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Daytime variation in ambient temperature affects skin temperatures and blood pressure: Ambulatory winter/summer comparison in healthy young women

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HIGHLIGHTS

- Ambient temperature changes induce alterations in distal skin temperature.
- Short-term changes in distal skin temperature and blood pressure are associated.
- Seasonal changes in distal skin temperature and blood pressure are not correlated.

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ABSTRACT

It is widely accepted that cold exposure increases peripheral vascular resistance and arterial blood pressure (BP) and, hence, increases cardiovascular risk primarily in the elderly. However, there is a lack of concomitantly longitudinal recordings at personal level of environmental temperature (PET) and cardiophysiological variables together with skin temperatures (STs, the "interface-variable" between the body core and ambient temperature). To investigate the intra-individual temporal relationships between PET, STs and BP 60 healthy young women (52 completed the entire study) were prospectively studied in a winter/summer design for 26 h under real life conditions. The main hypothesis was tested whether distal ST (T_{dist}) mediates the effect of PET-changes on mean arterial BP (MAP).

Diurnal profiles of cardiophysiological variables (including BP), STs and PET were ambulatory recorded. Daytime variations between 0930 and 2030 h were analyzed in detail by intra-individual longitudinal path analysis. Additionally, time segments before, during and after outdoor exposure were separately analyzed.

In both seasons short-term variations in PET were positively associated with short-term changes in T_{dist} (not proximal ST, T_{prox}) and negatively with those in MAP. However, long-term seasonal differences in daytime mean levels were observed in STs but not in BP leading to non-significant inter-individual correlation between STs and BP. Additionally, higher individual body mass index (BMI) was significantly associated with lower daytime mean levels of T_{prox} and higher MAP suggesting T_{prox} as potential mediator variable for the association of BMI with MAP.

In healthy young women the thermoregulatory and BP-regulatory systems are closely linked with respect to short-term, but not long-term changes in PET. One hypothetical explanation could serve recent findings that thermogenesis in brown adipose tissue is activated in a cool environment, which could be responsible for the counter-regulation of cold induced increase of BP in winter leading to no seasonal differences in MAP.

Our findings suggest that the assessment of diurnal patterns of STs and PET, in addition to the conventional ambulatory BP monitoring, might improve individual cardiovascular risk prediction.

Abbreviations: T_{dist}, distal skin temperature; T_{prox}, proximal skin temperature; PET, personal-level of environmental temperature; ST, skin temperature; BP, blood pressure; DBP, distal blood pressure; MAP, mean arterial blood pressure; SBP, systolic blood pressure; BAT, brown adipose tissue; SOL, sleep onset latency.

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1. Introduction

There is a higher mortality and incidence of vascular diseases including e.g. stroke, coronary ischemic events and heart failure in the general population (most pronounced in elderly) during winter than in other seasons [1–5]. The underlying mechanisms are not fully understood, however adverse effects of thermoregulatory adjustments seem to play an important role. For example, physiological, observational and epidemiological research has shown that cold exposure leads to cutaneous vasoconstriction with subsequent centralization of blood, increased cardiac preload, a rise in blood pressure (BP) and hemoconcentration [3,5,6].

The thermophysiological core/shell model developed by Aschoff [7] provides a possible explanation for the findings described above. In a cool environment the shell is large (relatively cool) and protects the core body against a rapid cooling (centralization of blood). In a warm environment, as well as during sleep, the shell is small (relatively warm) and the body loses its two-compartment system and is prone to cool [8]. Distal skin regions (e.g. hands, feet; belonging to the shell) are particularly suitable to lose body heat thanks to their physiological (abundant arteriovenous anastomoses) and physical (high surface to volume ratio) properties. Diverse controlled physiological and pharmacological laboratory studies have shown that changed distal skin temperature (T_{dist}) in relation to proximal skin temperature (T_{prox}) is associated with changes in core body temperature and body heat loss [7,9–12]. Furthermore, the difference between T_{dist} and T_{prox} has been validated as a measure for distal skin blood flow by plethysmographic and laser-Doppler-flowmetry methods [13–15], e.g. with lowered environmental temperature distal skin regions exhibit larger reduction in skin temperature (ST) and skin blood flow than proximal sites indicating redistribution of shell blood to the core [13,15]. Using wireless ST probes [16] T_{dist} and T_{prox} measurements easily provide information about the thermophysiological state of the human body also under ambulatory conditions, i.e. lower T_{dist} in relation to T_{prox} is indicative of a larger shell [8].

The relationship between ambient temperature and BP has mostly been studied in a cross-sectional design, however, for more accurate and reliable information longitudinal studies are needed [4]. In spite of the convincing amount of evidence for the influence of cold ambient temperature on BP it is amazing that in most studies BP measurements were compared only with outdoor environmental air temperature data provided by meteorological institutes. This shortcoming can be easily improved by direct personal-level environmental temperature recording (PET) [4,17,18]. Because of the obvious relationship that PET affects the body's physiology via the skin, it is a logical step to include also ST (the "interface-variable" between body core and ambient temperature) measurements with respect to ambient temperature induced changes in BP. Including ST measurements can further improve the understanding about mechanisms how changes in PET are transformed to changes in BP.

In a recent study under structured ambulatory conditions it could be shown that mean arterial BP exhibits an inverse 24 h pattern to STs most pronounced in distal skin regions in relation to proximal skin regions [19,20]. Unfortunately, no direct measurements of PET were recorded preventing detailed analyses and interpretation with respect to temporal changes in PET and its association with STs and BP.

