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Skin temperature and sleep-onset latency: Changes with age and insomnia

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Abstract

Throughout the 24-hour day, the occurrence of sleep and wakefulness is closely related to changes in body temperatures. Changes in skin temperature may causally affect the ability to initiate and maintain sleep. First, we briefly summarize a previously proposed neurobiological mechanism that couples skin temperature to sleep propensity. Next we review previous findings on the relation between skin temperature and sleep-onset latency, indicating that sleep propensity can be enhanced by warming the skin to the level that normally occurs prior to – and during – sleep. Finally, we present new data indicating age- and insomnia-related changes in the sleep-onset latency response to foot warming, and evaluate whether different methods of foot warming could provide an applicable strategy to address sleep complaints. Foot temperature manipulations included footbaths before sleep onset (*1*), and heatable bed socks applied either before (*2*) or after lights-off (*3*). In adults, sleep-onset was accelerated by warm and neutral bed socks after lights-off and correlated to the increase in foot temperature. This increase was attenuated in elderly subjects. In elderly subjects without sleep difficulties, sleep onset could be accelerated with neutral bed socks after lights-off and a warm footbath prior to lights-off. In elderly insomniacs, none of the treatments accelerated sleep onset. We illustrate that elderly subjects show an attenuated increase in foot temperature after lights-off and lose the relationship between pre-sleep heat-loss activation and sleep latency. The sensitivity of sleep propensity to foot warming changes with age and is attenuated in age-related insomnia.

Keywords: Sleep electroencephalogram; Core body temperature; Skin temperature; Thermoregulation; Sleep-onset latency; Ageing; Insomnia; Foot warming

1. Introduction

Both sleep initiation and termination are temporally related to the circadian rhythm of core body temperature (CBT) and skin temperature. The habitual sleep period coincides with the diurnal phase of lowered CBT and the rise of CBT heralds the end of the sleep period. Habitual sleep onset coincides with the maximal rate of decline in CBT [1,2]. This decline is to a large extent caused by increased skin blood flow, and consequently skin warming and heat loss. Moreover, the habitual sleep period coincides with the diurnal phase of increased skin temperature. A functional link between skin temperature and sleep has been suggested by Kräuchi and colleagues [3,4]. In a series of controlled laboratory studies, they showed that the gradient between the skin temperature of the hands and feet and the proximal skin temperature was highly correlated with subsequent sleep-onset latency. A key question is whether this correlation merely results from a single underlying sleep propensity increase that first shows in autonomous measures like skin vasodilation and only later in the central nervous system, as measured by the sleep-electroencephalogram (EEG). An alternative hypothesis [5] proposed that changes in skin temperature causally affect the ability to initiate and maintain sleep. The neurobiological mechanism proposed to underlie this causal relation is as follows.

1.1. Neurobiology and behavior

It has been shown that a subpopulation of warm-sensitive neurons (WSNs) in the preoptic area and anterior hypothalamus (POAH) spontaneously increases its firing rate at sleep onset. Experimental local warming of the POAH induces a similar increase in firing rate and facilitates sleep [6–8]. Consequently, it has been proposed that sleep would be facilitated when brain temperature exceeds a threshold level [6]. However, this

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proposition is in opposition to the chronobiological perspective – namely, that sleep propensity is actually minimal during the phase of high CBT. We proposed the warm-sensitive neurons involved in sleep regulation to be sensitive to skin temperature as well. The circadian phase of elevated skin temperature coincides with the period of maximal sleep propensity, and animal studies show that the activity of a high percentage of locally warm-sensitive neurons is strongly modulated by thermoafferent projections to the POAH originating in the skin [9]. Afferents conveying information about skin temperature modulate the firing rate of thermosensitive neurons in the POAH at least as strong as does local brain temperature. In case of simultaneous differential local brain temperature and skin temperature manipulations, the latter dominate the POAH response [9,10]. In addition, a recent *human* neuroimaging study demonstrated hypothalamic activation with warming of the skin [11]. Thus, the changes induced by direct local CBT warming and leading to sleep-related alterations in firing rate – changes that can be observed in experimental conditions – may well be induced by warming of the skin under more natural conditions.

The behaviors that occur while preparing for sleep strongly favor an increase in skin temperature. The postural change from upright or sitting to a supine position [12,13], the use of bedding to create a microclimate of 34 °C to 36 °C [14–16], and the relaxation associated with the preparedness to sleep that is signaled by lights-off [17] – all promote an increase in skin temperature. Since warming of the skin due to these changes occurs already before sleep onset, it could affect the process of falling asleep.

1.2. More evidence for a modulatory role of circadian changes in skin temperature

Several studies have shown that temperatures of the skin and, more specifically, temperatures of the skin of the extremities (i.e. hands and feet) increase prior to sleep onset. The potential role of skin temperature in sleep onset, was already recognized by Magnussen in 1939 [18]. He reported that peripheral vasodilation and hence an increase in peripheral skin temperature indicated "Schlafbereitschaft" or "sleep preparedness". Also, Kleitman reported on an increase in toe temperature before sleep onset [19]. Brown confirmed the elevation of toe temperature around sleep onset, and suggested that it was related to the onset of the first period of slow-wave sleep rather than to sleep onset [20]. Van den Heuvel and colleagues also reported on increased peripheral temperatures in the hand and foot prior to and after habitual sleep onset [21]. Kräuchi and colleagues showed that the degree of heat loss at the skin of the hands and feet relative to the proximal part of the body (distal to proximal gradient, or DPG) was the best physiological predictor of a fast sleep onset under strictly controlled experimental conditions [3,4]. Fronczek et al. [22] demonstrated that the DPG was increased in relation to the very short sleep-onset latencies of narcoleptic subjects, and that the association between skin temperature and sleep-onset latency was even stronger for proximal and distal skin temperature per se than for their difference. Lack and Gradisar focused on finger temperature on a finer timescale and showed that a rapid increase prior to the onset of sleep [23]. In another study, Gradisar and Lack concluded that the rise in finger temperature before sleep onset drives the decline in core body temperature, which in turn is related to sleep onset [24]. Recently, we showed that in a natural setting both distal and proximal skin temperature strongly increase around habitual bed times [25].

