



Original Article

Distal–proximal skin temperature gradient prior to sleep onset in infants for clinical use

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Abstract **Background:** The objective of this study was to explore the possibility of using distal–proximal skin temperature gradient (DPG) to predict sleep-onset latency of night-time sleep for infants at home.

Methods: Foot (for distal) and abdominal (for proximal) skin temperature during sleep onset in healthy infants, aged 4–9 months, was continuously recorded using a temperature logger at home. Sleep-onset latency during each study night was defined as the interval from lights-off to sleep onset, determined on actigraphy. Association of DPG profile after lights-off with sleep-onset latency on the study nights was evaluated.

Results: Data for 43 nights from 28 infants were available for analysis. With regard to low DPG ($<-2.5^{\circ}\text{C}$) at lights-off, $>60\%$ of infants fell asleep within 30 min if DPG was increased to $\geq-2.5^{\circ}\text{C}$ within 15 min after lights-off. If DPG remained at $<-2.5^{\circ}\text{C}$ at 15 min after lights-off, however, only 20% of infants fell asleep within 30 min. In addition, if infants were still awake at 15 min after lights-off and the DPG at that time was $<-2.5^{\circ}\text{C}$, they were not likely to quickly fall asleep (predictive value was 0.875).

Conclusions: Increase in DPG by 15 min after lights-off is a key determinant for sleep-onset latency.

Key words actigraphy, child care, circadian rhythm, sleep, skin temperature.

Human circadian rhythms are not present at birth and neonates spend most of their time sleeping. Thereafter, beginning at age 4 months, most infants start to sleep in an adult-like circadian rhythm throughout the day, with longer sleep at night.^{1,2} At this stage, most parents can read the state of alertness of their infant based on the infant's activities, and estimate a suitable time to put their infant to sleep. It is usual, however, that the infant unexpectedly takes a long time to fall asleep after lights-off in the bedroom and requires constant attention from their parents. Therefore, parents' distress would be relieved if they could have a more reliable, objective indicator of the likelihood that their infant will actually fall asleep.

Habitual sleep onset coincides with the maximum rate of decline in core body temperature during the late evening.^{3,4} During the course of sleep onset, body heat loss is extremely enhanced, and distal skin regions (e.g. feet or hands) are the major sites of vasomotor heat loss.^{5,6} This heat loss process is largely dependent on the opening of arteriovenous anastomoses located in glabrous regions of the skin (e.g. fingertips, toe, nose, eyelids, lips and earlobes), which rapidly increases blood flow in distal skin regions and enhances heat redistribution from the core to the cooler peripheral skin.^{7,8} Thus, the distal skin region shows

a rapid increase in temperature toward sleep onset, a trend that is the inverse of the core body temperature.^{5,6}

Recently, a number of studies have demonstrated a correlational link between pre-sleep increases in distal skin temperature and sleep propensity.^{5,6,9–13} Distal skin blood flow and hence heat loss were well correlated with a gradient between skin temperature of the hands and feet and the proximal skin temperature (distal–proximal skin temperature gradient; DPG).¹⁴ Kräuchi *et al.* reported that, under laboratory conditions with a constant routine protocol, DPG was shown to be the best predictor for sleep-onset latency among a variety of prospective candidates, including core body temperature and rate of change of core temperature, heart rate, melatonin onset, and subjective sleepiness rating.¹⁰ These previous findings suggest that DPG may be a useful clue in predicting sleep propensity in infants, who cannot talk about their own sleepiness to their parents. In most infants, the circadian rhythms of both skin temperature and motor activities appear by 3 months and become robust at 6 months.^{15,16} Thus, most healthy 4-month-old infants are expected to acquire circadian rhythms with synchronized skin temperature and sleep–wake cycles.

The aims of this study were to explore the possibility of using DPG to predict sleep-onset latency in infants at home. We continuously recorded proximal and distal skin temperature during sleep onset in healthy infants aged 4–9 months, and evaluated the ability of pre-sleep DPG to predict sleep-onset latency in infants from a clinical perspective.

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Methods

Participants

The study protocol was approved by the Ethics Committee of Akita University Graduate School of Medicine. In order to recruit participants, we approached mothers who had delivered healthy babies and visited a public hospital for the 4 months postnatal health examination for their babies. To establish an optimal study group, the eligibility criteria included a singleton, term, and uneventful delivery of a healthy baby, and a normal postnatal course of development. Mothers who agreed to participate in the study received written and verbal explanations about the nature of the study and ethics considerations.