The main objective of this prospective ambulatory study with healthy young women was to test the hypothesis whether the temporal association between PET and BP is mediated via T_{dist}, and whether this relationship is different in winter and summer. Healthy young women were chosen, first, because they are particularly sensitive to cool environment [21,22] and second, it could be expected that in the same subject acute outdoor effects can be found in BP, but not long-term seasonal effects [2,4]. Using a multivariate approach including diverse variables, e.g. PET, T_{dist} and BP, the comparison of intra-individual difference between acute and long-term effects could disclose possible mechanisms to explain why seasonal differences in BP are not present in younger subjects. In a first step potential seasonal differences in diurnal patterns of the measured variables and their interrelationships were analyzed. This approach includes day–night comparisons allowing one to specify whether environmental influences on STs and BP are dependent on time of day. In a further step daytime variation in the variables between 0930 and 2030 h were compared within subjects followed by a detailed analysis of outdoor effects. Furthermore, the present study should serve as database to compare future subject groups including e.g. men and elderly.

2. Methods

2.1. Study population and design

The study, including all experimental procedures and the informed consent form, has been approved by the local ethics committee (Ethikkommission beider Basel). Before admission to the study, each subject signed an informed consent form and was explicitly informed that she could stop the study at any time. However, none complained about the study and all subjects who did not complete the study did so for scheduling reasons.

Sixty healthy female residents (age: 25.0 ± 0.6) of the city of Basel (Switzerland) including rural agglomeration fulfilled the defined exclusion/inclusion criteria (Table 1) and were studied in a winter vs. summer design during 26 h. In order to obtain a study sample comprising a high variance with respect to STs women with (N = 32) and without (N = 28) thermal discomfort with cold extremities were selected [19].

Subjects were recruited via an announcement in an internet platform of the University of Basel informing potential volunteers about the opportunity to participate in a scientific research project. The screening questionnaire including the inclusion/exclusion criteria questions of Table 1 was sent to 394 potential study subjects, 194 sent the questionnaire back. Of the sixty study subjects, 39 women started in winter (02/12/11–09/03/12) and finished in summer (04/06/12–12/09/12), and 21 women started in summer (04/06/12–12/09/12) and finished in winter (04/12/12–14/03/13). Fifty-two subjects completed the entire study, six dropped out after winter 2011/2012 and two after summer 2012.

In order to get a more homogenous group of women with respect to female sex hormones, women without contraceptives and with regular menstrual cycle were studied during their luteal phase. This phase was defined as the interval between day 14 and the end of the menstrual cycle. 25 women with and 35 without taking contraceptives were studied. All subjects were asked to maintain their normal daily activities and sleep wake schedules, however, without sporting activities and not taking a shower or a bath.

Table 1
Exclusion criteria.

Exclusion criteria are defined as follows
• Age < 20 and >35 yr
• Body mass index (BMI) < 18 kg/m^2 and >28 kg/m^2.
• Acute or chronic mental or physical disease.
• Nickel or other skin allergies.
• Medication in the last month, except contraceptives.
• Irregular menstrual cycle (>±2 days).
• Shiftwork within 3 months or transmeridian travel within 1 month before the study begin.
• Pregnancy (pregnancy test was performed before study begin).
• Smoking, not abstinent at least for 3 months.
• Drug consumption.
• Excessive caffeine (≥5 cups/day) or alcohol consumption (>1 glass unit/day).
• Excessive sporting activities (>3 days per week).
• Not to experience thermal discomfort with cold extremities or not to be a control subject usually perceiving during winter according to [24].

Table 2
BMI and sleep characteristics in summer and winter measured/estimated during study days (mean ± SEM).

Variable	Summer	Winter
BMI (kg/m^2)	22.43 ± 0.38	22.67 ± 0.39
Lights on (h)	7.55 ± 0.17	7.68 ± 0.18
Lights off (h)	23.70 ± 0.13	23.80 ± 0.13
Sleep duration (h)	7.85 ± 0.16	7.88 ± 0.14
Sleep onset latency (SOL) (h)	27.49 ± 3.48[a]	32.08 ± 4.18[a]
Usual sleep onset latency (min) (estimated for the last 4 weeks)	15.59 ± 1.90	15.00 ± 1.74
Leeds sleep Evaluation Questionnaire		
Getting to sleep	43.5 ± 1.9[b]	38.9 ± 1.8[b]
Quality of sleep	27.3 ± 2.5[b]	28.0 ± 2.1[b]
Awake following sleep	49.4 ± 2.1	48.5 ± 1.9

No significant summer–winter differences were found.
Note: Compared to usual sleep, sleep continuity and sleep initiation (getting to sleep and SOL) were significantly impaired on study days.
[a] Sleep onset latencies estimated during study days were significantly longer (about doubled) than usual ($p < 0.0001$).
[b] Getting to sleep and quality of sleep estimated for study days were significantly ($p < 0.002$) worse than usual (= 50 mm).

Detailed subject characteristics for winter and summer including sleep behavior and BMI are presented in Table 2.

2.2. Sleep/wake, indoor/outdoor diaries

Immediately after awakening estimated bedtime, lights-off time, sleep onset latency, sleep disturbances (waking bouts, get-up times during night), wake-up time (lights-on), get-up time in the morning, sleep quality, restorative sleep, and sleepiness before lights-off were written in their sleep-wake diaries including the Leeds Sleep Evaluation Questionnaire [25]. Additionally, subjects noted timing of activity, time spent outdoors, and time of special events e.g. temperature sensor removal.

2.3. Ambulatory blood pressure measurements

24-h blood pressure monitoring with integrated pulse wave analysis was performed using an automated oscillometric ambulatory system (Mobil-O-Graph NG®, IEM GmbH, Stolberg, Germany). Diastolic (DBP), systolic (SBP) and mean arterial blood pressure (MAP), heart rate and pulse wave analysis variables (e.g. pulse wave velocity, augmentation index) were recorded in 15-min intervals during the wake phase and in 30-min intervals during the sleep phase. In order to reduce missing data within time series all measurements were averaged in 1-h bins. This paper focuses on classical blood pressure (BP) variables such as DBP, SBP and MAP and heart rate; the results of pulse wave analysis will be published in details elsewhere.