1.3. Thermal manipulations

In addition to the observational, correlational studies on diurnal changes in skin temperatures in relation to sleep onset, several studies have investigated the effect of manipulating body temperature on sleep-onset latency, by applying warm baths, warm blankets or water-perfused suits. Horne and colleagues showed in young adults that whole-body warming in the early afternoon induced sleepiness both during and following the warm baths, and decreased sleep-onset latency [26,27]. Other studies of bathing have demonstrated shorter sleep-onset latencies following passive body heating in the evening, but not after heating in the morning, and it has been suggested that the drop in core body temperature following heating of the body underlies these findings [28,29]. Sung and Tochihara showed that immersion of the body or the feet and lower legs only in a hot water bath before bedtime affected core temperature only marginally, but did result in an elevated skin temperature during the first part of the night and improved sleep-onset latency [30].

Other studies have applied passive body heating in elderly subjects. Kanda and colleagues [31] reported an increase in ease of falling asleep for both young and elderly subjects after taking a hot bath in the evening. Dorsey and colleagues [32–34] showed that taking a hot bath 1.5 to 2 h before bedtime resulted in a significant increase in SWS, but did not report on sleep onset.

It has been suggested that the mechanism by means of which passive heating of the body affects sleep is that warming promotes a subsequent steep fall in core body temperature, mimicking the decrease in CBT seen in the hours preceding habitual bedtime [26–28,30–32,34,35]. We have subsequently proposed that it is not so much the steep decrease in core body temperature but rather the underlying heat-loss activation that increases skin blood flow, and thereby skin temperature and heat loss, that is causally involved in the increase in sleep propensity. Of the aforementioned studies, only the study of Sung and Tochihara included both polysomnography and skin temperature measurements [30]. Of note, in this study, the sleep-promoting effects subsided as soon as a pre-sleep hot footbath-induced increase in skin temperature had normalized after 2 h of sleep.

Two studies explored the effects of sleeping with an electric blanket. Fletcher and colleagues found no effects on core body temperature in the first 3 h of sleep, but did not report on sleep onset or skin temperature [36]. Okamoto-Mizuno and co-workers showed an elevated foot temperature and bed microclimate temperature when using an electric blanket, but did not find an effect on sleep onset [37].

Using a thermo-suit for more controlled skin temperature manipulations, we showed reduced sleep-onset latencies with subtle warming of the proximal skin in the comfortable

and thermoneutral range [38]. Distal manipulation was not effective, possibly due to the very small range of the manipulated temperature.

In summary, temperatures of the skin and, more specifically, temperatures of the skin of the extremities (i.e. hands and feet) increase prior to sleep onset. The speed of sleep onset is related to (this increase of) skin temperature. Direct or indirect warming of the skin prior to onset of sleep speeds up sleep onset and might be a useful treatment for subjects with sleep-onset difficulties.

1.4. New studies

Recent data from our group give some clues regarding the possibilities of thermal manipulation as a tool for improvement of sleep onset. In this study we explored the effects on sleep-onset latency of home-applicable temperature treatments that affect only skin, not core body, temperature. Both timing and temperature of the foot warming are of crucial importance. A foot temperature manipulation that is too warm might induce arousal during sleep initiation, whereas the effect of a manipulation prior to sleep that is too mild might not last until the start of the lights-off period. In short, we examined the effectiveness of both warm and thermoneutral footbaths prior to lights-off, and of wearing warm socks prior to and during lights-off, in young adults and elderly subjects with no difficulties in getting to sleep and in elderly subjects with difficulties in getting to sleep. Since decreased sleep quality (shorter sleep duration, slower sleep onsets, early awakenings and fragmented sleep) [39,40] in the elderly may be determined in part by age-related changes in thermoregulation (i.e. decreased amplitude and decreased stability), the treatments might be suitable for ameliorating these age-related effects.

We hypothesized that warming the foot will decrease sleep-onset latency.

We addressed the following three questions. First, is sleep-onset latency modulated by distal skin temperature manipulation over a somewhat wider range than we applied previously? Second, does the distal skin temperature, *prior to* sleep onset, correlate with sleep-onset latency [3,4] – crucial for a fast subsequent initiation of sleep – or is the distal skin temperature *during* the period from lights-off to sleep onset the crucial factor? Third, to what extent are the effects of distal skin manipulations on sleep onset still effective in elderly, who in general show attenuated thermoreception and peripheral blood flow? [41]. With the possible application of such treatments in mind, we chose to conduct the distal temperature manipulation with home-applicable treatments, both in young and elderly subjects. Since poor sleep is a frequent complaint in the elderly [42] we included both elderly subjects who slept well and those who slept poorly.