Distal and proximal skin temperature recording

The study was conducted between September 2011 and December 2012. To avoid masking effects of hot environmental temperatures on diurnal skin temperature rhythms,¹⁷ data were not collected between 1 July and 31 August 2012. Temperatures of the foot (for distal) and abdominal (for proximal) skin regions in infants were continuously recorded at 5 min intervals using a temperature logger (LT-8A; Gram, Saitama, Japan) with a relative accuracy of 0.01°C. The families' homes and the infants' usual sleep situations were used as study conditions. For proximal and distal skin temperature recordings, the mother attached two thermistor probes to the infant with adhesive tape, one just above the navel, in the middle of the abdomen and the other at the base of the first digit of the foot. The third probe was placed near the infant's face to measure the ambient temperature around the infant. Each recording was started at least 10 min before the infant's usual bedtime, and was continued until the next morning. We asked all of the mothers to put their infants to sleep in a quiet room in the supine position. Until the infants fell asleep, mothers were not allowed to sleep beside the infants or to give milk. In principle, the infants' bedding and clothing were freely chosen by parents, but we instructed all of the mothers to avoid excessive bedding and clothing, and not to let the infants wear socks during sleep. When infants were put to bed in chilly sheets in the winter season, mothers were asked to wait for at least 15 min before turning the lights off after the infants were put down to sleep. We requested that mothers first record temperatures of infants for 1 night, and then to record again for the following night if possible.

After each recording was finished, skin temperature data were entered into a personal computer and analyzed using software (Gram, Saitama, Japan). Given that the variations in proximal skin temperature in all nightly recordings were found to be relatively small, some measurements were deleted if proximal skin temperatures deviated by more than threefold the standard deviation from the mean of all study nights. DPG at measurement points was calculated as the difference between distal minus proximal skin temperature. Because distal skin temperature is usually lower than proximal temperature, most DPG were expressed as negative values. Thus, when distal skin temperature increased toward the proximal skin temperature, DPG was increased to zero. The infants' ambient temperature during each

study night was determined by the mean from lights-off to sleep onset.

Evaluation of sleep onset on actigraphy

Time of sleep onset for each infant while recording the temperature was determined by an actigraph, a wristwatch-like acceleration sensor (Micro-mini RC; Ambulatory Monitoring, Ardsley, NY, USA). Mothers were requested to attach the actigraph to the infants' left ankle during temperature measurement. Motility levels were sampled in the zero-crossing mode at 1 min intervals. The resolution of the actigraph was set at 0.01 G/s. The activity data recorded by the actigraph was later downloaded using ACTme (version 3.10.0.3; Ambulatory Monitoring), and periods of sleep or wake were determined by an algorithm developed by Sadeh¹⁸ using Action-W (version 2.4.20; Ambulatory Monitoring). Sleep-onset latency during each study night was defined as the interval from lights-off to sleep onset determined on actigraphy.

Childcare practices

On each day of temperature recording, mothers were asked to record childcare practices, including bathing and feeding, and the status of the infant, including sleep start/end times and crying/fussy behavior. The timetable record consisted of columns of 5 min intervals from 0 to 24 h. We requested that recording be started in the early morning of the recording day and continued until the next morning. The times at which the infant was taken out of a hot bath, last feeding before bedtime, and lights-off were indicated according to number of minutes in separate columns.

Statistical analysis

IBM SPSS Statistics (version 20.0 Static Base and Advanced Statistics, IBM Japan, Tokyo, Japan) was used for all statistical analysis. The correlations and group differences were tested using parametric or non-parametric analysis according to the distribution of variables. DPG distribution was assumed to be normal and homoskedastic according to the Kolmogorov–Smirnov test; thus, parametric testing was done. The data from the study nights included both 1 night and 2 consecutive nights from each infant. For statistical analysis of group differences, we regarded the unit of analysis as 1 night, but in order to evaluate group differences for infant characteristics, the unit of analysis was the infant; two nights of data from one infant in the same group were regarded as one infant's data. Data are expressed as mean \pm SD when variables were normally distributed and as median (range or interquartile range [IQR]) when variables were not normally distributed. Statistical significance was set at two-sided $P < 0.05$.