2.4. Temperature measurements

Temperature recordings were performed with wireless temperature sensors (DS 1922L, Thermochron iButtons®; resolution 0.0625 °C, accuracy 0.5 °C; Maxim, Dallas, USA) in one-minute intervals. All subjects received the same iButton in winter and summer for each skin site. The temperature sensors were fixed to the skin with thin air-permeable adhesive surgical tapes (Fixomull®; Beiersdorf, Hamburg, Germany) on both sides of the body, left and right on these regions: ankle (inner side, between talus and Achilles' tendon above the shoes), wrist (palmar side), thigh (in the middle of quadriceps) in addition to the infraclavicular region and one temperature sensor on the stomach and another on the sternum. Mean value of ankles, wrists and thighs is defined as distal skin temperature (T_{dist}), while proximal skin temperature (T_{prox}) is constituted by the average of infraclavicular regions, sternum and stomach. We excluded data during and half an hour after exchanging a surgical tape when a probe was detached. None of the subjects lost a ST probe. In order to register personal-level environmental temperature (PET) during the wake phase temperature sensors were placed within a mesh net bag tied outside the clothes on the right hip e.g. to a waist belt. During the sleep phase the mesh net bag was installed at bedside table.

2.5. Overview of data analyses

The statistical analyses were performed in three steps. First, all variables were tested with respect to seasonal differences in diurnal time courses and 24-h mean levels. For this purpose we averaged the data for winter and summer seasons into 24 one-hour time-bins. In addition inter-relationships between variables were tested with respect to diurnal time courses, daytime values, night values and 24-h means. Second, in order to shed light on possible mechanisms in associations between intra-individual daytime variation of PET, ST and BP mediation analysis was carried out. Finally, in order to examine in detail short-term seasonal effects of outdoor exposure during daytime on PET, ST and BP variables separate analyses were performed.

2.6. Outdoor exposure analysis

According to times noted in the diary the last BP measurement before outdoor exposure was taken for the “pre-exposure” value (PRE), at least one BP measurement during the outdoor exposure for the “exposure” value (EXP, if more than one measurement was available the mean was calculated), and the first indoor BP measurement after outdoor exposure was declared as the “post-exposure” value (POST). An average of ST measurements from 2 min before to 2 min after the BP measurement was calculated for each time segment (PRE, EXP and POST). If a subject was outdoors more than once an average for all variables was performed per time segment and season.

2.7. Statistical methods

In order to test whether a variable exhibits a significant diurnal time course either between hourly time segments or between time segments PRE, EXP and POST analyses of variance for repeated measures were calculated of all measured variables with factors DIURNAL TIME COURSE (T) (or EXPOSURE, E) and SEASON (S) as fixed factors and SUBJECTS as random factor (mixed effects models). Variables showing significant interaction term S × T were analyzed as follows: Diurnal day–night differences (a measure of diurnal amplitude), daytime segment between 0930 and 2030 (all subjects were awake within this time span) and night segment between 0130 and 0630 h (all subjects slept within this time span) were averaged. Mixed effects models were calculated using the package “nlme” in R version 3.0.1.

Based on previous findings [19] we applied a multilevel structural equation model to explain changes in MAP by changes in PET and ST. Path-analysis was performed by a two-level model with measurements nested within participants [26]. In this model person mean centering is used by default, i.e. measurements on the within-person level denote deviations from each individual's mean. We used a random intercept model, i.e. only intercepts were allowed to vary between individuals but not slope parameters. Of particular interest were intra-individual changes between 0930 and 2030 h. Possible confounding effects of slow fluctuations in the time series (temporal trends) were first removed by a cubic polynomial fit. The multilevel structural equation model was analyzed using Mplus Version 5.2. [27]. Correlations between variables tested by linear regression analyses were performed by Statistica™ 6 software (StatSoft, Tulsa, OK, USA).

Means, SEM and p-values are reported. A p-value < 0.05 is considered significant.

3. Results

3.1. Seasonal differences in BMI and sleep characteristics

Table 2 shows that BMI and none of the sleep characteristics exhibit differences between winter and summer. Sleep was significantly impaired on study days compared to the subject's usual sleep as indicated by subjective estimation of sleep continuity and sleep initiation.

3.2. Analyses of diurnal profiles and winter–summer differences

In Fig. 1a & b diurnal time courses (24 hourly means) of all variables are shown in winter and summer. For all variables two-way-ANOVA for repeated measures revealed significant diurnal time courses (main effect: T) (see Table 3). All variables, except T_{dist} and T_{prox} exhibited higher values during daytime than night. PET was highest in the late afternoon (see below). Each separate ST followed more or less similar

