# Combined Facial Heating and Inhalation of Hot Air Do Not Alter Thermoeffector Responses in Humans

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# COMBINED FACIAL HEATING AND INHALATION OF HOT AIR DO NOT ALTER THERMOEFFECTOR RESPONSES IN HUMANS

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Running Head: Regional thermosensitivity

**ABSTRACT**

The influence of thermoreceptors in human facial skin on thermoeffector responses is equivocal; furthermore, the presence of thermoreceptors in the respiratory tract and their involvement in thermal homeostasis has not been elucidated. This study tested the hypothesis that hot air directed on the face and inhaled during whole-body passive heat stress elicits an earlier onset and greater sensitivity of cutaneous vasodilation and sweating than that directed on an equal skin surface area away from the face. Six men and 2 women completed 2 trials separated by ~1 week. Participants were passively heated (water-perfused suit; core temperature increase ~0.9 °C) while hot air was directed on either the face or on the lower leg (counterbalanced). Skin blood flux (laser-Doppler flowmetry) and local sweat rate (capacitance hygrometry) were measured at the chest and one forearm. During hot-air heating, local temperatures of the cheek and leg were 38.4 ± 0.8 °C and 38.8 ± 0.6 °C, respectively ($p=0.18$). Breathing hot air combined with facial heating did not affect mean body temperature onsets ($p=0.97$ and 0.27 for arm and chest sites, respectively) or slopes of cutaneous vasodilation ($p=0.49$ and 0.43 for arm and chest sites, respectively), or the onsets ($p=0.89$ and 0.94 for arm and chest sites, respectively) or slopes of sweating ($p=0.48$ and 0.65 for arm and chest sites, respectively). Based on these findings, respiratory tract thermoreceptors—if present in humans—and selective facial skin heating do not modulate thermoeffector responses during passive heat stress.

**Key Words:** Thermoregulation, Regional thermosensitivity, Skin blood flow, Sweat rate, Passive heat stress

## INTRODUCTION

In humans, the hypothalamus integrates afferent signals from thermoreceptors located in the body core, as well as in the skin, to effect thermoregulatory responses. These thermoreceptors can be categorized as cold- or warm-sensitive, and the distribution and density of the two types varies across the body surface (9, 29). Generally, both cold- and warm-sensitive receptors are located just under the skin and are separated into so-called spots; typically cold spots outnumber warm spots by 3–10 times (7). The density of cold- or warm-sensitive neurons (or cold or warm "spots") in a particular skin region may affect thermoeffector responsiveness. However, some have suggested little variation in thermoeffector responsiveness to thermal provocation among different skin areas (27); then again, evidence (albeit in a small sample) exists that the face causes greater thermoeffector reactivity than other skin areas (24), possibly because of the high density of thermosensors in this area (29). Research involving animals supports the hypothesis of regional differences in thermoreceptor density and/or sensitivity. For example, in goats, Jessen and colleagues (12) showed that thermoeffector responses to deep muscle cooling were small, suggesting that the density and/or sensitivity of this tissue in driving efferent thermoregulatory responses is perhaps less than that of the skin, which can be very influential in the overall thermoregulatory effector response (11).

In addition to skin, the presence of thermoreceptors in other body areas has been demonstrated. In humans, these areas include the abdomen, nasal vestibule (the part lined with skin), and larynx (9, 15, 22, 34, 35). Furthermore, findings from animal studies suggest the presence of thermoreceptors in the superficial part of the respiratory tract (1, 6, 8, 16, 29). For instance, sheep (1) and dogs (8, 16) breathed more rapidly when the surface temperature of the upper respiratory tract was raised, thereby supporting the presence of thermoreceptors in these

68 "evaporating" surfaces (8). To our knowledge, however, the presence of respiratory-tract
69 thermoreceptors—especially warm-sensitive neurons—nor their influence on thermoregulation,
70 have been clearly elucidated in humans. Given the equivocacy of research regarding the
71 influence of facial skin on thermoeffector responsiveness and the lack of knowledge regarding
72 the influence of respiratory tract thermoreceptors on the same, the purpose of this study was to
73 investigate the combined influence of facial and respiratory tract heating on thermoeffector
74 responsiveness in humans. We hypothesized that combined heating of the face and respiratory
75 tract during a whole-body heat stress would elicit earlier core temperature thresholds for
76 cutaneous vasodilation and sweating along with enhanced slopes of the increase in these
77 variables relative to the increase in mean body temperature.