Results

Infant characteristics and childcare factors

Data for 49 nights from 31 infants were obtained, including data for 2 consecutive nights from 18 infants, but recordings of 2 nights were excluded because temperature measurement was found to be unreliable, probably due to poor attachment of thermistor probes. Furthermore, recordings from 4 nights were

Table 1 Subject characteristics

Characteristics (<i>n</i> = 28)	<i>n</i> (%) or median (range)
Male	13 (46.6)
Firstborn babies (number, %)	13 (46.4)
Gestational age (weeks)	39 (37–41)
Birth weight (g)	3088 (2508–3960)
Weight at 4 months (g)	6710 (5628–8250)
Age at time of study (weeks)	25 (18–36)
Breast-feeding only	15 (53.6)
Sleeping in parental bed	23 (82.8)
Sleeping in the supine position	28 (100)
Childcare factors during study nights (<i>n</i> = 43)	
Ambient temperature (°C)	19.4 (12.6–26.5)
Length of daytime nap (min)	180 (30–420)
Time of sleep onset	21:54 (19:40–01:23)
Lights-off	21:26 (19:15–00:23)
Time of evening hot bath [†]	19:15 (16:00–22:05)
Time of last feeding	21:05 (16:12–23:30)
Sleep-onset latency (min)	34 (4–95)
Interval from evening bath to lights-off (min) [†]	115 (14–392)
Interval from last feeding to lights-off (min)	31 (0–296)

[†]Study nights when infants had a bath before 16:00 hours (*n* = 2) were excluded.

excluded due to deviation from protocol, such as infants falling asleep before lights-off or severe crying immediately after lights-off. Three recordings from infants who cried for short periods (<5 min) after lights-off were not excluded. Finally, data of 43 nights from 28 infants, 13 boys and 15 girls, including data of 2 consecutive nights from 15 infants, were used for analyses. Maternal age ranged from 23 to 39 years and no mothers smoked or drank alcohol. Infant characteristics (*n* = 28) and childcare factors for the study nights (*n* = 43) are summarized in Table 1.

Time course of DPG

Individual DPG profiles surrounding sleep onset (30 min before sleep onset–30 min after sleep onset) for all study nights (*n* = 43), with reference mean (\pm SD) proximal and distal skin temperatures over time, are given in Figure 1. There was no notable change in mean proximal skin temperature during that interval. In contrast, mean distal skin temperature gradually rose until 10 min after sleep onset, and stabilized afterwards. Thus, most DPG recordings had an upward curve toward sleep onset, but there were seven exceptional curves that did not show any significant rise during that interval. The slope of the mean DPG rise during the 30 min interval before sleep onset was calculated to be 0.075°C/min.

Figure 2 shows the time course of DPG with actigraph activity data in an infant (18-week-old boy) who had no significant increase in DPG with sleep onset. In this infant, onset of DPG rise was delayed considerably (approx. 45 min) after sleep onset. A rise in DPG with large (>30 min) absolute interval between initial DPG rise and sleep onset was also observed in four other infants, with no significant rise of DPG surrounding sleep onset.

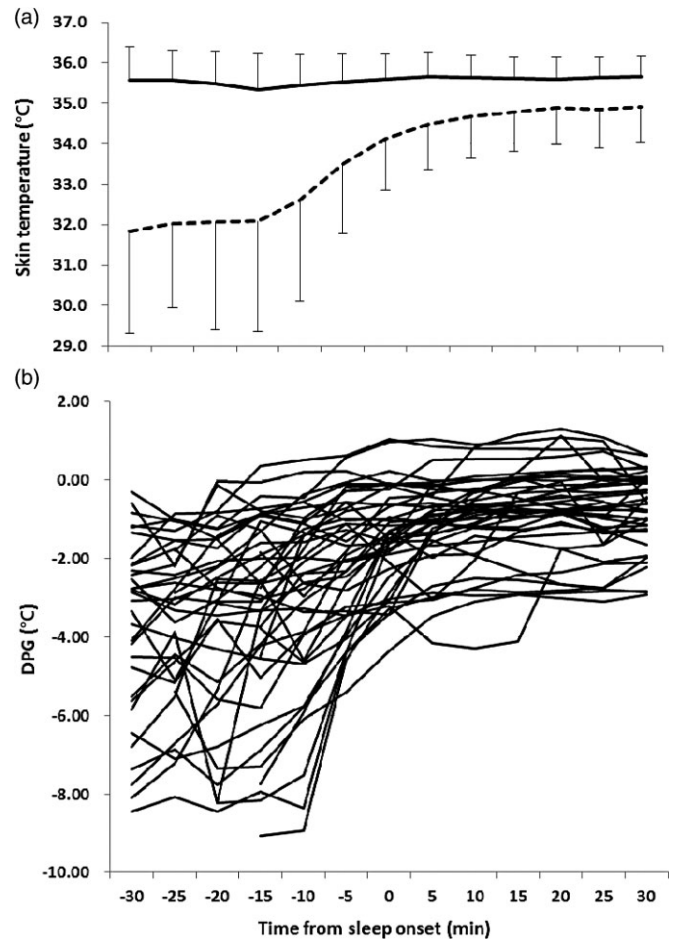


Fig. 1 (a) Mean \pm SD (—) proximal skin temperature and (---) distal skin temperature; (b) distal–proximal skin temperature gradient (DPG) vs time for 43 study nights.