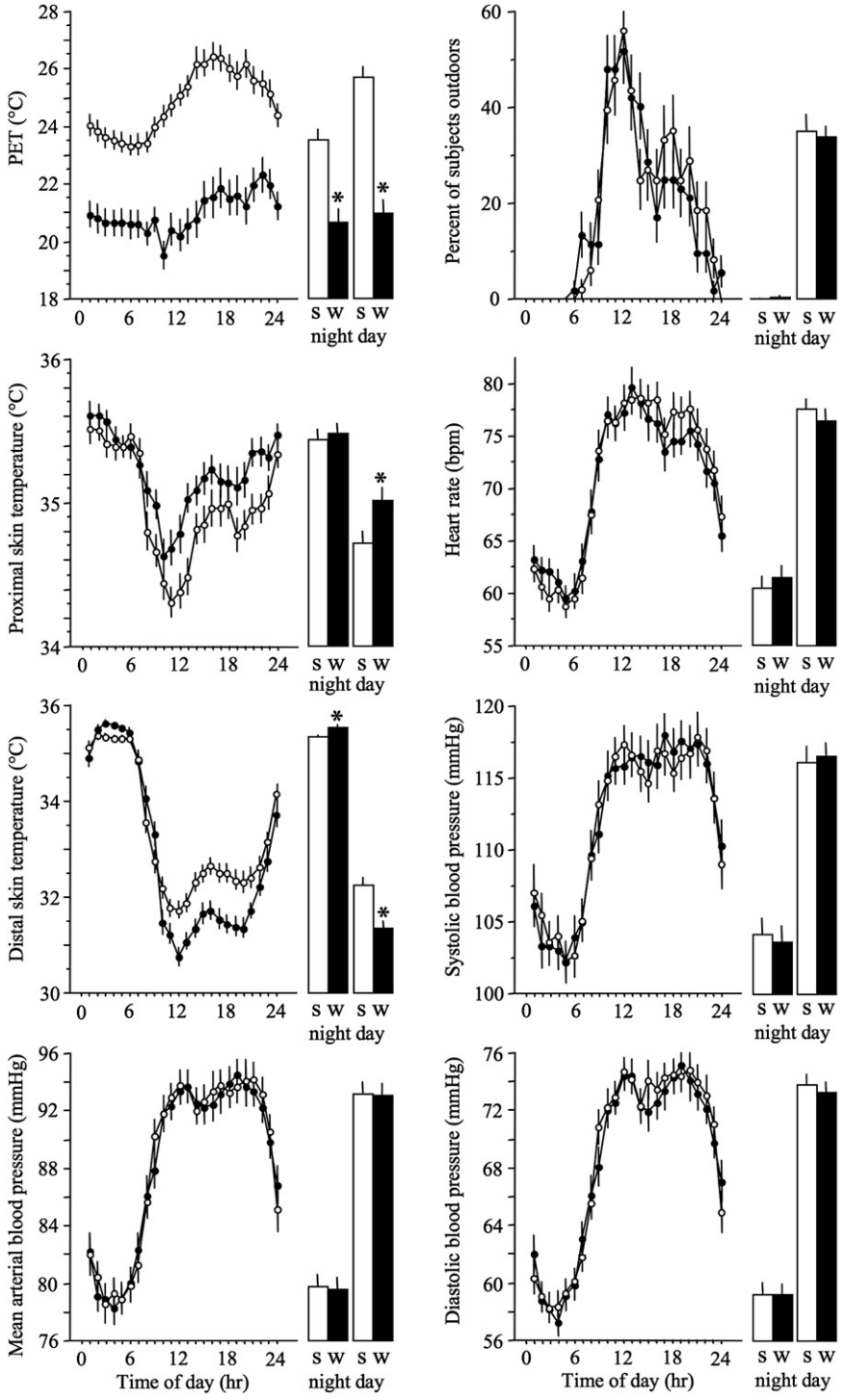

Fig. 1. Diurnal time courses in winter and summer. In the left panel from top to down diurnal profiles of personal level of environmental temperature (PET), proximal skin temperature, distal skin temperature and mean arterial blood pressure are shown in hourly mean values. In the right panel from top to down diurnal time courses of, percentage of subjects spent time outdoors, heart rate, systolic and diastolic blood pressure. Besides the time courses the corresponding daytime (mean between 0930 and 2030 h) and night (mean between 0130 and 0630 h) values are presented in bars for winter and summer. Mean ± SEM of N = 52 subjects; summer values: white dots and white bars, winter values: black dots and black bars. *$p < 0.05$, for statistics see Table 3.

Table 3
Two-way ANOVA for repeated measures with factors season (S, winter vs. summer) and time course (T, 24 hourly mean values, see Fig. 1).

Variable	Summer	Winter	S	Time course (T)	S × T
	Mean ± SEM	Mean ± SEM	p	p	p
PET	24.86 ± 0.32	21.04 ± 0.37	.0001	0.0001	0.0001
T_{dist}	33.34 ± 0.10	32.93 ± 0.08	.0001	0.0001	0.0001
T_{prox}	34.99 ± 0.07	35.22 ± 0.06	.0004	0.0001	0.0023
MAP	88.53 ± 0.78	88.34 ± 0.71	n.s.	0.0001	n.s.
OUTDOORS	19 ± 2	19 ± 1	n.s.	0.0001	n.s.
Heart rate	71.13 ± 1.07	70.64 ± 1.07	n.s.	0.0001	n.s.
DBP	68.72 ± 0.69	68.42 ± 0.65	n.s.	0.0001	n.s.
SBP	112.03 ± 1.06	111.96 ± 0.93	n.s.	0.0001	n.s.

Note: For all variables significant time courses were found. In contrast to PET, T_{dist} and T_{prox} none of the cardiophysiological variables revealed any significant seasonal differences.
PET: personal level of environmental temperature, T_{dist}: distal skin temperature, T_{prox}: proximal skin temperature, MAP: mean arterial blood pressure, DBP: diastolic blood pressure, SBP: systolic blood pressure, OUTDOORS: percentage of subjects spent time outdoors at least once per hour.

time profiles with highest values during the night (data not shown). T_{prox} and T_{dist} were highest during night (0130–0630 h) and lowest in the late morning (10–12 h) followed by a bimodal pattern with a second maximum in the afternoon (around 16 h) and a second minimum in the evening (around 20 h). The cardiophysiological measures DBP, SBP and MAP, and heart rate showed similar diurnal time courses with bimodal pattern during daytime. Furthermore, the intraindividual diurnal time courses (SUBJECTS as random factor) of all those cardiophysiological variables were negatively correlated with T_{dist} (all significant, $p < 0.0001$; e.g. MAP vs. T_{dist}: 24 hourly time points, N = 52 subjects, df = 1247, intra-individual $r = -0.774$, $p < 0.0001$) and to a lesser extent also with T_{prox} (all significant, $p > 0.0001$; e.g. MAP vs. T_{prox}: $r = -0.453$, $p < 0.0001$). However, based on the fact that diurnal time courses of T_{dist} and T_{prox} are interrelated ($r = 0.610$, $p < 0.0001$) multiple regression analyses (dependent variable: MAP) canceled out the effect of T_{prox} ($r = 0.036$, n.s.) — only T_{dist} appeared as a significant factor in the model ($r = -0.703$, $p < 0.0001$). A further analysis revealed that the subjects were more outdoors in the morning than afternoon, which resembles the pattern of heart rate — both were significantly correlated (24 hourly time points, N = 52 subjects, df = 1247, intra-individual $r = 0.467$, $p < 0.0001$).

