Sex differences in thermoeffector responses during exercise at fixed requirements for heat loss

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Gagnon D, Kenny GP. Sex differences in thermoeffector responses during exercise at fixed requirements for heat loss. J Appl Physiol 113: 746–757, 2012. First published July 12, 2012; doi:10.1152/japplphysiol.00637.2012.—To assess potential mechanisms responsible for the lower sudomotor thermosensitivity in women during exercise, we examined sex differences in sudomotor function and skin blood flow (SkBF) during exercise performed at progressive increases in the requirement for heat loss. Eight men and eight women cycled at rates of metabolic heat production of 200, 250, and 300 W/m² of body surface area, with each rate being performed sequentially for 30 min. The protocol was performed in a direct calorimeter to measure evaporative heat loss (EHL) and in a thermal chamber to measure local sweat rate (LSR) (ventilated capsule), SkBF (laser-Doppler), sweat gland activation (modified iodine-paper technique), and sweat gland output (SGO) on the back, chest, and forearm. Despite a similar requirement for heat loss between the sexes, significantly lower increases in EHL and LSR were observed in women (P = 0.001). Sex differences in EHL and LSR were not consistently observed during the first and second exercise periods, whereas EHL (348 ± 13 vs. 307 ± 9 W/m²) and LSR on the back (1.61 ± 0.07 vs. 1.20 ± 0.09 mg·min⁻¹·cm⁻²), chest (1.33 ± 0.06 vs. 1.08 ± 0.09 mg·min⁻¹·cm⁻²), and forearm (1.53 ± 0.07 vs. 1.20 ± 0.06 mg·min⁻¹·cm⁻², men vs. women) became significantly greater in men during the last exercise period (P < 0.05). At each site, differences in LSR were solely due to a greater SGO in men, as opposed to differences in sweat gland activation. In contrast, no sex differences in SkBF were observed throughout the exercise period. The present study demonstrates that sex differences in sudomotor function are only evidenced beyond a certain requirement for heat loss, solely through differences in SGO. In contrast, the lower EHL and LSR in women are not paralleled by a lower SkBF response.

A lower thermosensitivity of whole body evaporative heat loss could be related to either a central (neural activity) and/or peripheral (effector response) modulation of temperature regulation. The onset threshold of thermoeffector responses has typically been used to represent central modifications of temperature regulation, whereas the thermosensitivity is thought to represent a peripheral modulation (36). Additionally, it is generally accepted that any factor that exhibits a central modulation of temperature regulation must shift the onset threshold of both local sweat production and skin blood flow (18). For example, factors, such as sex hormones (47), hyperosmolality (41), and heat acclimation (1), consistently shift the onset threshold of both heat loss responses, with inconsistent (acclimation) or no changes (sex hormones, osmolality) in thermosensitivity. Finally, if sex modulates the level of thermal afferent and/or efferent neural activity, sex differences in thermoeffector responses should be evident at any combination of exercise intensity and environmental conditions (i.e., requirement for heat loss).

In contrast, a peripheral modulation of sudomotor function would be expected to result in sex differences in the thermosensitivity of the response, without any differences in the onset threshold for sweating and skin blood flow. Furthermore, the lower sweat rate in women would be associated with a lower sweat gland output (39), and differences in local sweat rate and/or evaporative heat loss would only be evidenced above a certain requirement for heat loss. Although a number of studies have examined sex differences in sweat rate during exercise, insight into potential physiological differences between men and women are limited due to employed experimental protocols (15, 42) and a lack of considering confounding physical differences (13). Nonetheless, recent observations suggest that sex-related differences in local sweat rate may only be observed above a certain exercise intensity (25), suggesting that sex differences in sudomotor function are not evidenced at all requirements for heat loss. To our knowledge, however, no study has specifically examined whether sex differences in sudomotor function and/or skin blood flow are only evidenced above a certain requirement for heat loss during exercise. Such information would provide valuable physiological insight to determine whether the lower sudomotor thermosensitivity observed in women during exercise is associated with a central and/or peripheral modulation of temperature regulation.