DPG at lights-off, childcare factors and sleep-onset latency

Distal–proximal skin temperature gradient or proximal and distal skin temperature at lights-off on each study night were determined by calculating the means of two DPG measurements just before and just after lights-off. Mean \pm SD DPG, and proximal and distal skin temperature at lights-off for all study nights were $-4.28 \pm 2.42^\circ\text{C}$, $35.15 \pm 0.75^\circ\text{C}$ and $30.76 \pm 2.54^\circ\text{C}$,

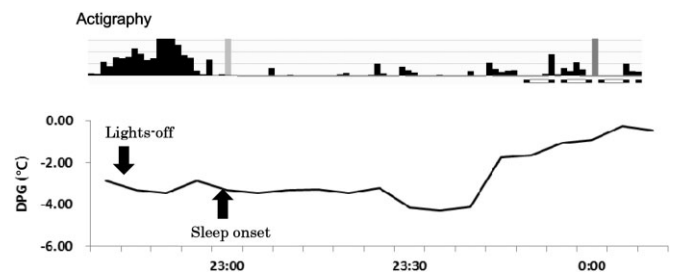


Fig. 2 Distal–proximal skin temperature gradient (DPG) vs time in an infant showing no significant increase of DPG surrounding sleep onset.

Table 2 Associations between main childcare factors and temperature at lights-off

	No. nights	Proximal skin temperature (°C) (mean ± SD)	Distal skin temperature (°C) (mean ± SD)	DPG (°C) (mean ± SD)
Ambient temperature				
≥20°C	19	35.14 ± 0.85	31.67 ± 1.77	-3.50 ± 1.65
<20°C	24	35.14 ± 0.85	30.05 ± 2.85	-4.890 ± 2.77
<i>P</i> [†]		0.908	0.036	0.059
Interval from evening bath to lights-off				
≤90 min	18	35.12 ± 0.59	31.54 ± 1.55	-3.58 ± 1.60
>90 min	25	35.18 ± 0.86	30.21 ± 2.97	-4.79 ± 2.79
<i>P</i> [†]		0.824	0.089	0.108
Interval from last feeding to lights-off				
≤60 min	26	34.92 ± 0.82	31.12 ± 2.51	-4.19 ± 2.44
>60 min	17	35.31 ± 0.67	30.22 ± 2.56	-4.43 ± 2.46
<i>P</i> [†]		0.097	0.258	0.749
Crying episode 30 min before lights-off				
Yes	8	35.20 ± 0.75	31.611 ± 2.62	-3.53 ± 1.62
No	35	34.96 ± 0.76	31.43 ± 2.19	-4.45 ± 2.55
<i>P</i> [†]		0.425	0.418	0.338

[†]Student's *t*-test. DPG, distal–proximal skin temperature gradient.

respectively. DPG at lights-off was not correlated with proximal skin temperature ($r = 0.154$, $P = 0.331$), but was strongly correlated with distal skin temperature ($r = 0.913$, $P < 0.0001$). Thus, DPG at lights-off for each infant was highly dependent on distal skin temperature.

Associations between main childcare factors and proximal and distal skin temperature and DPG at lights-off are listed in Table 2. We estimated that high ambient temperature ($\geq 20^\circ\text{C}$), short interval from evening bath (≤ 90 min), short interval from last feeding (≤ 60 min) and crying episode 30 min before lights-off might have a significant positive impact on DPG or skin temperature at lights-off, but significant impact was detected only for high ambient temperature (vs distal skin temperature, $P = 0.036$). There were no significant correlations between DPG and sleep-onset latency (correlation coefficient, by Spearman's rank test: -0.103 , $P = 0.512$).

DPG profile according to sleep-onset latency

Prior to the study, we expected that pre-sleep DPG rise across 2 nights would occur in a similar way, but this did not happen in nearly half of the infants. Therefore, the unit of analysis was defined as each night, not as each infant.

Because DPG profile after lights-off was highly variable among study nights, we were unable to utilize an appropriate quantitative index of DPG change (e.g. slope of the DPG rise from lights-off). Therefore, in order to estimate ability of DPG to predict sleep-onset latency in infants, we simply compared DPG between two groups divided according to sleep-onset latency. The criterion of sleep-onset latency, "30 min", was based on the practical assumption that most parents would usually be happy if their infant fell asleep within 30 min after lights-off. Nineteen nights when infants ($n = 13$) fell asleep within 30 min after lights-off were grouped as "short sleep-onset latency nights", while the other 24 nights with 19 infants were grouped as "long sleep-onset latency nights". Among 18 infants with two consecutive nights of data, the study nights of four infants were grouped

separately into the long and short sleep-onset latency nights. The two sleep-onset latency groups were similar with regard to infant characteristics and childcare factors (data not shown), indicating that influences from these factors on length of sleep-onset latency appeared to be similar.