2. Materials and methods

2.1. Subjects

Eight healthy young adults free from sleep complaints (21–39 years old; mean±SE: 27.00±2.41 years, 4 males), eight healthy elderly subjects free from sleep complaints (56–80 years old; mean±SD: 65.75±7.91 years, 4 males) and eight elderly subjects with sleep complaints but otherwise healthy (51–66 years old; 59.13±5.41 years, 4 males) participated with informed consent. All participants were free of medication known to affect sleep or the circadian system, cardiovascular medication or psychotropic medication. One female adult used oral contraceptives. Subjective sleep quality and complaints were measured using the 75-item Sleep Disorders Questionnaire (SDQ) a Dutch adaptation [43] of the SDQ [44] and the Pittsburgh Sleep Quality Index (PSQI) [45]. Poor sleepers were defined by an SDQ-Insomnia score >2.5, a PSQI >5 and a score ≤3 on the SDQ subscales narcolepsy, apnea, restless legs and psychiatry. The adult females participated between day 4 and day 12 of the menstrual cycle (mid-follicular phase) and all elderly females were post-menopausal. The protocol was approved by the Medical Ethics Committee of the Academic Medical Center of the University of Amsterdam.

2.2. Procedures

The participants were instructed to keep a regular as possible sleep–wake pattern by minimizing variability in bedtime and wake-up time in the 2 weeks prior to the experiment, which was verified with a sleep diary [46] and with actigraphy (Actiwatch, Cambridge Neuro-Technology Ltd., Cambridge, UK). One week before the experiment, participants visited the sleep-laboratory for an introductory session and became habituated to the bedroom and the equipment. Participants were instructed to refrain from caffeine, alcohol and tobacco for 8 h before arriving at the sleep laboratory and were questioned about compliance with this instruction. In brief, the experiment consisted of determining 6 sleep-onset latencies on a single day for each subject while manipulating foot skin temperature with home-applicable methods. The subjects reported to the sleep laboratory at 08:30 where they were prepared for polysomnography. Ambient room temperature was kept at approximately 21 °C. The subjects wore their habitual nightclothes, and they were covered by a sheet and a blanket during lights-off. The experiment started at 09:30 and consisted of 6 consecutive blocks with durations of 1.5 h each. As shown in Fig. 1, each block consisted of the following strictly standardized procedures: It started at 0:00 (block-time) by setting the bed in semi-supine position and requiring the subjects to leave the bed, wear a bathrobe and slippers and sit behind a desk. At 0:10 they were

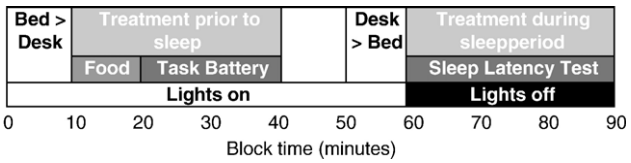

Fig. 1. Schematic view of the experimental design within a block. At 00:10, in 4 of the 6 conditions, foot temperature was manipulated for 30 min by applying warm (42 °C) or neutral (32 °C) footbaths (FBPRE), or by means of non-heated or heated bed socks (SOCKPRE). At 00:60 in the two remaining of the 6 conditions temperature was manipulated for 30 min by applying non-heated or heated bed socks during the lights-off period in bed (SOCKBED).