The present study, therefore, examined sex differences in the onset threshold and thermosensitivity of sudomotor function (local and whole body) and skin blood flow during exercise performed at increasing requirements for heat loss. To determine if sex differences in sudomotor function are only evidenced above a certain requirement for heat loss, the experimental paradigm included one continuous exercise bout divided into three consecutive periods, performed at increasing
levels of metabolic heat production. We hypothesized that sex differences in sudomotor function would only be evidenced at the highest requirement for heat loss. Furthermore, we hypothesized that these differences would be paralleled by a lower thermosensitivity of the response, without any differences in the onset threshold. In contrast, we hypothesized that no sex differences in skin blood flow would be observed, in terms of both the onset threshold and thermosensitivity.

METHODS

Ethical Approval

The present experimental protocol was approved by the University of Ottawa Health Sciences and Science Research Ethics Board. Written, informed consent was obtained from all volunteers before their participation in the study.

Participants

Expected sex differences in end-exercise whole body evaporative heat loss (16) and local sweat rate (25) were used to calculate (β = 0.8, α = 0.05) a minimum sample size of six participants in each group, assuming an effect of 20% and standard deviation of 12%. Sixteen participants, eight men and eight women, were recruited within the university community and volunteered for the study. To minimize the influence of differences in hormonal status across the menstrual cycle, female participants performed each experimental session within the 1st and 10th day after the onset of their self-reported menses. Three female participants were taking oral contraceptives: one used Aviane (pill 1: 0.1 mg levonorgestrel/0.020 mg ethinyl estradiol, pill 2: placebo), another used Tri-Cyclen (pill 1: 0.180 mg norgestimate/0.025 mg ethinyl estradiol, pill 2: 0.215 mg norgestimate/0.025 mg ethinyl estradiol, pill 3: 0.250 mg norgestimate/0.025 mg ethinyl estradiol, pill 4: placebo), and the other used Triquilar (pill 1: 50 µg levonorgestrel/30 µg ethinyl estradiol, pill 2: 75 µg levonorgestrel/40 µg ethinyl estradiol, pill 3: 125 µg levonorgestrel/30 µg ethinyl estradiol, pill 4: placebo). These three female participants performed the experimental sessions during the no pill/placebo phase of oral contraceptive use. Hormonal status was confirmed by taking a venous blood sample on the day of each experimental session. Participants had to be withdrawn or repeated based on blood sample results. All participants volunteered for one preliminary and two experimental sessions during the no pill/placebo phase of oral contraceptive use. Hormonal status was confirmed by taking a venous blood sample on the day of each experimental session. Participants had to be withdrawn or repeated based on blood sample results. Participants were healthy, nonsmoking, and free of any known cardiovascular, metabolic, and respiratory diseases. Participant characteristics are presented in Table 1.

Experimental Design

All participants volunteered for one preliminary and two experimental sessions. During the preliminary session, training history, body height, mass, and density, as well as maximum oxygen uptake, were determined. Training history was assessed by having the participants quantify their physical activity levels using the quantitative (3 mo) and 7-day physical activity recall questionnaires proposed by Kohl et al. (30). Body height was determined using a stadiometer (Detecto, Webb City, MO), whereas body mass was measured using a digital high-performance weighing terminal (model CBU150X, Mettler Toledo, Mississauga, ON, Canada). Body surface area was subsequently calculated from the measurements of body height and mass (9). Body density was measured using the hydrostatic weighing technique and used to calculate body fat percentage (46). Maximum oxygen uptake was determined by indirect calorimetry (MOXUS system, Applied Electrochemistry, Pittsburgh, PA) during a progressive incremental exercise protocol (5) performed on an upright, seated, constant-load cycle ergometer (Corival, Lode BV, Groningen, the Netherlands).