The time course of individual DPG profiles after lights-off in short or long sleep-onset latency nights is given in Figure 3. In short sleep-onset latency nights (Fig. 3a), the time course of most DPG recordings had an upward curve immediately after lights-off. In long sleep-onset latency nights (Fig. 3b), however, the tendency of steady increase after lights-off was less evident in many recordings. When mean DPG were compared between the two groups at each measurement time after lights-off (Table 3), significant differences appeared at 5 min after lights-off ($P = 0.049$), and became very evident at 15 min after lights-off ($P = 0.008$). Therefore the DPG that differentiated the two groups was -2.5°C , which first appeared at 15 min after lights-off.

Prediction of sleep-onset latency using DPG at 15 min after lights-off

For infants with low DPG at time of lights-off, DPG that increased by 15 min after lights-off might be a key determinant for sleep-onset latency. Therefore, we compared sleep-onset latency with DPG at lights-off and at 15 min after lights-off. Based on group differences between the long and short sleep-onset latency nights at 15 min after lights-off (Table 3), we determined low or high DPG using -2.5°C as the reference temperature. At lights-off, DPG was $< -2.5^\circ\text{C}$ for 34 study nights (79.1% of all study nights). Thereafter, DPG increased to $\geq -2.5^\circ\text{C}$ within 15 min for 19 nights (group A: DPG at lights-off $< -2.5^\circ\text{C}$ and DPG at 15 min after lights-off $\geq -2.5^\circ\text{C}$), but not during 15 nights (group B: DPG at lights-off $< -2.5^\circ\text{C}$ and DPG at 15 min after lights-off $< -2.5^\circ\text{C}$). At lights-off, DPG was already $\geq -2.5^\circ\text{C}$ for 9 nights (group C). Regarding data for 2 consecutive nights from 15 infants, 2 consecutive nights for eight infants were classified into separate groups.

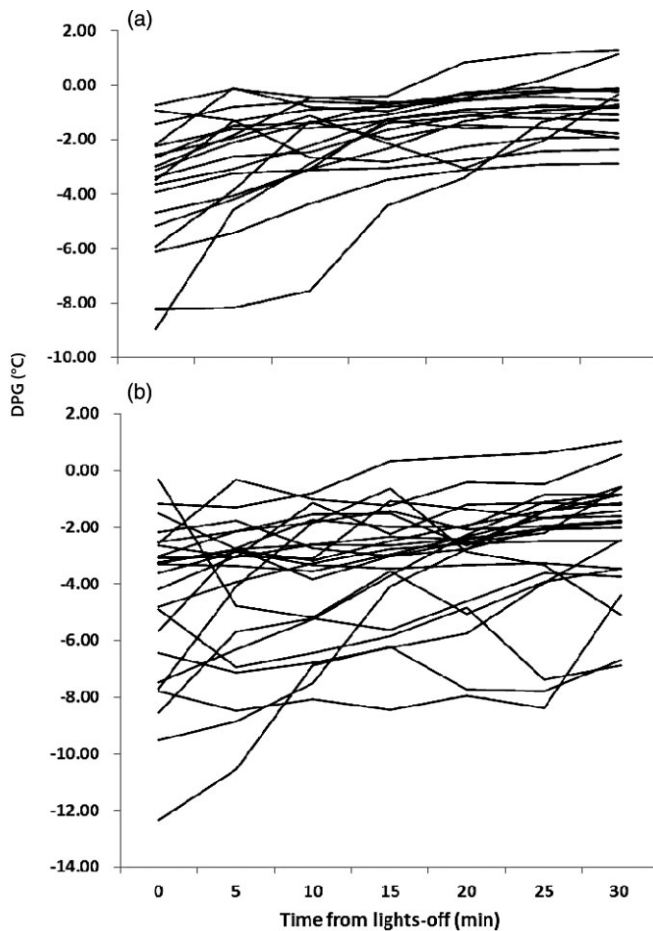


Fig. 3 Distal–proximal skin temperature gradient (DPG) after lights-off for (a) short (≤ 30 min, $n = 19$ nights) and (b) long (> 30 min, $n = 24$ nights) sleep-onset latency.