Seasonal influences on the data were only statistically significant for T_{dist}, T_{prox} and PET as manifested in significant main effects season (S) and interaction terms S × T (Table 3), all cardiophysiological variables didn't reveal significant seasonal differences. Detailed analyses disclosed significantly reduced daytime mean values (averaged hourly means between 0930 and 2030 h) in T_{dist} during winter compared to summer (31.36 ± 0.13 vs. 32.25 ± 0.15 °C, $p < 0.0001$). The changes were most pronounced in thigh (31.47 ± 0.21 vs. 32.73 ± 0.16 °C, $p < 0.0001$) and wrist (31.75 ± 0.15 vs. 32.76 ± 0.14 °C, $p < 0.0001$) and lowest in ankle (30.86 ± 0.23 vs. 31.24 ± 0.22 °C, $p < 0.09$), however, all values were higher in summer than winter allowing the interpretation of the averaged measure of T_{dist}. In contrary, T_{prox} during daytime was significantly increased in winter (35.02 ± 0.09 vs. 34.72 ± 0.08 °C, $p < 0.05$). Detailed ST analyses for daytime values revealed specifically in infraclavicular skin region a significant seasonal difference (winter: 35.34 ± 0.09; summer: 34.85 ± 0.09, $p < 0.0001$). During night (averaged hourly means between 0130 and 0630 h) a small but significant higher T_{dist} was found in winter than summer (35.53 ± 0.05 vs. 35.33 ± 0.05 °C, $p < 0.002$), and T_{prox} did not differ (35.49 ± 0.07 vs. 35.44 ± 0.07 °C; n.s.). As expected, PET revealed lower values in winter than in summer, whereas the differences are bigger during daytime than at night (daytime: 20.91 ± 0.46 °C vs. 25.75 ± 0.37; night: 20.77 ± 0.47 vs. 23.56 ± 0.34 °C; both $p < 0.0001$).

3.3. Intra-individual mediation analyses between PET, skin temperatures and MAP during daytime (0930–2030 h)

We tested whether the intraindividual relationship between PET and MAP was mediated by T_{dist} and/or T_{prox} using a multilevel structural equation model. Results are presented in Table 4 and Fig. 2. Only results at the within-subjects level are presented because all between-subjects effects didn't reach statistical significance.

For the winter data, there was a significant total 'within subject' effect ($p < 0.001$) with a 0.43 mm Hg in MAP increase per 1 °C decrease in PET (Table 4). The corresponding indirect path via T_{dist} was also significant ($p < 0.001$) since neither the indirect path via T_{prox}, nor the direct path from PET to MAP was significant. This indicates that the effect of intra-individual variation in PET on MAP is nearly completely mediated by T_{dist}. For example, a decrease of 1 °C in PET during winter leads to a decrease of 0.19 °C in T_{dist} and to an increase of 0.31 mm Hg in MAP (Table 4). Similarly to path analysis of winter data analysis of summer data revealed a significant indirect path from PET to T_{dist} and MAP (Table 4). However, an additional significant indirect path from PET to T_{prox} and MAP was found with similar negative coefficients as described for T_{dist}. Both indirect paths lead to a significant total indirect effect of similar extent as found in winter. In contrast to the winter analysis PET in summer showed a significant positive direct path to MAP that canceled out the negative indirect paths, leading to a non-significant total effect.

3.4. Analyses of outdoor exposure

Fig. 3 summarizes outdoor exposure analysis of the main variables. Overall conditions mean PET values were higher in summer than in winter ($p < 0.05$) and each point was statistically different from the other ($p < 0.05$). During EXP T_{dist} and T_{prox} diminished in winter but increased in summer ($p < 0.05$). The post-exposure (POST) values for T_{dist} were significantly different from pre-exposure values (PRE) ($p < 0.05$), whereas POST T_{prox} was comparable to PRE.

In winter, values for MAP, SBP and heart rate were increased during EXP, and POST values did not differ from PRE values. Detailed analyses revealed that SBP and heart rate were significantly increased during EXP in winter, whereas in summer only SBP was significantly decreased. DBP showed similar but weak changes (n.s.) according to outdoor exposure. All these findings didn't exhibit a significant influence of BMI (BMI as covariate n.s.).

3.5. Between subject correlations

In order to test whether BMI was associated with overall 24 h-means of MAP (average of summer and winter values, N = 52 women), T_{dist} and T_{prox} linear regression analyses were performed. BMI showed a significant positive correlation with MAP ($r = 0.302$, $p < 0.030$) and a negative one with T_{prox} ($r = -0.353$, $p < 0.011$), and no significant association with T_{dist} was found ($r = 0.068$, n.s.). Additionally, BMI correlated significantly with heart rate ($r = 0.315$, $p < 0.03$) and SBP ($r =$

Table 4
Mediation analyses among PET, T_{dist}, T_{prox} and MAP.

Effects	Winter	Summer
Indirect		
(PET → T_{dist} → MAP)	**−0.30 ± 0.08, p < 0.001**	**−0.25 ± 0.07, p < 0.001**
(PET → T_{prox} → MAP)	−0.01 ± 0.03, n.s.	**−0.15 ± 0.07, p < 0.028**
Total indirect	**−0.31 ± 0.08, p < 0.001**	**−0.39 ± 0.09, p < 0.001**
Direct effect (PET → MAP)	−0.12 ± 0.12, n.s.	**0.49 ± 0.17, p < 0.003**
Total within	**−0.43 ± 0.10, p < 0.001**	0.10 ± 0.18, n.s.

The obtained models were just identified and fitted the data perfectly (CFI = 1, TLI = 1, RMSEA = 0). All 'between subject' effects didn't reach statistical significance. Bold values are statistically significant ($p < 0.05$).
Note: There is a significant indirect effect from PET to T_{dist} to MAP in both seasons.