For each experimental session, participants reported to the laboratory between 700 and 900. The participants were asked to drink 500 ml of water the night before, as well as the morning of, each experimental session and to refrain from alcohol, caffeine, and exercise 24 h before experimentation. On arrival at the laboratory, the participants provided a urine sample, weighed themselves nude, and changed into shorts, sandals, as well as a sports bra for female participants. They subsequently sat upright for a 60-min instrumentation period at an ambient room temperature of 24°C. Following instrumentation, participants entered a thermal chamber for one of the experimental sessions, while they entered a whole body calorimeter for the other session. The order in which the sessions were performed was balanced both within and between sexes. The thermal chamber was regulated to an ambient air temperature of 40.1 ± 0.2°C and a relative humidity of 24 ± 2% (~11.31 g/kg specific humidity), and a fan placed in front of the participant provided an airflow of 1.04 ± 0.20 m/s. The calorimeter was regulated to an ambient air temperature of 40.08 ± 0.15°C, a specific humidity of 5.47 ± 2.82 g/kg (~12% relative humidity), and an air mass flow of 7.74 ± 0.25 kg air/min. In both cases, participants rested for a 30-min baseline period in the upright seated posture. Subsequently, they performed 90 min of continuous upright seated cycling exercise. The exercise period was performed at fixed rates of metabolic heat production equal to 200, 250, and 300 W/m², with each level being 30 min in duration. The participants did not stop exercising between each exercise period. At the end of exercise during the experimental session performed in the thermal chamber, all instrumentation was removed, except for the laser-Doppler flow probes, and the participants remained seated for a 45-min local heating period to determine maximum skin blood flow (see details below). A final nude body weight measurement was obtained at the end of the experimental session.

Body mass, by influencing rate of metabolic heat production, and body surface area, by affecting heat exchange, are the main physical characteristics that can influence local and whole body sweat rate during exercise (22). As such, we employed fixed rates of metabolic heat production during non-weight-bearing exercise (i.e., cycling) to negate any influence of differences in body mass, while we adjusted the rate of metabolic heat production per unit of surface area to negate any differences in the surface area available for heat exchange. Previous studies have shown that the level of local and whole body sweat rate achieved during exercise is determined by the ratio of the required evaporation for heat balance (Ereq) and the maximum evaporation possible (Emax) in a given environment (2, 43). Since men and women performed the exercise bout in the same environmental conditions (producing the same Emax), the use of fixed rates of metabolic heat production expressed per unit of body surface area (producing the same Ereq) ensured that the Ereq-to-Emax ratio, and

<table>
<thead>
<tr>
<th>Sex</th>
<th>Age, yr</th>
<th>Body Mass, kg</th>
<th>Height, cm</th>
<th>AT, m²</th>
<th>Fat Mass, kg</th>
<th>FFM, kg</th>
<th>VO2max</th>
<th>l/min</th>
<th>ml·kg⁻¹·min⁻¹</th>
<th>ml·kg⁻¹·Framin⁻¹·min⁻¹</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men</td>
<td>27 ± 6</td>
<td>73.9 ± 13.5*</td>
<td>174 ±10*</td>
<td>1.88 ± 0.22*</td>
<td>11.0 ± 5.4</td>
<td>62.9 ± 10.4*</td>
<td>3.78 ± 0.70*</td>
<td>51.4 ± 6.8*</td>
<td>60.2 ± 7.8</td>
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</tr>
<tr>
<td>Women</td>
<td>28 ± 5</td>
<td>60.7 ± 3.7</td>
<td>166 ± 5</td>
<td>1.67 ± 0.07</td>
<td>13.0 ± 2.7</td>
<td>47.6 ± 3.3</td>
<td>2.68 ± 0.36</td>
<td>44.1 ± 4.5</td>
<td>56.1 ± 3.9</td>
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</tr>
</tbody>
</table>

Values are mean ± SD. AT, body surface area; VO2max, maximum oxygen consumption; FFM, fat free mass. *Significantly different from women (P ≤ 0.05).
throughout the measurement periods, the wrist cuff was inflated to a hand, such that the forearm did not touch anything. Before (5 sec) and supported at heart level by placing custom supports at the elbow and 10th and 20th min of each exercise period. The right forearm was wa). Cuffs were placed around the wrist and upper arm, and a mercury-in-rubber strain gauge was placed around the widest part of the experimental trial. To determine maximum skin blood flow, a laser-Doppler velocimetry output in arbitrary perfusion units divided by mean arterial pressure and expressed as a percentage of maximum. Forearm vascular conductance (in ml·100 ml tissue⁻¹·min⁻¹·mmHg⁻¹) was calculated by dividing forearm blood flow by mean arterial pressure. Esophageal temperature was measured with a general purpose thermocouple temperature probe (Mallinckrodt Medical, St. Louis, MO). The probe was inserted 40 cm past the entrance of the nostril, while the participants sipped water (100–300 ml) through a straw. Skin temperature was measured at 10 sites using thermocouples (Concept Engineering, Old Saybrook, CT) attached to the skin with surgical tape. Mean skin temperature was subsequently calculated using a 10-point weighting of the regional proportions determined by Hardy and DuBois (21). Temperature data were collected using a HP Agilent data acquisition module (model 3497A) at a rate of one sample every 15 s and simultaneously displayed and recorded in spreadsheet format on a personal computer with LabVIEW software (version 7.0, National Instruments).