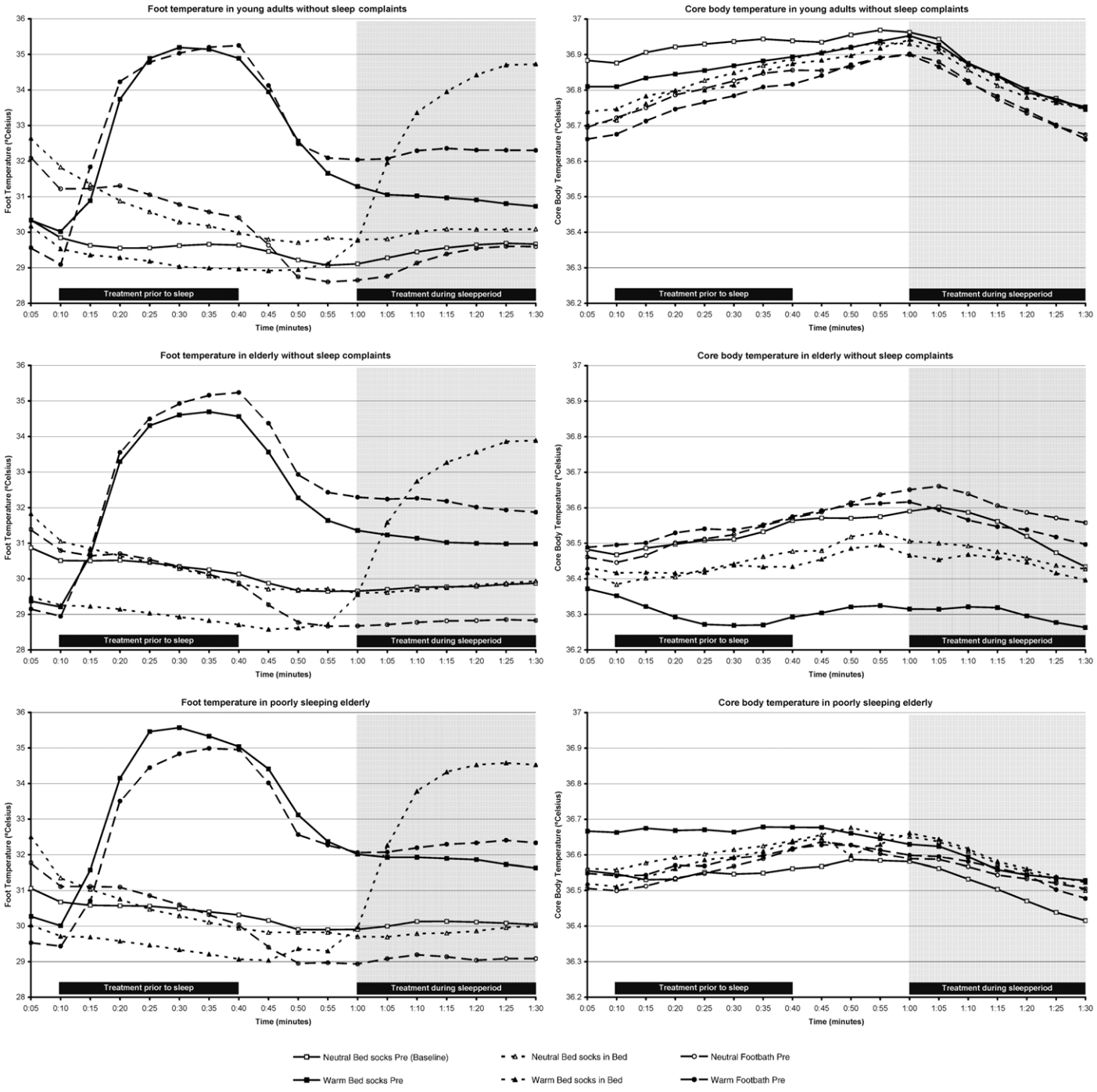

Fig. 2. The average core body (T_{re}) and foot temperatures (T_{foot}) for the six treatments throughout every single experimental block per group. Lights-off period is in gray.

served a drink (200 ml decaffeinated tea; 4.25 kcal, 17.8 kJ; Iced Tea Mix, Diet Decaffeinated Lemon, Lipton, Englewood Cliffs, USA) and an isocaloric snack of the subject's choice (200 kcal, 837.2 kJ) at room-temperature, to be consumed in approximately 10 min. Also at 00:10, in 4 of the 6 conditions, foot temperature was manipulated for 30 min by applying warm (42 °C) or neutral (32 °C) footbaths (FBPRE), or by means of non-heated or heated bed socks (SOCKPRE). At 00:20 a self-paced computerized neurobehavioral task battery was started, taking around 20 min to complete. This battery included assessment of subjective thermal comfort using a 100 mm visual analogue scale (VAS) ranging from uncomfortable to comfortable. At 00:50, the subjects were required to leave the desk and to use the bathroom if needed and returned to bed. At 01:00 in the two remaining of the 6 conditions temperature was manipulated for 30 min by applying non-heated or heated bed socks during the lights-off period in bed (SOCKBED). For all conditions at 01:00, the bed was set in supine position, the lights switched off and the participants were asked to try to sleep. Sleep onset was determined online (Multiple Sleep Latency Test, MSLT) [47,48] and subjects were awakened directly after sleep-onset determination (see below). When woken up, subjects were kept awake in bed in

the supine position, and with the light turned on (<10 lux). The maximum time allowed for falling asleep was 30 min, thus completing the 1.5 h of a block.

Within the sequence of the manipulations, the thermoneutral and warm levels of each condition (FBPRE, SOCKPRE, SOCKBED) were paired. All conditions and their two levels were optimally counterbalanced over subjects within each group.

2.3. Temperature manipulations and measurement

Foot temperature was manipulated by means of a footbath (Philips, HP5225/B, Eindhoven, The Netherlands) and Hot Socks (Nature's Choice, Prinsenbeek, The Netherlands). The loose-fitting bed socks have a removable filling at the sole part of the sock. The filling contains grains and can be heated using a microwave oven. When applying the warm footbath, the bath was filled with 2.8 l water of 42 °C and the heating of the footbath was turned on. When using the thermoneutral footbath, the bath was filled with 2.8 l water of 32 °C and the heating of the footbath was turned off. When using the warm bed socks, the 2 fillings were heated for 90 s at 620 W using a microwave oven. This resulted in a temperature of the sole of the sock of approximately 66 °C, gradually declining to 43 °C in 30 min. When applying the thermoneutral bed socks, the fillings were not heated and were at room temperature.

Body temperature was obtained using 3 thermistors (P-8432, ICBT, Tokyo, Japan). Core body temperature (T_{re}) was measured using a rectal thermistor that was self-inserted 13 cm into the rectum. Foot temperature (T_{foot}) was measured at the medial metatarsal area at the plantar sites of the left and right foot. The skin thermistors were attached to the skin with thermal probe covers (ref 090-2764, ConMed Corporation, Utica, USA) that reflect ambient heat. Temperature was digitally recorded at 1 Hz (Embla A10 and Somnologica software, Flaga hf, Reykjavik, Iceland) and sampled offline at 0.1 Hz. Based on visual inspection of the data, an automated procedure was applied to remove occasional artefacts, defined for core body temperature as outside the range 35.5 °C–38 °C. In addition, visually obvious artefacts (abrupt steep changes in skin temperature, >0.3 °C/min, or in core body temperature, >0.1 °C/min, outside the time-window of the foot-temperature manipulation) were removed and omitted from analyses. The average temperature of both feet was used for subsequent analyses.