78 **METHODS**

79 *Ethical approval*

80 The study and consent were approved by the institutional review boards at the University
81 of Texas Southwestern Medical Center at Dallas and at Texas Health Presbyterian Hospital
82 Dallas, and participants provided written informed consent before participating. The study
83 conformed to the standards set by the *Declaration of Helsinki*.

84 *Subjects*

85 Six men and 2 women voluntarily consented to participate. This sample size was
86 sufficient to detect a moderate effect of d = 0.5 SD (30) for the difference in onset threshold
87 between treatments, assuming $\alpha = 0.05$, power $\approx 0.75$, and the correlation between paired
88 comparisons was $\approx 0.9$ (26). Subjects were nonsmokers and free of any cardiovascular,
89 metabolic, or neurological disease as determined by health history questionnaire. Their mean ±

SD physical characteristics were as follows: age = 36 ± 9 y, height = 178 ± 13 cm, and weight = 78 ± 12 kg. The phase of the menstrual cycle was not controlled.

*Design*

A repeated measures experimental design was used in which each subject served as his/her own control, with trials completed in a counterbalanced order. On average, 7 ± 4 days separated trials.

The primary dependent variables were the elevations in mean body temperature at the onset of cutaneous vasodilation and sweating at forearm and chest sites, along with the slope of the rise in these variables relative to mean body temperature during face heating/hot air breathing versus leg heating of an equal skin surface area.

*Instrumentation*

Subjects were instructed to arrive at the laboratory after having refrained from consumption of alcohol during the previous 24 h and caffeine during the previous 12 h. Upon arrival, they provided a urine sample for measurement of urine specific gravity to determine hydration status. Intestinal temperature ($T_{in}$), as a measure of core temperature ($T_c$), was assessed with a temperature-sensing pill (HQ, Palmetto, FL) swallowed with < 50 mL of water. Generally the pills were swallowed ~90 min before the commencement of study procedures. Next, thermocouples (Type T, Omega Engineering, Stamford, CT) were taped to the lateral calf, lateral thigh, lower back, lower abdomen, upper back, and chest for measurement of mean skin temperature ($\overline{T}_{sk}$; TC-1000 Thermocouple Meter, Sable Systems, Las Vegas, NV) from the weighted average of these regional temperatures (33). Mean body temperature ($\overline{T}_b$) was calculated as (3, 32):

$$\overline{T}_b = 0.8 \cdot T_c + 0.2 \cdot \overline{T}_{sk}.$$

A thermocouple (Type T, Physitemp, Clifton, NJ) also was taped either on the cheek or the anterior aspect of the lower leg situated halfway between the knee and ankle, depending on the counterbalanced treatment for that day. Next, electrodes were placed on the torso for continuous measurement of heart rate from an electrocardiogram (HP Patient Monitor, Agilent, Santa Clara, CA) interfaced with a cardiotachometer (CWE, Ardmore, PA). Then subjects put on a tube-lined water-perfusion suit (Med-Eng, Ottawa, Canada) on top of shorts (and sports bra for women). The suit covered the whole body except for the face, head, feet, hands, 1 leg below the knee, and 1 forearm. This suit was used to manipulate $T_c$, $\overline{T}_{sk}$, and $\overline{T}_b$ by changing the temperature of the water perfusing the suit.