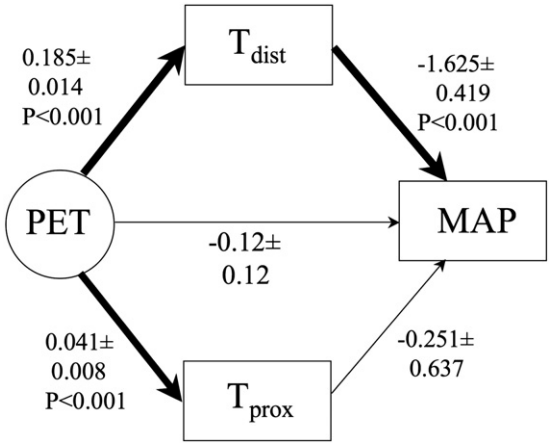

Fig. 2. Effects of short-term PET changes on distal and proximal skin temperatures and MAP. Path diagram (mediation analysis) of winter values. Path diagram (mediation analysis) showing the relation between intra-individual variations in personal-level environmental temperature (PET), distal skin temperature (T_{dist}), proximal skin temperature (T_{prox}) and mean arterial blood pressure (MAP) during winter. Significant paths, $p < 0.001$, are indicated by thick arrows (see Table 4). The thin line represents a non-significant path $p > 0.3$. Path coefficients are shown beside the path arrows. Note: Individual variation of PET exhibits its influence on MAP exclusively by an indirect path via T_{dist}.

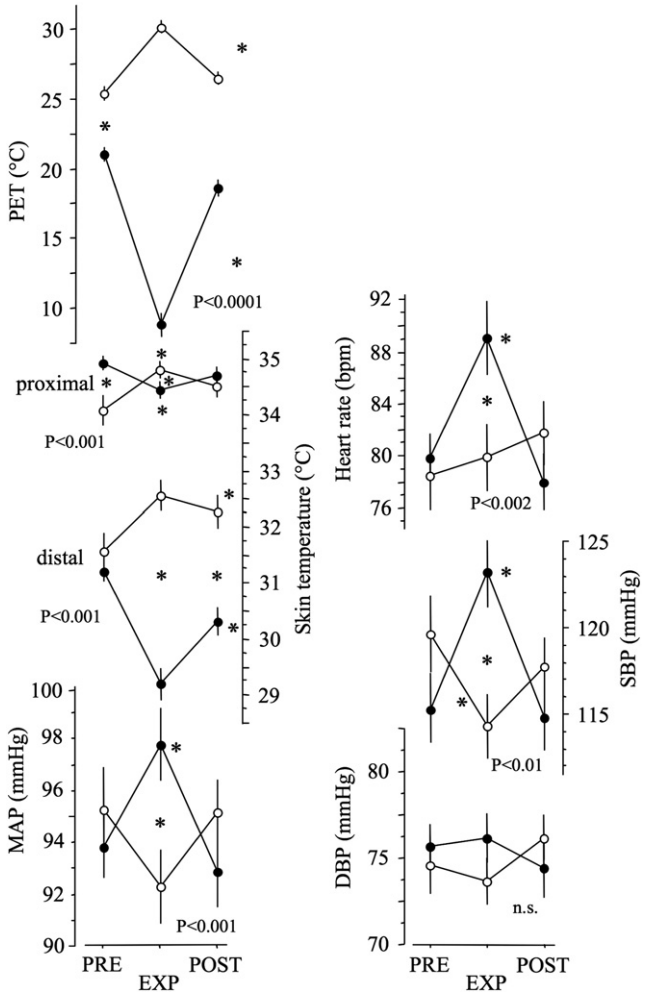

Fig. 3. Analyses of pre, during and after outdoors exposure data in winter and summer. In the left panel from top to down effects of pre (PRE), during (EXP) and post (POST)-outdoor exposure during winter and summer are shown on personal level of environmental air temperature (PET), distal and T_{prox} and mean arterial blood pressure (MAP). In the right panel effects on heart rate, systolic blood pressure (SBP), and diastolic blood pressure (DBP) are presented. Mean ± SEM; summer values: white dots, winter values: black dots; *$p < 0.05$.

0.334, $p < 0.02$). Furthermore, a significant negative correlation between T_{prox} and MAP was found (-0.361, $p < 0.0086$; T_{dist}: 0.069, n.s.). Similar results were found when daytime (0930–2030 h) values instead of 24 h-mean values were correlated with BMI (data not shown).

Linear regression analyses of summer–winter 24 h-means and in diurnal amplitude (day–night differences) revealed non-significant correlations between MAP and T_{dist} or T_{prox}. However, a significant correlation was found between summer–winter differences in daytime (0930–2030 h)-level of T_{dist}–T_{prox} gradient and summer–winter differences in log (sleep onset latency, SOL) ($r = -0.296$, $p < 0.04$). Similarly, a significant correlation between summer–winter difference in diurnal amplitude (day–night difference) and summer–winter difference in logSOL was found ($r = -0.332$, $p < 0.017$).

4. Discussion

This prospective ambulatory study in healthy young women gives an insight into how environmental temperature variation influences BP. The analyses focused mainly on three real life changes in environmental temperature, namely by diurnal (day–night), seasonal (winter–summer) and acute indoor–outdoor differences with respect to BP changes.

4.1. Diurnal profiles

During both seasons each ST followed more or less a similar diurnal profile with highest values during night and lowest in the morning (see Fig. 1a) confirming previous findings [24,28]. Additionally, all STs exhibit a bimodal pattern during daytime with a maximum in the afternoon, which has been described in many other studies [19,20,29]. The diurnal amplitude was higher in distal than proximal skin regions and hence the T_{dist} minus T_{prox} gradient (data not shown) varies as well during the diurnal time course. The different diurnal amplitudes of T_{dist} and T_{prox} are mainly a consequence of different daytime and not night values, confirming previous studies [19,24,28]. Furthermore, these findings implicate increased blood redistribution from the core to the shell, which has been shown to be primarily induced by sleep [19,20].