2.4. Sleep

Polysomnographic sleep recordings consisted of electroencephalography (EEG), electromyography (EMG) and electrooculography (EOG). The EEG was derived from two bipolar leads FpzCz and PzOz [49] with the E-net and Hydrodot system (Physiometrix Inc., Billerica USA). Submental EMG and horizontal EOG from the outer canthi were recorded using disposable Ag/AgCl electrodes (type 4203 Meditrace, Graphic Controls Corporation, Buffalo 11 USA). All PSG signals were digitally recorded at 200 Hz using the Embla A10 recorder and Somnologica software (both Flaga hf, Reykjavik, Iceland). Sleep onset was determined online during the experiment according to standard criteria [50], with sleep onset defined as three consecutive 30-s epochs of stage 1 sleep or one 30-s epoch of stage 2 (or deeper) sleep [48].Online determination of sleep stage was aided by the use of spectral views of the EEG signal, facilitating the observation of disappearance of the alpha (8–12 Hz) peak, dominance of the proportion of theta (4–8 Hz) over the proportion of alpha activity, or the clear appearance of spindle (12–15 Hz) peaks. Recordings of MSLT were visually scored offline by two independent scorers blind to the manipulations and, in case of differences, consensus was reached. sleep-onset latency (SOL) was defined as the time between lights-off and the sleep onset. If the subject did not sleep during the 30 min, sleep-onset latency was scored as 30 min.

2.5. Statistical analysis

All temperature measures were first averaged into 30-second bins. Mean foot and mean core body temperature were then calculated over block-time 00:20–00:40 ($T_{\text{-pre}}$) and block-time 01:00 until sleep onset ($T_{\text{-bed}}$) for statistical analyses. Additionally the linear rate of change (ROC, in 1 °C/min) in the interval lights-off (blocktime: 01:00) until sleep onset was calculated. For graphical purposes all temperature data were once again averaged in 5-min bins.

To determine the effects the passive cutaneous warming treatment on body temperatures and sleep-onset latency, hierarchical regression modeling (i.e. random coefficient analysis) was applied (MLwiN software, Centre for Multilevel Modelling, Institute of Education, London, UK). This method takes into account the interdependency of the data points inherent to the hierarchical structure of the design, in our case the sequential sleep-onset observations *i* that were nested within subjects *j* [51]. It moreover allows for varying numbers of missing data within a case.

Since the frequency distribution of SOLs was slightly skewed, a log transformation was applied.

For the 3 groups (young adults free from sleep complaints, elderly free from sleep complaints and elderly with sleep complaints) 5 separate analyses were run with either SOL, $T_{\text{re-pre}}$, $T_{\text{foot-pre}}$, $T_{\text{re-bed}}$ and $T_{\text{foot-bed}}$ as the dependent variable and the treatments as dummy coded predictors. The unwarmed bed socks pre-sleep was selected as reference condition (hereafter referred to as baseline), since it mostly resembles the situation before going to bed in daily living. In the subsequent analyses for sleep-onset latency the actual measured temperatures and temperature changes ($T_{\text{re-pre}}$, $T_{\text{foot-pre}}$, $T_{\text{re-bed}}$ and $T_{\text{foot-bed}}$ and $\text{ROC}_{T\text{foot-bed}}$) were entered in the equation.Time of day (hour) was entered in the models as covariate, and up to the third order and the square-root (hour^2, hour^3, $\sqrt{\text{hour}}$), as needed, to account for possible diurnal variation in SOL [52]. Maximum likelihood was used to estimate the regression coefficients, which were tested for significance with the Wald test [53]. Additional temperature-related and time-related independent variables were allowed in the model only if their coefficients were significant and if residual error of the model was reduced according to the likelihood ratio test [54]. Finally, the overall mean $\text{ROC}_{T\text{foot-bed}}$ was determined for the group of young subjects and the group of all elderly subjects *in the treatments*

without warming during the lights-off period, by the intercept of equation for the null-model (i.e. the model without independent variables) for the $ROC_{Tfoot\text{-}bed}$ of each group. Two-tailed significance levels were set at 0.05.

3. Results

3.1. Induced temperatures

For each group the average core body and foot temperatures per treatment are displayed in Fig. 2 and Table 1. Table 2 shows the regression model effect sizes of treatment and time on foot and core body temperature.

Foot temperature (T_{foot}) was significantly higher during the warm SOCKPRE and FBPRE manipulations as compared to the baseline condition in all the three groups and the effects lasted, albeit less strongly, during the lights-off period. Likewise the warm SOCKBED manipulation induced a significantly higher T_{foot} during the lights-off period for all the three groups. Moreover, the neutral FBPRE condition lowered $T_{foot\text{-}bed}$ in the elderly free from sleep complaints.

Rectal temperature (T_{re}) was significantly lower during the warm FBPRE manipulation as compared to the baseline condition in the young adults free from sleep complaints and this lasted, albeit less strongly, during the lights-off period. In the elderly free from sleep complaints, T_{re} was significantly lower during and after the warm SOCKPRE manipulation. In addition, $T_{re\text{-}bed}$ was lower after the warm FBPRE manipulation. The elderly with sleep complaints showed a higher $T_{re\text{-}pre}$ during the warm SOCKPRE condition, which did not last until the lights-off period. Inspection of the figures suggested that the observed differences in T_{re} were already present at the start of the

Table 1
The average core body (T_{re}) and foot temperatures (T_{foot}) per treatment condition per group