Subjects rested supine while 3-cm diameter local heaters (model PF 450, Perimed, North Royalton, OH) with accompanying laser-Doppler flow probes (model DP7a, Moor Instruments, Wilmington, DE) were taped to the upper chest and forearm uncovered by the suit to provide an index of skin blood flow. A local heater/skin blood flow probe combination was placed at each body site. A thermocouple (Type T, Physitemp, Clifton, NJ) was placed between the local heater and the skin to monitor local skin temperature at each site. Additionally, sweat rate was measured via capacitance hygrometry using acrylic capsules covering 2.83 $cm^2$ placed on the upper chest and forearm uncovered by the suit and adjacent to the local heaters. The capsules were ventilated with 100% nitrogen at a flow rate of 300 mL/min. Humidity of the effluent gas was measured with humidity-temperature probes that were interfaced with a humidity data processor (model HMP 35E ,Vaisala, Woburn, MA) placed ~ 1 m from the capsules. Two capsules were placed at each site, with the responses for each site averaged.

An inflatable blood pressure cuff was placed on the arm opposite the local heater/skin blood flow probe combination and was used to measure systolic and diastolic blood pressure via

136 electrosphygmomanometry of the brachial artery (Tango, SunTech Medical Instruments,
137 Raleigh, NC). Blood pressure was measured every 5 min throughout the protocol. Mean arterial
138 pressure was calculated as 1/3 pulse pressure + diastolic pressure.
139 All data collection took place in an environmental chamber maintained at 25.3 ± 0.6 °C,
140 46.9 ± 5.6% relative humidity.
141 *Procedure*
142 During a quiet supine resting period, 34 °C water perfused the suit, followed by ~10 min
143 of baseline data collection. Then, subjects were heated passively by perfusing 48-50 °C water
144 through the suit. Meanwhile, hot air (Honeywell, Hz-341BL, Morristown, NJ) was
145 simultaneously blown through ~15-cm diameter duct directed at either the uncovered lower leg
146 or the face, depending on the counterbalanced trial for that day. The end of the duct was placed
147 ~ 8 cm from the skin surface of the subject. The temperature of the air exiting the duct was
148 approximately 70 °C. No subjects complained of discomfort or pain in relation to the
149 temperature of the hot air directed at the face.
150 Whole-body heat stress progressed until participants reached an increase in $T_c$ of ~ 0.8
151 °C. At that point, the hot air blowing on the face or leg was removed and whole-body passive
152 heat stress continued in an effort to determine if an obvious change in thermoregulatory effector
153 responses occurred upon removal of this stimulus. After ~ 5 min of additional passive heating
154 without the hot air stimulus (to an increase in $T_c$ of ~ 0.9 °C), whole-body heat stress ceased and
155 the subjects were passively cooled by perfusing ~ 22 °C water through the suit while maximal
156 cutaneous vasodilation was elicited by locally heating the skin to ~ 42-43 °C (13, 14, 21). After
157 local heating for ~ 30 min, instrumentation was removed and the trial ended.
158

*Data Analysis*

Data were acquired continuously at a sampling rate of 50 Hz using a data acquisition system (Biopac, Santa Barbara, CA). All variables were averaged every 30 s for offline analysis. Paired samples t-tests were used to analyze mean differences between treatments for baseline and final temperature ($T_c$, $\overline{T}_{sk}$, $\overline{T}_b$) values. Cutaneous vascular responses were indexed as cutaneous vascular conductance (calculated as laser-Doppler flux divided by mean arterial blood pressure) and normalized to maximal values obtained during local heating. Segmental regression (2) using computer software (Prism 5, GraphPad Software, Inc., La Jolla, CA) was used to determine slopes and $\overline{T}_b$ onsets for cutaneous vasodilation and sweating, which were then analyzed between trials using paired samples t-tests. Obvious plateau data were omitted from the analysis, and in the event of a biphasic sweating response consisting of an early and late phase with different slopes (2, 17), only the initial (early) phase was analyzed. Data are presented as means ± SD, and all hypothesis tests used an $\alpha$ level of 0.05.