The modified Snellen direct air calorimeter (38) was employed to measure whole body evaporative heat loss. In order for evaporative heat loss to be a valid measure of whole body sweat production, we ensured that the environmental conditions provided a high-vapor pressure gradient between the skin surface and the surrounding air. Furthermore, we continually maintained this vapor pressure gradient by providing a high mass flow of dry air through the calorimeter. Inflow and outflow values of absolute humidity were collected at 8-s intervals throughout the trials. The real time data were displayed and recorded on a personal computer with LabVIEW software (version 7.0, National Instruments). Evaporative heat loss was subsequently calculated using the calorimeter outflow-inflow difference in absolute humidity, multiplied by the mass flow and latent heat vaporization of water at 30°C (50).

Indirect calorimetry was used for the measurement of metabolic energy expenditure (37). Expired gas was analyzed for oxygen (error of ±0.01%) and carbon dioxide (error of ±0.02%) concentrations using electrochemical gas analyzers (AMETEK model S-3A/l and CD 3A, Applied Electrochemistry, Pittsburgh, PA). For the calorimeter session, the gas analyzers were located outside of the calorimeter, and expired air was recycled back into the calorimeter to account for respiratory heat exchange. Before each session, gas mixtures of known concentrations were used to calibrate the gas analyzers and a 3-liter syringe was used to calibrate the turbine ventilimeter.

Urine-specific gravity was determined in duplicate using a handheld total solids refractometer (model TS400, Reichter, Depew, NY).

On the day of each experimental session, a venous blood sample (10 ml) was obtained from female participants to confirm that the session occurred in the follicular/low-hormone phase of the menstrual cycle. The blood samples were collected with a SST vacutainer (BD Vacutainer, Franklin Lakes, NJ) for the determination of plasma 17β-estradiol and progesterone. Plasma concentrations of 17β-estradiol and progesterone (50) were quantified by an independent external laboratory (Gamma-Dynacare Medical Laboratories, Ottawa, ON, Canada), with plasma concentrations representative of the follicular phase of the menstrual cycle of 46–604 pmol/l and 0.6–4.7 nmol/l, respectively.

For the additional experimental visit, blood samples were drawn without stasis after a minimum of 30-min baseline rest in the upright seated posture, as well as at 30, 60, and 90 min of exercise through an indwelling plastic catheter in a superficial vein. At each time point, period, which were averaged to give one forearm blood flow value per time point (in ml·100 ml tissue⁻¹·min⁻¹).

Systolic and diastolic blood pressures were determined by manual auscultation of the brachial artery at the 5th, 15th, and 25th minute of each exercise period, as well as during the local heating period to determine maximum skin vascular conductance. All auscultations were performed by the same experienced investigator. Mean arterial pressure was subsequently calculated as diastolic blood pressure plus one-third of pulse pressure. Skin vascular conductance was calculated as laser-Doppler velocimetry output in arbitrary perfusion units divided by mean arterial pressure and expressed as a percentage of maximum. Forearm vascular conductance (in ml·100 ml tissue⁻¹·min⁻¹·mmHg⁻¹) was calculated by dividing forearm blood flow by mean arterial pressure.

Measurements

Local sweat rate on the left upper back, chest, and forearm was measured from 3.8-cm² plastic capsules attached to the skin with adhesive rings and topical skin glue (Collodion IV, Maidvon Medical Products, Lake Worth, FL). Anhydrous compressed air was passed through each capsule at a rate of 1 l/min. Water content of the effluent air was measured using high-precision dew point mirrors (model 473, RH Systems, Albuquerque, NM). Local sweat rate was calculated using the difference in water content between effluent and influent air, multiplied by the flow rate and normalized for the skin surface area under the capsule.