	Foot temperature (°C)		Core body temperature (°C)	
	$T_{foot\text{-}pre}$	$T_{foot\text{-}bed}$	$T_{re\text{-}pre}$	$T_{re\text{-}bed}$
Young adults free from sleep complaints				
Neutral SOCKPRE (baseline)	**29.62 ± 0.91**	**29.40 ± 0.94**	**37.00 ± 0.15**	**36.90 ± 0.08**
Warm SOCKPRE	35.00±0.85*	31.17±0.67*	36.87±0.07	36.89±0.05
Neutral FBPRE	30.70±0.44	29.04±0.35	36.89±0.07	36.83±0.08
Warm FBPRE	35.06±0.32*	32.28±0.41*	36.83±0.12*	36.82±0.07*
Neutral SOCKBED	30.25±0.42	29.87±0.48	36.91±0.07	36.87±0.10
Warm SOCKBED	29.04±0.64	32.38±0.36*	36.91±0.09	36.90±0.08
Elderly free from sleep complaints				
Neutral SOCKPRE (baseline)	**26.79 ± 3.85**	**29.76 ± 0.59**	**36.63 ± 0.13**	**36.59 ± 0.13**
Warm SOCKPRE	34.55±0.63*	31.22±0.59*	36.35±0.17*	36.31±0.17*
Neutral FBPRE	30.23±0.39	28.78±0.56*	36.54±0.09	36.64±0.08
Warm FBPRE	34.96±0.42*	32.26±0.41*	36.55±0.08	36.58±0.10*
Neutral SOCKBED	30.18±0.81	29.65±0.73	36.45±0.14	36.49±0.14
Warm SOCKBED	28.87±0.80	31.94±0.78*	36.43±0.16	36.44±0.19
Poorly sleeping elderly				
Neutral SOCKBED (baseline)	**30.44 ± 0.48**	**30.04 ± 0.58**	**36.55 ± 0.09**	**36.59 ± 0.10**
Warm SOCKBED	35.35±0.62*	31.90±0.67*	36.67±0.10*	36.62±0.08
Neutral FBPRE	30.44±0.39	29.14±0.36	36.58±0.10	36.57±0.07
Warm FBPRE	34.78±0.56*	32.16±0.44*	36.59±0.09	36.59±0.08
Neutral SOCKBED	30.20±0.70	29.70±0.65	36.62±0.08	36.62±0.09
Warm SOCKBED	29.27±0.73	32.94±1.01*	36.61±0.10	36.61±0.10

Values are means±SE. SOCKPRE=bed sock pre, FBPRE=footbath pre, SOCKBED=bed sock in bed.
Due to missing data, directly comparing averages over time (pre and bed) and over treatment might be cumbersome.
* Significantly different from baseline condition.

Table 2
Estimates of the effects of treatment and time of day on foot (T_{foot}) and core body (T_{re}) temperature per group

	Young adults free from sleep complaints	Elderly free from sleep complaints	Poorly sleeping elderly
Body temperatures prior to sleep ($T_{\text{-pre}}$)			
Foot temperature (T_{foot})			
Intercept	29.57±0.60‡	26.79±1.57‡	30.44±0.55‡
Warm SOCKPRE	5.44±0.67‡	7.76±1.99‡	4.91±0.61‡
Warm SOCKBED	−0.58±0.70	2.09±1.99	−1.17±0.61
Neutral SOCKBED	0.63±0.70	3.39±1.99	−0.24±0.61
Warm FBPRE	5.45±0.70‡	8.17±1.99‡	4.34±0.61‡
Neutral FBPRE	1.08±0.70	3.44±1.99	0.00±0.61
no modulation by time			
Core body temperature (T_{re})			
Intercept	37.10±0.09‡	36.55±0.15‡	36.75±0.09‡
Warm SOCKPRE	−0.11±0.06	−0.17±0.07*	0.12±0.06*
Warm SOCKBED	−0.09±0.07	−0.01±0.07	0.08±0.06
Neutral SOCKBED	−0.09±0.07	0.01±0.07	0.10±0.06
Warm FBPRE	−0.17±0.07†	−0.07±0.70	0.08±0.06
Neutral FBPRE	−0.11±0.07	−0.05±0.07	0.07±0.06
Hour	0.10±0.03‡	0.11±0.03‡	0.08±0.02‡
√Hour	−0.29±0.07‡	−0.32±0.07‡	−0.30±0.06‡
Body temperatures after lights-off ($T_{\text{-bed}}$)			
Foot temperature (T_{foot})			
Intercept	28.97±0.54‡	29.49±0.57‡	29.79±0.60‡
Warm SOCKPRE	1.73±0.48‡	1.48±0.46‡	1.91±0.59**
Warm SOCKBED	2.47±0.52‡	1.86±0.47‡	2.54±0.61‡
Neutral SOCKBED	0.26±0.48	−0.42±0.47	−0.71±0.61
Warm FBPRE	2.64±0.48‡	2.26±0.46‡	2.00±0.59‡
Neutral FBPRE	−0.56±0.48	−1.20±0.46†	−1.06±0.59
Hour	0.16±0.06†		
$Hour^2$		0.02±0.01†	0.02±0.01*
Core body temperature (T_{re})			
Intercept	36.86±0.07‡	36.42±0.16‡	36.61±0.08‡
Warm SOCKPRE	−0.03±0.05	−0.18±0.07†	0.00±0.05
Warm SOCKBED	−0.06±0.05	−0.10±0.07	−0.01±0.05
Neutral SOCKBED	−0.08±0.05	−0.04±0.07	0.01±0.05
Warm FBPRE	−0.11±0.05*	−0.15±0.07*	−0.05±0.05
Neutral FBPRE	−0.09±0.05	−0.10±0.07	−0.06±0.05
Hour		0.03±0.01†	
$Hour^2$	0.003±0.001‡		
$Hour^3$			0.0002±0.0001*