**RESULTS**

Ambient temperature (25.3 ± 0.8 °C and 25.3 ± 0.5 °C for face and leg heating, respectively; $p = 1.0$) and humidity (46.9 ± 6.4% and 47.0 ± 5.2 for face and leg heating, respectively; $p = 0.70$) were consistent between trials. Likewise, subjects' hydration status (via urine specific gravity) and baseline core temperatures were not different between experimental trials ($p = 0.54$ and 0.38, respectively). As intended, whole-body passive heat stress increased $T_c$ ~ 0.9 °C during each experimental trial ($p = 0.59$ between treatments). $\overline{T}_{sk}$ increased ~ 4 °C during each trial and was not different between treatments ($p = 0.86$). Likewise, the local temperatures of the cheek (38.4 ± 0.8 °C) and leg (38.8 ± 0.6 °C), averaged throughout the heating phase of those respective trials, were not different ($p = 0.18$). Because of similar

baseline core and mean skin temperatures, along with similar increases in these measures during heat stress, the change in $\overline{T}_b$ also was not different between experimental treatments ($p = 0.79$). The increases in body temperature did not affect mean arterial pressure across time [78 ± 5 mm Hg and 80 ± 8 mm Hg for baseline and end of face or leg heating, respectively (collapsed across treatments); $p = 0.47$] or differentially between treatments [77 ± 4 mm Hg and 80 ± 8 mm Hg for face and leg heating treatments, respectively (collapsed across time); $p = 0.30$]. Heart rate, however, increased as a result of whole-body passive heat stress over time but was not different between treatments [68 ± 14 beats/min to 90 ± 17 beats/min for baseline and end of face or leg heating, respectively (collapsed across treatments); $p = 0.002$].

Table 1 shows that face/respiratory tract heating did not affect the $\overline{T}_b$ onset thresholds at arm or chest sites for cutaneous vasodilation and sweating. Regardless of site, there were no statistical differences in the slope of cutaneous vascular conductance versus $\overline{T}_b$ (Figure 1). It is noteworthy that 2 subjects had extraordinarily large responses for the face heating trial (> 2 SD from the mean; seen in Figure 1) resulting in large variances in the presented figure. This result had no effect on the statistical outcome, however, because even with these subjects excluded from the analysis, the slopes were still not different between treatments. Individual data at the arm site were mixed, with 5 participants having a higher slope under the face heating condition and 3 participants having a higher slope under the leg heating condition. At the chest site, results were equal—half the subjects had higher slopes under the face heating condition and half had higher slopes under the leg heating condition. Like cutaneous vascular conductance, face heating had no effect on the slope of the sweating responses at arm and chest sites (Figure 2).

Upon removal of the local heating stimulus (regardless of the location) no changes in thermoregulatory effector responses were identified for the subsequent 5 min. Given this observation, no further analysis was conducted.

## DISCUSSION

This study tested the hypothesis that combined facial and respiratory tract heating (via forced air) would modify thermoeffector (sweating and cutaneous vasodilation) responsiveness during passive heating relative to forced air heating of an equal surface area of the lower leg. This hypothesis was not supported since there were no mean differences between the $\overline{T}_b$ onset and sensitivities (slopes) of cutaneous vasodilation and sweating at either chest or forearm sites during face/respiratory tract heating relative to leg heating.

Evidence for thermoreceptors in the mouth, nasal surfaces, and upper respiratory tract has been reported in sheep and dogs (1, 8, 16), but data in humans are limited, especially for warm-sensitive neurons (9, 15, 31, 35). Clearly, the ability to detect temperature differences between warm and cold fluids and foods suggests the presence of temperature-sensitive neurons in the mouth and upper throat in humans, but whether such neurons are involved in whole-body thermal homeostasis has not been elucidated. Recent work by Morris and colleagues (22) showed that thermoreceptors capable of modulating sudomotor output in response to cold or warm fluid ingestion did not seem present in the mouth, but rather were likely present in the abdomen. The results of the present study do not rule out the presence of warm-sensitive thermoreceptors in the respiratory tract in humans, but they do suggest that such thermoreceptors, heated to the level imposed in the present study, do not modulate cutaneous vasodilation and sweating during conditions of whole-body passive heat stress with high $\overline{T}_{sk}$.