The number of active sweat glands was measured in an area adjacent to each local sweat rate site (to avoid removing the sweat capsule) at 30, 60, and 90 min of exercise using the modified iodine-paper technique with computer-assisted analysis (14). The number of glands determined by computer analysis was divided by the surface area of the paper to give a value of active sweat glands per square centimeter. The sweat output per gland was calculated by dividing the sweat rate at the corresponding measurement period by the number of active sweat glands.

Local skin blood flow was estimated using laser-Doppler velocimetry (PeriFlux System 5000, Perimed AB, Stockholm, Sweden). Before the start of the experimental trial, laser-Doppler flow probes (integrating probe 413, Perimed AB, Stockholm, Sweden) were affixed with an adhesive ring to the left upper back, chest, and forearm in a site adjacent to the sweat capsules that demonstrated pulsatile activity. The probes were not moved from their location throughout the experimental trial. To determine maximum skin blood flow, a local heating period to 42°C for 30 min and then to 44°C for an additional 15 min was performed at the end of the experimental trial. Blood flow to the right forearm was measured using venous occlusion plethysmography (model A16, D.E. Hokanson, Bellevue, WA). Cuffs were placed around the wrist and upper arm, and a mercury-in-rubber strain gauge was placed around the widest part of the forearm. Measurements were performed for 2-min periods at the 10th and 20th min of each exercise period. The right forearm was supported at heart level by placing custom supports at the elbow and hand, such that the forearm did not touch anything. Before (5 sec) and throughout the measurement periods, the wrist cuff was inflated to a pressure of 250 mmHg to occlude the circulation of blood to the hand, while the cuff around the upper arm inflated (50 mmHg) and deflated in cycles of 15 s. This procedure yielded eight measurements per time
one sample (~5 ml) was drawn and transferred into a K2 EDTA vacutainer (BD Vacutainer) to determine hematocrit and hemoglobin, while two additional samples (~10 ml) were drawn and transferred into SST vacutainers (BD Vacutainer) for the measurement of plasma osmolality. Hematocrit and hemoglobin concentrations were determined using the Coulter method (Coulter A-T diff 2 analyzer, Beckman Coulter, Miami, FL) and used to estimate changes in plasma volume (8). To determine plasma osmolality, both samples were immediately centrifuged at normal room temperature, and osmolality was determined in duplicate by freezing point depression (Osmometer, Advanced Instruments).

Data Analysis

For all variables, minute averages were performed to carry out the statistical analyses. To account for the relative influence of core and mean skin temperatures on the activation of sweat production (24, 35, 36) and increases in skin blood flow (53, 54), mean body temperature was calculated as follows: 0.9 × esophageal temperature + 0.1 × mean skin temperature (45). The onset threshold and thermosensitivity of local sweat rate and whole body evaporative heat loss during each exercise period were determined using the linear portion of each response plotted against mean body temperature and analyzed using segmented regression analysis (6). Since skin blood flow did not increase with each exercise period (see RESULTS section), the onset threshold was determined during the first exercise period only, by plotting skin blood flow (as a percentage of maximum) over time and determining visually the point at which it increased over three consecutive measurements. The corresponding mean body temperature at that time point was taken as the onset threshold (32, 49). The thermosensitivity was determined as the slope of the relationship between skin vascular conductance and mean body temperature, plotted using the values at baseline, as well as at the end of each exercise period.

Statistical Analysis

All dependent variables were compared between groups (men and women) within each experimental condition (chamber and calorimeter). Independent samples T-tests were used for single comparisons between groups, while a two-way mixed-model analysis of variance was used for multiple comparisons using the repeated factor of time and the nonrepeated factor of group. When a significant main effect was found, multiple comparisons using the repeated factor of time and Bonferroni approach. The level of significance for all analyses was set at a 0.05 level of P ≤ 0.05. Statistical analyses were performed using commercially available statistical software (SPSS 19.0 for Windows, SPSS, Chicago, IL). Segmented regression analysis was performed using GraphPad Prism 5.0 (GraphPad Software, La Jolla, CA). Participant characteristics, training history, and exercise intensities are presented as means ± SD, while all other variables are reported as mean ± 95% confidence intervals.