No significant differences were detected for infant characteristics or childcare factors among the three groups (Table 4). Median sleep-onset latency in groups A, B and C was 26 min (IQR, 15–40 min), 47 min (IQR, 35–76 min) and 31 min (IQR, 19–39 min), respectively, with significant differences among the three groups (Kruskal–Wallis test, $P = 0.025$). Regarding 34 nights with low DPG ($< -2.5^{\circ}\text{C}$) at lights-off (group A and B), sleep-onset latency was significantly shorter in group A

($P < 0.014$). The incidence of short sleep-onset latency nights in groups A, B and C was 12/19 (63.1%), 3/15 (20.0%) and 4/9 (44.4%), respectively, and the differences were significant (χ^2 for independence test, $P = 0.036$).

In addition to the aforementioned findings, we investigated DPG at 15 min after lights-off as a predictor for short sleep-onset latency nights. The predictive values of $\text{DPG} \geq -2.5^{\circ}\text{C}$ at 15 min after lights-off are presented in Table 5. The sensitivity and specificity of $\text{DPG} \geq -2.5^{\circ}\text{C}$ for prediction of “short sleep-onset latency nights” were 0.789 and 0.583, respectively, but, because 13 infants (30.2%) were already asleep at 15 min after lights-off, the sensitivity and specificity of the criterion in the real sense were 0.800 and 0.583, respectively, when sleeping infants were removed from analysis. Due to the low specificity, the positive predictive value was as low as 0.444. The negative predictive value, however, was as high as 0.875.

Discussion

According to laboratory studies with a constant routine protocol, DPG increased sharply after lights-off,¹⁰ and some authors have suggested that the more the distal skin temperature increased toward the proximal temperature, the less time it took to fall asleep.^{11,19} Thus, the initial expectation in this study was use of DPG at lights-off for prediction of sleep-onset latency. We soon found, however, that this was difficult because of poor correlation between DPG at lights-off and sleep-onset latency. Furthermore, we failed to observe immediate elevation of DPG after lights-off in many study nights. But, when the time course of DPG after lights-off was compared according to length of sleep-onset latency, we found a possible clinical application for low DPG ($< -2.5^{\circ}\text{C}$) at lights-off. That is, if infants with low DPG at lights-off are still awake at 15 min after lights-off and DPG at that time is $< -2.5^{\circ}\text{C}$, they are not likely to quickly fall asleep.

Contrary to expectation, sleep-onset latency for infants with high DPG ($\geq -2.5^{\circ}\text{C}$) at lights-off was not always reduced, being distributed widely from 4 to 68 min. If high DPG at lights-off indicated that adequate vasomotor heat loss had already occurred before lights-off, the infants would fall asleep soon after lights-off. More than half of the recording profiles in infants with high DPG, however, showed significant, but slow elevation in DPG after lights-off, suggesting that high DPG at lights-off in such infants was not the result of vasomotor heat loss but was due to

Table 3 Mean DPG vs sleep latency

Time after lights-off	DPG ($^{\circ}\text{C}$)		P^{\dagger}
	Short sleep-onset latency nights, ($n = 19$) (mean \pm SD)	Long sleep-onset latency nights, ($n = 24$) (mean \pm SD)	
0 min	-3.80 ± 2.26	-4.65 ± 2.96	0.303
5 min	-2.73 ± 2.00	-4.20 ± 2.60	0.049
10 min	-2.18 ± 1.70	-3.72 ± 2.18	0.016
15 min	-1.70 ± 1.09	-3.17 ± 2.06	0.008
20 min	-1.31 ± 1.13	-3.05 ± 2.03	0.002
25 min	-0.97 ± 0.99	-2.70 ± 2.26	0.003
30 min	-0.81 ± 1.07	-2.23 ± 2.02	0.008

† Student's t -test. DPG, distal–proximal skin temperature gradient.

Table 4 Main infant characteristics vs change in DPG

	Group A	Group B	Group C	<i>P</i> [†]
	(<i>n</i> = 19, 15 infants) Mean ± SD or median (IQR)	(<i>n</i> = 15, 13 infants) Mean ± SD or median (IQR)	(<i>n</i> = 9, 8 infants) Mean ± SD or median (IQR)	
DPG at lights-off (°C)	-4.28 ± 1.70	-5.85 ± 2.51	-1.68 ± 0.96	
DPG at 15 min after lights-off (°C)	-1.47 ± 0.59	-4.40 ± 1.70	-1.61 ± 1.34	
Weight at 4 months of age (g) [‡]	6890 (6245–7400)	6560 (64 909–7 208)	6840 (6515–7300)	0.845
Age at study (weeks) [‡]	30 (23–32)	25 (20–32)	21 (19–29)	0.220
Ambient temperature (°C)	19.4 (16.4–21.9)	19.4 (16.7–21.6)	21.0 (17.2–24.2)	0.282
Interval from hot bath to lights-off (min)	120 (69–168)	122 (51–150)	115 (55–173)	0.917
Interval from last feeding to lights-off (min)	27 (0–66)	30 (12–92)	14 (0–85)	0.214
Sleep-onset latency (min)	26 (15–40)	47 (35–76)	31 (19–39)	0.025