Using vastly different approaches, some studies have proposed greater thermosensitivity—and therefore, greater influence on thermoeffector responsiveness—in facial skin relative to skin at other body sites (20, 24). The reason for the discrepant findings in the present study is likely related to the different experimental approaches. The cited studies had small sample sizes (n = 5 and 2, respectively), did not match the various surface areas of treated skin, and controlled $T_c$ and $\overline{T}_{sk}$ temperatures in a manner different from our study (20, 24). For instance, Libert et al. (20) kept $\overline{T}_{sk}$ constant by simultaneously cooling and heating various body segments while observing sweating changes in other areas not being cooled or heated. Nadel et al. (24) used thermal irradiation to selectively heat various skin areas while evaluating sweating at the thigh, though $T_c$ and $\overline{T}_{sk}$ were essentially uncontrolled. As mentioned, their sample size was small (n = 2), likely explaining why data were not analyzed statistically. In another study, Crawshaw et al. (4) evaluated the effects of local cooling various sites on thigh sweating during exposure to a hot ambient environment (39 °C); like Nadel et al. (24), data were not analyzed statistically, probably because of the small sample size (n = 3). Lastly, only sweat rate was measured in these studies and thus no conclusions regarding skin blood flow can be ascertained.

In contrast to these studies, we used a whole-body heat stress approach using a water-perfused suit to progressively increase $T_c$ and $\overline{T}_{sk}$. This approach resulted in $\overline{T}_{sk}$ approximating 38 °C. This, combined with the ~0.9 °C increase in $T_c$, may have been such a robust afferent signal that it may have masked any differential thermosensitive afferent feedback during the face heating component. That said, potential threshold differences, as well as sensitivities, to the perturbations were assessed at much lower $T_c$ relative to that achieved at the end of the heat stress.

While $T_c$, $\overline{T}_{sk}$, and $\overline{T}_b$ were not clamped in the present study, the changes in these temperatures to the heat stress were not different between treatments, demonstrating that the influence of these variables on the outcome measures was likely uniform between treatments. Our findings are therefore in agreement with those of Patterson et al. (27) who elevated and then clamped $T_c$ and $\overline{T}_{sk}$ and also did not observe differences in sweat output at the face, hand, forearm, or upper arm during selective heating of the face relative to selective heating of these respective measurement sites. A tendency for higher sweating when the face was heated led the authors to conclude that the absence of a statistical difference in sweating to facial heating does not necessarily mean that the facial skin region is not more thermosensitive, and therefore more influential on thermoeffector responsiveness, than other regions. Our findings, however, do not support this assertion. Taken together, the findings from the present study and those of Patterson et al. (27) do not support the notion of greater thermosensitivity in facial skin relative to other body sites. So, regardless of whether $T_c$ and $\overline{T}_{sk}$ are progressively increasing or clamped, as long as they are similar between respective trials, selective heating of facial skin does not modulate sweating. Furthermore, since Patterson et al. (27) did not measure skin blood flow and since the approach used did not permit identification of thermoeffector threshold or slope differences, our findings extend those of Patterson et al. (27) in demonstrating: 1) skin blood flow also is not modulated by heating facial skin relative to heating skin of a similar surface area at a different body site, 2) facial heating does not alter the $\overline{T}_b$ threshold for the onset of cutaneous vasodilation and sweating or the associated slopes of those responses, and 3) breathing hot air in conjunction with facial skin heating does not modulate thermoregulation during whole-body passive heat stress with high $\overline{T}_{sk}$.

*Limitations*

Previous studies have used esophageal temperature ($T_{es}$) to determine slopes and onset thresholds of thermoregulatory effector responses (23). We contend, however, that since thermoregulatory cutaneous vasodilation and sweating are integrated responses based on afferent signals from both peripheral (i.e., skin) and internal thermoreceptors (28, 36), the use of $\overline{T}_b$ to determine slopes and onset thresholds is appropriate. Furthermore, the use of $\overline{T}_b$ rather than $T_c$ does not affect the interpretation of the results.