RESULTS

Participant Characteristics

There were no differences in age between groups (P = 0.607). However, men had a significantly greater height (P = 0.040) and body mass (P = 0.018). The differences in body mass were due to differences in fat free mass (P = 0.001), as fat mass did not significantly differ between groups (P = 0.563). Furthermore, men had a greater maximum oxygen consumption, both in absolute values (P = 0.001) and relative to body mass (P = 0.025). However, there were no significant differences between groups in maximum oxygen consumption when expressed as a function of fat free mass (P = 0.204).

Training History

During the 3 mo before their participation in the study, men and women reported engaging in physical activities long enough to work up a sweat, on average 6 ± 3 (range: 3–10) and 7 ± 2 (range: 5–12) times/wk, respectively (P = 0.433). On average, men exercised 11 ± 8 (range: 2–25) h/wk, while women exercised 11 ± 6 (range: 2–22) h/wk (P = 0.972). During the 7 days before their participation in the study, men and women reported performing vigorous physical activity for 4 ± 3 (range: 0–8) and 5 ± 2 (range: 1–8) h, respectively (P = 0.744). Men and women also reported performing moderate physical activity for 4 ± 3 (range: 0–9) and 4 ± 4 (range: 0–13) h, respectively (P = 0.933).

Experimental Session 1: Whole Body Evaporative Heat Loss

On the day of the experimental session, plasma concentrations of 17β-estradiol and progesterone for the female participants averaged 406 ± 139 pmol/l and 1.6 ± 0.1 nmol/l, respectively. Urine-specific gravity did not differ between groups (men: 1.016 ± 0.009 vs. women: 1.011 ± 0.008, P = 0.244). By design, rate of metabolic heat production did not differ between groups during the first (men: 200 ± 3 vs. women: 200 ± 7 W/m², P = 0.856), second (247 ± 2 vs. 248 ± 5 W/m², P = 0.646), and third (302 ± 3 vs. 300 ± 4 W/m², P = 0.412) exercise periods. The external workloads associated with these rates of metabolic heat production did not differ between groups (men: 71 ± 9, 96 ± 13, 116 ± 15 W vs. women: 67 ± 6, 92 ± 9, 109 ± 11 W, respectively, P = 0.321), but represented a lower percentage of maximum oxygen consumption in men (36 ± 5, 45 ± 6, 55 ± 7% vs. 45 ± 6, 57 ± 5, 68 ± 5%, respectively; P = 0.001).

Despite exercising at similar requirements for heat loss, changes over time in whole body evaporative heat loss significantly differed between groups (P = 0.002, Fig. 1A). Although evaporative heat loss was similar at the end of the first (P = 0.418) and second (P = 0.394) exercise periods, it became greater in men at the end of the third exercise period (348 ± 26 vs. 305 ± 17 W/m², men vs. women, P = 0.015). When examined in relation to the requirement for heat loss (Fig. 1A), evaporative heat loss reached a similar percentage of the Ereq needed for heat balance in men and women during the first (P = 0.480) and second (P = 0.402) exercise periods. However, during the third exercise period, evaporative heat loss reached 84 ± 5% of Ereq in women, whereas it represented 94 ± 5% in men (P = 0.024). These differences were primarily due to a “leveling off” of evaporative heat loss in women, such that it did not significantly change over time during the last 10 min of the exercise period (P > 0.1), whereas evaporative heat loss significantly increased with time until the 26th min of exercise in men (P < 0.05). The onset threshold for evaporative heat loss did not differ between men and women at the start of each exercise period (all P > 0.1, Table 2). The thermosensitivity of evaporative heat loss did not differ between the sexes during the first two exercise periods (both P > 0.1), but was greater in men during the last exercise period (P = 0.007, Table 3 and Fig. 1B).

At the end of the 30-min baseline period, esophageal temperature averaged 36.69 ± 0.12°C in men and 37.03 ± 0.18°C in women (P = 0.01). During the exercise period, changes over time in esophageal temperature significantly differed between
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Fig. 1. Sex differences in evaporative heat loss (EHL) relative to the required evaporation for heat balance (Ereq; A), as well as in EHL as a function of changes in mean body temperature (B) during exercise performed at increasing rates of metabolic heat production (200, 250, 300 W/m²). Dashed lines represent the beginning of each exercise period. Values are means ± 95% confidence intervals. *Significantly different EHL between men and women (P < 0.05). Δ, Change.