Values are means±SE. Regression model was as follows: $T_{ij}=\beta_{0ij}+\beta_1*\text{warm bed sock pre}_{ij}+\beta_2*\text{warm bed sock bed}_{ij}+\beta_3*\text{neutral bed sock bed}_{ij}+\beta_4*\text{warm footbad pre}_{ij}+\beta_5*\text{neutral footbad pre}_{ij}+\beta_6*\text{hour}_{ij}+\beta_7*\text{hour2}_{ij}+\beta_8*\sqrt{\text{hour}}_{ij}+\beta_9*\text{hour}^3_{ij}$ (see text; subscripts indicate ith observation for subject j). The treatments were included in the model as dummy coded predictors. Hour (time), defined as the number of hours since the start of the first included sleep latency test, starting with 0 for the first block. Time variables that were not significant in all 3 groups are not displayed. SOCKPRE=bed sock pre, FBPRE=footbath pre, SOCKBED=bed sock in bed. *P 0.05; †P 0.01; ‡P 0.001.

treatments – except for the decreases in T_{re} both prior to and during the lights-off in elderly free from sleep complaints, where a change from the start of block is seen. Both $T_{re\text{-}pre}$ and $T_{re\text{-}bed}$ were modulated by time of day.

In summary: The effects of the warm manipulation were reflected in the foot temperatures during manipulation and were maintained during the subsequent lights-off period. The neutral footbath treatment in the elderly free from sleep complaints actually lowered foot temperature during the lights-off period, probably through evaporative heat loss. Only pre-sleep foot warming, by means of heated bed socks in the elderly free from sleep complaints, appeared to affect rectal temperature.

3.2. Sleep-onset latency

Table 3 shows the average sleep-onset latencies associated with the different treatments. Table 4 shows the regression model effect sizes of treatment and time on sleep-onset latency.

In young adults, the baseline sleep-onset latency averaged 15.69±3.47 min. LOG(SOL) was 0.22±0.08 shorter in the warm SOCKBED condition and 0.20±0.08 in the neutral SOCKBED condition as compared to the baseline condition, but unaffected by FBPRE or SOCKPRE manipulations. In the elderly free from sleep complaints, the baseline sleep-onset latency averaged 11.19±3.32 min. LOG(SOL) was 0.16±0.06 shorter in the neutral SOCKBED condition and 0.12±0.06 shorter in the warm FBPRE condition, but unaffected by the other manipulations. In the elderly with sleep complaints, the baseline average sleep-onset latency averaged 10.50±2.87 min. Sleep-onset latency was not affected by any treatment. In the elderly without sleep complaints, LOG(SOL) was also modulated by hour^2.

We next addressed the question whether SOL could be predicted by the manipulation-induced changes in rectal and foot temperature, either before or after lights-off. Within the young adult group it turned out that the rate of change (ROC) of the $T_{foot\text{-}bed}$ was significantly associated with SOL. The steeper the increase in foot temperature, the faster the sleep onset is. For every 1 °C/min faster increase in $T_{foot\text{-}bed,}$ LOG(SOL) decreased by 0.34±0.15. In elderly subjects, both with and without sleep complaints, none of the possible predictors for SOL reached significance. Subsequently, we found that, in general, the rate of change of foot temperature was significantly less for elderly compared to young adults. In the treatments without warming during the lights-off period, the rate of change in foot temperature after lights-off was 59% less in the elderly (0.04 °C/min) compared to the young adults 0.10 °C/min) (P=0.02).

In summary: In young adults, sleep onset was accelerated by wearing either warm or neutral bed socks after lights-off, and the rate of change of the foot temperature after lights-off was related to this faster sleep onset. In elderly subjects free from sleep complaints, sleep onset was accelerated by a warm footbath prior to sleep or wearing neutral bed socks during lights-off. In elderly subjects with sleep complaints, none of the foot-warming strategies used was effective in changing SOL. Unlike young subjects, elderly subjects did not show an association between sleep-onset latency and the rate of change in foot temperature, or any other temperature variable, and showed an attenuated increase in foot temperature after lights-off compared to the young subjects.

Table 3
Sleep-onset latency by treatment condition per group

	Sleep-onset latency (min.)		
	Young adults free from sleep complaints	Elderly free from sleep complaints	Poorly sleeping elderly
Neutral SOCKPRE (baseline)	15.69±3.47	11.19±3.32	10.50±2.87
Warm SOCKPRE	12.94±3.21	9.81±2.71	9.38±3.41
Neutral FBPRE	15.13±3.29	9.50±2.26	11.81±3.02
Warm FBPRE	15.56±3.45	8.13±1.45*	8.06±1.69
Neutral SOCKBED	11.38±3.21*	8.00±1.83*	7.63±1.57
Warm SOCKBED	11.25±3.77*	10.56±2.33	8.31±1.25

Values are means±SE.
*Significantly different from baseline.

Table 4
Estimates of the effects of manipulations as dummy coded predictor variables and time of day on log transformed sleep-onset latency per group

	Sleep-onset latency LOG(SOL)		
	Young adults free from sleep complaints	Elderly free from sleep complaints	Poorly sleeping elderly
Intercept	1.13±0.11‡	0.90±0.09‡	0.92±0.10‡
Warm SOCKPRE	−0.13±0.08	−0.04±0.06	−0.13±0.09
Warm SOCKBED	−0.22±0.08†	−0.04±0.06	−0.04±0.09
Neutral SOCKBED	−0.20±0.08*	−0.16±0.06†	−0.10±0.09
Warm FBPRE	−0.02±0.08	−0.12±0.06*	−0.07±0.09
Neutral FBPRE	−0.03±0.08	−0.06±0.06	0.07±0.09
Hour^2		0.003±0.001†	