[†]Kruskal–Wallis test. [‡]In order to evaluate group differences for the characteristics of infants, the unit of analysis was the infant; two nights of data from one infant in the same group were regarded as one infant's data. Group A, DPG at lights-off < -2.5°C and DPG at 15 min after lights-off ≥ -2.5°C; group B, DPG at lights-off < -2.5°C and DPG at 15 min after lights-off < -2.5°C; group C, DPG at lights-off ≥ -2.5°C. DPG, distal–proximal skin temperature gradient.

relatively higher set points of DPG before onset of real pre-sleep heat-loss. For such infants, DPG rise after lights-off occurred slowly to a minor extent. Therefore, if we were able to determine that infants, at lights-off, were in a given status before onset of pre-sleep heat-loss, determining a reference value of DPG according to level at lights-off might increase ability to predict sleep onset.

What is evident in this study is a lack of individual stability in the pattern of pre-sleep DPG rise. Thus, with regard to the possibility of using DPG to predict infant sleep onset, the discussion should focus on how to stabilize this pattern in infants at home. One key observation is that the patterns were to some extent dependent on DPG at lights-off. When DPG at lights-off was relatively lower, subsequent DPG rise tended to occur more rapidly with a large magnitude. Therefore, interventions to set a relatively constant, lower DPG in infants at lights-off seems to increase stability of DPG patterns. For that purpose, relatively low ambient temperatures were thought to be advantageous, because distal skin temperature is well correlated with ambient temperature.²⁰ Furthermore, external interventions associated with enhancement of pre-sleep heat loss, including a hot bath in the evening or the shortening of the interval from last feeding to bedtime, may be feasible.²¹ Although the present study failed to demonstrate significant influences of such childcare practices

on DPG at lights-off or induction of DPG rise after lights-off, it is likely that the influence of a single intervention would be masked by other interventions under uncontrolled conditions at home.

Another possible intervention to stabilize DPG patterns in infants may be to provide more definite external clues to strengthen the biological circadian rhythm, in order to initiate vasomotor heat loss from distal skin regions immediately after lights-off. The external clues include intensity of the light. Increasing the intensity of the light and the length of light exposure during the day may be beneficial for infant circadian entrainment.²² Furthermore, because melatonin secretion appears to be the hormonal signal that induces selective vasodilatation in the distal skin regions,¹⁰ complete darkening of the bedroom after lights-off, which may reinforce the melatonin surge, could facilitate DPG rise after lights-off. We observed, however, wide dissociations between DPG rise and sleep onset in some infants, and the phenomenon might reflect the underlying intrinsic problems of the infants: asynchronous timing between sleep–wake and body thermal rhythms. In conjunction with this problem, two previous studies noted immature patterns of melatonin circadian rhythms in some infants aged 3–9 months, suggesting that asynchronous physiological circadian rhythms are not rare in infants at this age.^{23,24}

Table 5 Predictive value of DPG at 15 min after lights-off for sleep-onset latency

	<i>n</i>	Short sleep-onset latency nights	Long sleep-onset latency nights	Sensitivity	Specificity	PPV	NPV
All nights (<i>n</i> = 43)							
DPG ≥ -2.5°C	25	15	10	0.789	0.583	0.600	0.778
DPG < -2.5°C	18	4	14				
Total	43	19	24				
Nights when infants awoke (<i>n</i> = 34)							
DPG ≥ -2.5°C	18	8	10	0.800	0.583	0.444	0.875
DPG < -2.5°C	16	2	14				
Total	34	10	24				

DPG, distal–proximal skin temperature gradient; NPV, negative predictive value; PPV, positive predictive value.

Conclusions

In the present study, we found an increase in DPG prior to sleep onset in a number of nightly recordings of infants, aged 4–9 months, suggesting that vasodilation of distal skin regions and hence heat loss preceded sleep onset in many infants at home. Although the usability of DPG to predict sleep-onset latency appears to be limited, low DPG ($<-2.5^{\circ}\text{C}$) at 15 min after lights-off is suggested to indicate difficulty in falling asleep quickly. The present results seem to be more useful for parents during the winter season when pre-sleep distal skin temperature or DPG tends to be lower. The present conclusions may be more remarkable because relations between DPG and sleep-onset were found in infants even under conditions of considerable variance. Furthermore, this observational study indicates that improving our understanding of the relationship between natural DPG profile and sleep onset in infants will increase the precision with which we are able to predict sleep onset at home.