The close association between blood redistribution from the core to shell was underlined by the result that diurnal time courses of T_{dist} with MAP are strongly correlated than T_{prox} with MAP [19]. However, STs (most pronounced T_{dist}) and MAP are known to be multifactorially influenced, e.g. by locomotor activity, sleep, food and fluid intake, postural changes, and emotional events [2,4,5,19,30,31], but also by environmental changes, e.g. in air temperature [1,5,17,19,31]. The observed (overt) diurnal profiles are a combination of all these masking effects in addition to the endogenous underlying time courses [32,33] and therefore specific for a selected study sample. In the present real life ambulatory study these effects cannot be fully disentangled.

In contrast to the significant association of the diurnal profiles of MAP with T_{dist} their diurnal amplitudes (daytime-night differences) were not significantly correlated in the present study consisting of young subjects. Therefore, it can be concluded that sleep induced dipping is not dependent on peripheral vasodilatation in young women, as recently described in a 30 years older study sample [19]. Previous studies have reported that sleep induced BP-dipping is less pronounced in elderly [34], indicating that blood redistribution from the core to shell at sleep wake transition would be less effective to reduced blood pressure.

4.2. Seasonal effects on diurnal profiles

The study was carried out in both winter and summer; one sample part started in summer the other in winter. Therefore, a potential bias

in the data analysis by order effects was controlled and could be excluded. Additionally, during both seasons sleep timing did not differ and sleep initiation and sleep continuity were similarly impaired during the study days, both indicating that seasonally modified sleep behavior, as a confounder variable, is rather unlikely. However, both intra-individual seasonal differences in daytime levels and diurnal amplitudes of T_{dist}–T_{prox} gradient were significantly associated with seasonal differences in SOL. This result confirms under ambulatory conditions controlled laboratory studies showing distal vasoconstriction before bedtime delays the onset of sleep [8,9,21]. It further indicates, and that in contrast to the blood pressure regulatory system, seasonal differences in STs have affected the sleep regulatory system. Whether seasonal differences in BP exist during SOL remains to be studied using BP recordings with higher time resolution than in the present study. In a previous study carried out in elderly subjects significant seasonal differences in diverse sleep variables (e.g. SOL) as well as in STs have been reported whereas different methodologies prevent a final conclusion whether the discrepancy is caused by aging [27]. For clarification direct seasonal comparisons of different age groups using the same protocol are needed. In our study all cardiophysiological measures didn't differ between winter and summer. For example, heart rate (an indirect measure of activity and energy expenditure [32,35]) and indoor/outdoor behavior, significantly inter-correlated measures, showed similar diurnal profiles in summer and winter. This indicates similar behavioral activities in our study sample during winter and summer, which in turn could explain the non-seasonal difference in intra-individual daytime variation of MAP. The present study sample consists mainly of students, instructed to carry out the same activity in both seasons, thus the finding could be different in other subject groups showing seasonally different behavior (e.g. gardeners). A further limitation of the study is that only healthy young women were investigated which in principle prevents an extrapolation of the findings to other subject groups e.g. elderly, men and patients with medication.

In contrast to PET and ST, MAP did not reveal seasonal changes, confirming previous results in healthy young subjects [1]. As a consequence linear regression analyses of seasonal differences (summer–winter values) between MAP and ST (distal and proximal) revealed non-significant correlations. These findings raise the question why in contrast to the short-term changes in PET and T_{dist} long-term changes (i.e. winter to summer differences in mean daytime levels) are not transformed to changes in MAP. In other words, short-term increase and decrease in BP during winter and summer, respectively, do not lead to long-term seasonal changes in daytime mean levels of BP. This further implicates, at least in young subjects, that additional mechanisms have to be activated to counteract the changes in MAP, which should have occurred according to the seasonal changes in ST and hence changes in peripheral vascular resistance. In any case, similar daytime level of BP during winter and summer cannot be explained solely by the observed seasonal changes in vasoconstrictory activity i.e. reduced T_{dist}. Usually distal skin regions are more directly exposed to environmental air than proximal regions, and are additionally more sensitive to changes in environmental air temperature changes [36]. Surprisingly T_{prox} was higher in winter than in summer. Separate analyses of each T_{prox} revealed significant higher winter values during daytime specifically in infraclavicular ST.

One explanation for this finding could be that the subjects wore warmer clothing in winter than in summer specifically on infraclavicular skin regions, which seems to be rather unlikely. Furthermore, a recent study has shown, that increased supraclavicular ST reflects increased brown adipose tissue (BAT) activity occurring during cold exposure [37,38]. In our study we measured ST not directly in the supra-, but in the infraclavicular skin region, in which BAT activity is also affected by cold exposure [37,39]. Therefore, it can be hypothesized that in our study higher infraclavicular ST in winter might also indicate cold induced BAT activity during the cold season [40], whereas, it can be assumed that measurements directly on supraclavicular skin regions would reveal even larger seasonal differences. It has also been shown that BAT activity exhibits a marked seasonal variation in diverse anatomical depots, including the supraclavicular region, with higher values in winter than summer [41,42]. Moreover, in comparison to peripheral vasoconstriction activation of thermogenesis in BAT is a rather slow mechanism, which represents a further counter-regulation of a decline in core body temperature in cool environment [36,43,44]. A reduction of core body temperature during cold exposure is associated with an increase in BP [43]. It has been reported that reduced non-shivering thermogenesis during cold exposure in elderly might lead to impaired defense of core body temperature and hence to increased blood pressure [23]. In spite of the diverse findings, further prospective studies are needed to verify this post-hoc hypothesis. Such studies should include contemporaneous measurements of BAT activity, diverse STs and BP variables in young and elderly subject during winter and summer.