Another possible limitation is the use of $T_{in}$ instead of $T_{es}$, given that use of $T_{in}$ may have resulted in slower response times than if we had used $T_{es}$ (19, 25). Nonetheless, $T_{in}$ has been shown to closely track esophageal temperature under resting and exercise conditions and during thermal transients (19, 25), and it has been used previously for assessing onset thresholds and thermoeffector sensitivity (18). Furthermore, we were concerned that breathing hot air could possibly affect the temperature reading independent of blood/core body temperature had we used $T_{es}$, given that inspired air temperature has been shown to influence $T_{es}$ (5, 10). Finally, $T_{in}$ was used during both treatments so any delays in identification of a threshold would have been the same between treatments and therefore would not have adversely affected the interpretation of the results.

It is acknowledged that the present design did not permit the ability to distinguish the potential effect of facial skin thermosensitivity from that of respiratory tract thermosensitivity. A future study with an additional treatment of hot-air breathing alone—without simultaneous face heating—is necessary to make that distinction.

293 *Perspectives and Significance*

294 Directing hot air on the face and simultaneously breathing that air did not affect the $\overline{T}_b$
295 onsets for cutaneous vasodilation and sweating or the slopes of those responses relative to the
296 increase in $\overline{T}_b$ during passive heating with elevated $\overline{T}_{sk}$. The present data do not rule out the
297 possibility of thermoreceptors in the respiratory tract, but it can be concluded that under the
298 thermal conditions employed in the present study—using a water-perfused suit to induce whole-
299 body passive heat stress—if such thermoreceptors are present they have little or no involvement
300 in regulating thermoeffector responsiveness.
301
302

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**DISCLOSURES**

The authors cite no conflicts of interest.

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401 **FIGURE LEGENDS**

402

403 Figure 1. Individual and mean ± SD cutaneous vascular sensitivity, defined as the increase in
404 cutaneous vascular conductance (CVC) per 1 °C increase in $\overline{T}_b$, at arm (top panel) and chest
405 (bottom panel) sites. There was large inter-subject variability in the slopes for the facial heating
406 protocol because of a couple incidences of large, rapid cutaneous vasodilatory responses.
407 Regardless, no differences between face and leg treatments were observed, even when these data
408 were re-analyzed with those data points removed ($p = 0.49$ for arm site and 0.43 for chest site).

409

410 Figure 2. Individual and mean ± SD sweat sensitivity, defined as the increase in sweat rate per 1
411 °C increase in $\overline{T}_b$, at arm (top panel) and chest (bottom panel) sites (mean ± SD). There was
412 large inter-subject variability, especially at the chest site because of a couple incidences of robust
413 sweating responses. Nevertheless, no differences between face and leg treatments were observed
414 ($p = 0.48$ for arm site comparison and $p = 0.65$ for chest site comparison).