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References

- McMillen IC, Kok JS, Adamson TM, Deayton JM, Nowak R. Development of circadian sleep-wake rhythms in preterm and full-term infants. *Pediatr. Res.* 1991; **29** (4 Pt 1): 381–4.
- Mirmiran M, Maas YG, Ariagno RL. Development of fetal and neonatal sleep and circadian rhythms. *Sleep Med. Rev.* 2003; **7**: 321–34.
- Lack LC, Lushington K. The rhythms of human sleep propensity and core body temperature. *J. Sleep Res.* 1996; **5**: 1–11.
- Murphy PJ, Campbell SS. Nighttime drop in body temperature: A physiological trigger for sleep onset? *Sleep* 1997; **20**: 505–11.
- 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.* 1994; **267** (3 Pt 2): R819–29.
- 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.
- Johnson JM, Kellogg DL Jr. Thermoregulatory and thermal control in the human cutaneous circulation. *Front. Biosci. (Schol. Ed)* 2010; **2**: 825–53.
- Braverman IM. The cutaneous microcirculation: Ultrastructure and microanatomical organization. *Microcirculation* 1997; **4**: 329–40.
- van den Heuvel CJ, Noone JT, Lushington K, Dawson D. Changes in sleepiness and body temperature precede nocturnal sleep onset: Evidence from a polysomnographic study in young men. *J. Sleep Res.* 1998; **7**: 159–66.
- 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.
- Lack L, Gradisar M. Acute finger temperature changes preceding sleep onsets over a 45-h period. *J. Sleep Res.* 2002; **11**: 275–82.
- Gradisar M, Lack L. Relationships between the circadian rhythms of finger temperature, core temperature, sleep latency, and subjective sleepiness. *J. Biol. Rhythms* 2004; **19**: 157–63.
- van Marken Lichtenbelt WD, Daanen HA, Wouters L *et al.* Evaluation of wireless determination of skin temperature using iButtons. *Physiol. Behav.* 2006; **88** (4–5): 489–97.
- Rubinstein EH, Sessler DI. Skin-surface temperature gradients correlate with fingertip blood flow in humans. *Anesthesiology* 1990; **73**: 541–5.
- Zornoza-Moreno M, Fuentes-Hernández S, Sánchez-Solis M, Rol MÁ, Larqué E, Madrid JA. Assessment of circadian rhythms of both skin temperature and motor activity in infants during the first 6 months of life. *Chronobiol. Int.* 2011; **28**: 330–37.
- Glotzbach SF, Edgar DM, Boeddiker M, Ariagno RL. Biological rhythmicity in normal infants during the first 3 months of life. *Pediatrics* 1994; **94** (4 Pt 1): 482–8.
- Sarabia JA, Rol MA, Mendiola P, Madrid JA. Circadian rhythm of wrist temperature in normal-living subjects: A candidate of new index of the circadian system. *Physiol. Behav.* 2008; **95**: 570–80.
- Sadeh A. Activity-based assessment of sleep-wake patterns during the 1st year of life. *Infant Behav. Dev.* 1995; **18**: 329–37.
- Fronczek R, Overeem S, Lammers GJ, van Dijk JG, Van Someren EJ. Altered skin-temperature regulation in narcolepsy relates to sleep propensity. *Sleep* 2006; **29**: 1444–9.
- Nardin RA, Fogerson PM, Nie R, Rutkove SB. Foot temperature in healthy individuals: Effects of ambient temperature and age. *J. Am. Podiatr. Med. Assoc.* 2010; **100**: 258–64.
- Kanda K, Tochiyama Y, Ohnaka T. Bathing before sleep in the young and in the elderly. *Eur. J. Appl. Physiol. Occup. Physiol.* 1999; **80**: 71–5.
- Tsai SY, Thomas KA, Lentz MJ, Barnard KE. Light is beneficial for infant circadian entrainment: An actigraphic study. *J. Adv. Nurs.* 2012; **68**: 1738–47.
- Sadeh A. Sleep and melatonin in infants: A preliminary study. *Sleep* 1997; **20**: 185–91.
- Shinohara H, Kodama H. Relationship between circadian salivary melatonin levels and sleep-wake behavior in infants. *Pediatr. Int.* 2011; **53**: 29–35.