4.3. Short-term effects during daytime

With the aid of intra-individual path-analyses of daytime longitudinal data recorded between 0930 and 2030 h, it was possible to disclose that changes in PET during winter lead to inverse changes in MAP, confirming previous studies, e.g. [4,17]. However, for the first time it could be shown that this relationship is mediated by an indirect effect (path) through changes in T_{dist}: changes in real life variations in PET lead to parallel changes in T_{dist} and this in turn to inverse changes in MAP. During summer, the indirect path via T_{dist} could be confirmed but a further significant indirect path from PET to MAP via T_{prox} was found contributing to a similar total within effect as during winter (Table 4). Additionally, a direct positive path from PET to MAP occurred which is responsible for the lack of total within effect of PET on MAP (so-called 'inconsistent mediation' [27]) which cannot be explained without further investigations.

In contrast to significant 'within-subject effects' path-analyses of daytime data revealed non-significant 'between-subject effects' for both seasons. This indicates that individual ST levels are not predictive for blood pressure in young subjects, which is in contrast to reports in the elderly [2,4,5,19,30].

A similar conclusion can be drawn from the finding that subjects with and without thermal discomfort with cold extremities (a person's trait) did not differ with respect to MAP responses to changes in PET and T_{dist} (data not shown). It can be presumed that short-term changes of PET within hour(s) affect MAP independent of the person's long-term acclimatization of the thermoregulatory system.

4.4. Short-term indoor/outdoor-changes

A separate analysis of selected data segments before, during and after staying outdoors revealed additional and similar findings as the path analysis disclosed from the entire daytime data (0930–2030 h). Outdoor exposure during winter reduced PET by −12.5 °C and T_{dist} by −2 °C, and increased MAP by 4 mm Hg, which resembles the changes found by path analysis of winter data (i.e. PET −1 °C, T_{dist} −0.19 °C, MAP +0.31 mm Hg, see above) indicating a similar association between PET, T_{dist} and MAP in both approaches. Moreover, based on the described results, a seasonal decline of 1 °C in T_{dist} during winter (see Fig. 1), an increase of 1.625–2 mm Hg MAP could be expected, which should have been found with a statistical power of 0.83–0.93. This calculation indicates that seasonal differences in mean daytime MAP do not exist. Acute increases and decreases of PET during outdoor exposure induced parallel changes in ST with larger extent of changes in winter than in summer. MAP was changed in the opposite direction, whereby the extent of changes did not differ between the two seasons. Additionally, the large changes in PET during outdoor exposure revealed that SBP and heart rate were elevated in winter compared to summer, but not

DBP. These findings confirm previous studies showing a higher sensitivity of SBP to seasonal changes than DBP [1].

4.5. BMI and 24 h-mean values of skin temperatures and cardiophysiological measures

In our non-obese sample a significant correlation between BMI and 24 h-mean values of MAP was found, confirming previous findings [45,46]. The increase in MAP has been explained by increased sympathetic output to inner organs in heavier subjects [45,46]. A further significant association (negative correlation) was found between BMI and T_{prox} (T_{dist}, n.s.). Fat insulates the skin from the core reducing thereby conductive heat loss [47,48]. This effect could further contribute to an increased peripheral resistance, at least in proximal skin regions, and hence to centralization of blood and to an increase in MAP. In fact a negative correlation between T_{prox} and MAP was found. However, this preliminary finding needs to be verified in a larger prospective study including detailed measurements of body composition. Nevertheless, 24-h mean levels of proximal rather than T_{dist} seem to be associated with 24-h mean levels of MAP, i.e. T_{prox} is a possible mediator variable for BMI-effects on MAP.

4.6. Possible mechanisms on how PET affects MAP

In the present study outdoor exposure leads to changes in T_{dist} between 29 and 33 °C, which are within the range of more or less linear dependency between T_{dist} and distal skin blood flow [13–15,49]. Therefore it can be assumed that changes in T_{dist} indicate changes of distal skin blood flow [13,15]. It has been observed that in a cool environment cutaneous blood vessels constrict and subsequently blood withdraws from the shell (most pronounced from extremities) to the core [7,36]. This centralization of blood acutely increases central hemodynamic stress and MAP [6]. Furthermore, beside direct cooling responses on local vascular mechanism, indirect sympathetic vasomotor reflexes are also involved [50]. The inverse occurs in a warm environment, whereby the lowered MAP is attributed to cutaneous vasodilatation, but also to loss of water and salt from sweating [50]. Therefore, the observed significant indirect path via T_{dist} in winter and summer can be interpreted as part of the sympathetic vasomotor reflex loop. The thermophysiological core–shell model of the human body developed by Aschoff [7] may explain the findings described above, whereby T_{dist} and T_{prox} measurements easily provide information about the thermoregulatory state of the human body, i.e. cooler T_{dist} in relation to T_{prox} is indicative of a large shell [8,9]. However, it is important to keep in mind that skin temperature recordings provide an indirect measure of skin blood flow which represents a study limitation. Therefore, it is necessary to confirm the present study findings by additional more direct measurements of skin blood flow e.g. by measuring thermal conductivity.

5. Conclusions

The present ambulatory study provides evidence that intra-individual daytime changes in PET affect T_{dist} in parallel and BP inversely suggesting a possible causative mechanism chain for short-term real life changes in BP. In contrast, despite the distinct winter–summer differences in PET and STs, no seasonal differences in BP occurred supporting the notion that long-term changes in the core-to-shell relationship of blood distribution do not affect BP, at least not in healthy young women. This selected subject group allowed disclosing mechanisms why seasonal differences in STs do not lead to seasonal differences in BP. One hypothetical explanation for this observation could serve recent findings that not only peripheral vasoconstriction is activated in a cool environment, but also thermogenesis in BAT, the latter could be responsible for the counter-regulation of cold induced increase of BP in winter. This hypothetical concept needs to be proofed in prospective studies, e.g. comparing elderly with young subjects in winter and summer, and in both genders. Our findings suggest that the assessment of diurnal patterns of ST in addition to the conventional ambulatory BP monitoring will lead to improved personalized management of antihypertensive therapies tailored to the individual, which could be of special interest for the elderly.

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