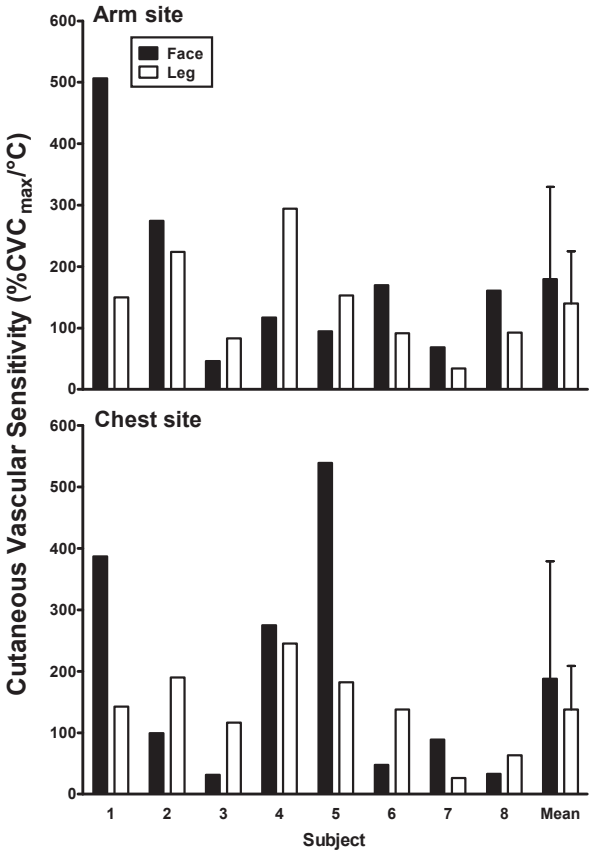
415

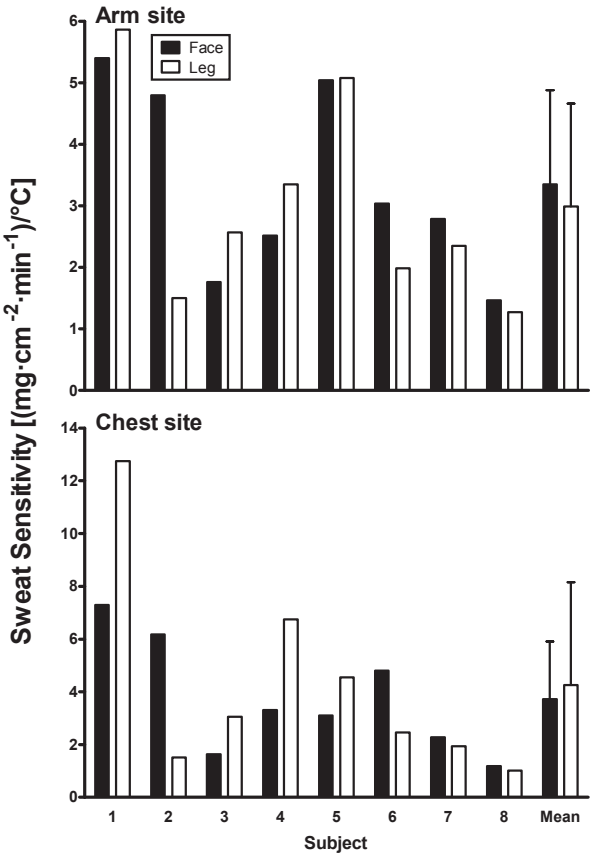
**TABLE**

Table 1. Mean ± SD onset thresholds for cutaneous vasodilation and sweating during face and leg heating.

| | Onset of Cutaneous Vasodilation | | | | | | Onset of Sweating | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Arm Site | | | Chest Site | | | Arm Site | | | Chest Site | | |
| | Face | Leg | P value | Face | Leg | P value | Face | Leg | P value | Face | Leg | P value |
| $\overline{T}_b$ (°C) | 37.1 ± 0.4 | 37.1 ± 0.3 | 0.97 | 37.1 ± 0.2 | 37.1 ± 0.3 | 0.27 | 37.2 ± 0.4 | 37.2 ± 0.3 | 0.89 | 37.2 ± 0.3 | 37.2 ± 0.3 | 0.94 |
| $\Delta\overline{T}_b$ (°C) | 0.6 ± 0.4 | 0.5 ± 0.2 | 0.64 | 0.6 ± 0.2 | 0.5 ± 0.2 | 0.85 | 0.7 ± 0.3 | 0.6 ± 0.2 | 0.54 | 0.7 ± 0.3 | 0.6 ± 0.2 | 0.60 |

Sweat rate data are the average from 2 capsules at each site. $\overline{T}_b$ = mean body temperature; $\Delta\overline{T}_b$ = change in mean body temperature from baseline during heat stress. No comparisons were significantly different.


Arm site
Face
Leg
Chest site
Cutaneous Vascular Sensitivity (%CVC$_{max}$/°C)
600
500
400
300
200
100
0
1
2
3
4
5
6
7
8
Mean
Subject


Arm site
Face
Leg
Chest site
Sweat Sensitivity [(mg·cm-2·min-1)/°C]
0
1
2
3
4
5
6
0
2
4
6
8
10
12
14
1
2
3
4
5
6
7
8
Mean
Subject