Values are means±SE. Regression model was as follows: $LOG(SOL)_{ij}=\beta 0_{ij}+\beta_1 * \text{warm bed sock pre}_{ij}+\beta_2 * \text{warm bed sock bed}_{ij}+\beta_3 * \text{neutral bed sock bed}_{ij}+\beta_4 * \text{warm footbad pre}_{ij}+\beta_5 * \text{neutral footbad pre}_{ij}+\beta_6 * \text{hour}_{ij}+\beta_7 * \text{hour2}_{ij}+\beta_8 * \sqrt{\text{hour}_{ij}}+\beta_9 * \text{hour}^3{}_{ij}$ (see text; subscripts indicate ith observation for subject j). The treatments were included in the model as dummy coded predictors. Hour (time), defined as the number of hours since the start of the first included sleep latency test, starting with 0 for the first block. Time variables that were not significant in all 3 groups are not displayed. SOCKPRE=bed sock pre, FBPRE=footbath pre, SOCKBED=bed sock in bed. *P 0.05; †P 0.01; ‡P 0.001.

4. Discussion

The aim of the present study was to investigate whether sleep-onset latency could be modulated by home-applicable foot-temperature manipulations, which result in changes in foot temperature of approximately 6 °C. Moreover, we addressed the question whether sleep-onset latency is indeed related to the distal skin temperature *prior to* sleep onset, shown to be correlated with sleep-onset latency [3,4], or rather to the distal skin temperature *during* the period from lights-off to sleep onset. Furthermore, it was investigated whether the effects of distal skin manipulations on sleep onset would be equally effective in elderly, who in general show attenuated thermoreception [41] compared to younger subjects. Results showed that wearing bed socks from the time of lights-off decreased

sleep-onset latency, at least in young adults. Whereas we did not find changes in sleep-onset latency during very subtle distal warming [38], the more robust warming with heated bed socks and also the more subtle change in foot temperature due to wearing non-heated bed socks, did affect sleep-onset latency in the present protocol.

The faster increases of foot temperature after lights-off seemed to be involved in this faster sleep onset, suggesting a role for the rate of change rather than the level of distal temperature. The results from the elderly subjects without sleep problems were less clear. Both neutral bed socks during lights-off and a warm footbath prior to sleep decreased SOL, but SOL could not be related to any specific induced temperature change. It might be that, in the elderly, skin temperature is not as effective a sleep-inducing signal as in the young. In fact aging affects thermoreception and peripheral blood flow negatively [41], which in turn reduce the ability to warm the peripheral skin. A post-hoc analysis revealed that the most effective treatment before sleep in elderly subjects without sleep problems was rated as being most comfortable in both these and young subjects. Increased comfort might be a more relevant factor than temperature input in the elderly subjects. The treatments used were not successful in accelerating sleep onset in elderly people with sleep complaints. It might be possible that the manipulation of skin temperature in the feet would be more effective in improving nocturnal sleep at habitual bedtimes.

In young adults, the rate of change of the foot temperature after lights-off appeared crucially involved in sleep-onset latency whereas, in elderly subjects, both the rate of change of foot temperature and the effects of the treatments were significantly less. It is conceivable that the reduced ability to show a fast increase in distal temperature plays a key role in the complaints of difficulties with sleep initiation frequently noted in the elderly. Regular exercise provides a way to improve the vasodilatory response [55], which may be involved in the finding that regular exercise is associated with a reduction in the prevalence of disturbed sleep in a large population of healthy middle-aged to elderly subjects [56].

The average SOL was shorter in the older groups, particularly the poor sleepers. In this particular daytime protocol, they might benefit from their increased daytime sleepiness and their familiarity with daytime napping.

In summary, home-applicable methods for warming the feet may be effective in accelerating sleep onset in young subjects, but the effect is less pronounced in elderly subjects. A steep increase in foot temperature is associated with a rapid onset of sleep. The reduced ability of elderly subjects to show such a steep increase in foot temperature may be involved in the attenuated efficacy in them of foot warming to promote sleep onset. It is conceivable that sleep-promoting manipulation of temperature may become more effective in elderly subjects if they are supplemented by interventions (such as regular exercise) that improve the vasodilatory response.

Taken together, direct or indirect warming of the skin may accelerate sleep onset. This is in line with the previously proposed neurobiological mechanism that changes in skin temperature modulate brain areas involved in sleep regulation [5]. Skin warming may thus be applied to accelerate sleep onset. However, it is not yet known at what location on the body skin warming is most effective. Most correlational studies stress the importance of distal skin temperature, but the only study that applied both proximal and distal skin temperature *manipulation* simultaneously, showed that proximal skin warming was most effective [38].

Another point of debate is which property of the temperature signal is crucial. Whereas the results of the present study and others show that the *level* of proximal or distal skin temperature is essential [22,30,38], others suggest the importance of the distal to proximal skin temperature difference, i.e. the *gradient* in skin temperature [3,4,23,24].

Both timing and temperature of the skin warming play a key role. A too warm skin during or just prior to sleep initiation might induce arousal and elevation of core body temperature. Skin warming methods that also induce an increase of core body temperature should therefore be applied at approximately 1.5–2 h before bedtime, whereas moderate skin warming methods that manipulate the skin temperature close to the ceiling of its normal diurnal pattern *without* affecting core temperature can be applied just prior or during sleep initiation.

In elderly subjects, enhancement of skin vasodilation and its concomitant increase in skin temperature may be crucial to promote sleep onset. Such enhanced skin vasodilation can for example occurs after passive body heating, which indeed promoted sleep in elderly subjects [31–34].

In summary, skin warming is effective in accelerating sleep onset. In young adults the application of a mild thermal skin manipulation is effective, whereas in elderly the induction of a vasodilatory response seems to be crucial for accelerating sleep onset.

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