the sexes (time × sex interaction, P = 0.010). Although the change in esophageal temperature during the first (0.36 ± 0.09 vs. 0.52 ± 0.18°C, P = 0.145) and second (0.24 ± 0.04 vs. 0.33 ± 0.13°C, men vs. women, P = 0.215) exercise periods did not significantly differ between the sexes, it was significantly greater in women (0.61 ± 0.16°C) compared with men (0.37 ± 0.07°C, P = 0.018) during the last exercise period. In contrast, no sex differences in mean skin temperature were observed throughout the exercise period (P = 0.490), averaging 35.52 ± 0.26, 35.60 ± 0.26, and 35.82 ± 0.29°C for men and 35.83 ± 0.26, 35.94 ± 0.39, and 36.24 ± 0.58°C for women at the end of the first, second, and third exercise period, respectively. Furthermore, no sex differences in heart rate were observed at the end of the first (108 ± 7 vs. 113 ± 7 beats/min, P = 0.351), second (125 ± 11 vs. 135 ± 10 beats/min, P = 0.212), and third (143 ± 12 vs. 153 ± 10 beats/min, men vs. women, P = 0.251) exercise period. Overall, the change in body weight was significantly greater in men during the exercise period (1.70 ± 0.12 vs. 1.45 ± 0.10 kg in women, P = 0.008). However, it represented a similar percent change in both groups (−2.32 ± 0.20 vs. −2.38 ± 0.14%, men vs. women, P = 0.596).

Experimental Session 2: Local Heat Loss Responses

On the day of the experimental session, plasma concentrations of 17β-estradiol and progesterone for the female participants averaged 225 ± 138 pmol/l (P = 0.205 vs. calorimeter session) and 1.7 ± 0.5 nmol/l (P = 0.520 vs. calorimeter session), respectively. Urine specific gravity did not differ between groups (men: 1.018 ± 0.010 vs. women: 1.009 ± 0.008, P = 0.061). By design, rate of metabolic heat production did not differ between groups during the first (men: 197 ± 16 vs. women: 204 ± 3 W/m², P = 0.246), second (252 ± 2 vs. 250 ± 3 W/m², P = 0.076), and third (303 ± 2 vs. 305 ± 6 W/m², P = 0.412) exercise periods. The external workloads associated with these rates of metabolic heat production did not differ between groups (men: 68 ± 7, 86 ± 10, and 105 ± 16 W vs. women: 60 ± 9, 81 ± 12, and 93 ± 13 W, P = 0.140), but represented a lower percentage of maximum oxygen consumption in men (37 ± 5, 46 ± 7, and 55 ± 7% vs. 46 ± 4, 58 ± 4, and 69 ± 5%, P ≤ 0.001).

Local sweat rate. Despite exercise being performed at fixed requirements for heat loss, changes in local sweat rate on the back (P < 0.001), chest (P ≤ 0.001), and forearm (P < 0.001) significantly differed over time between sexes. Upper back sweat rate (Fig. 2A) was similar at the end of the first exercise period (P = 0.483), but became greater in men at the end of the second (P = 0.012), and third (P = 0.004) exercise periods. Similarly, chest sweat rate (Fig. 3A) did not differ between groups at the end of the first (P = 0.802) and second (P = 0.382) exercise periods, but was greater in men at the end of the last (P = 0.044) exercise period. In contrast, forearm sweat rate (Fig. 4A) was significantly greater in men at the end of each exercise period (P ≤ 0.05). The onset threshold for local sweat rate at all sites (Table 2), as well as at the onset of each exercise period, did not differ between men and women (P > 0.1). There were no sex differences in the thermosensitivity of local sweat rate at all sites during the first exercise period (P > 0.1, Table 3). During the second exercise period, no differences in thermosensitivity were observed between the sexes on the chest and forearm (P > 0.1), while it was greater in men on the upper back (P = 0.014). In contrast, the thermosensitivity at all sites was significantly greater in men during the last exercise period (P ≤ 0.01, Table 3). The mean of all three local sweat rate measurements against the change in mean body temperature is presented in Fig. 5A. The change in body weight was significantly greater in men during the exercise period (2.02 ± 0.15 vs. 1.59 ± 0.09 kg in women, P ≤ 0.001). However, it represented a similar percent change in both groups (−2.78 ± 0.25 vs. −2.62 ± 0.13%, men vs. women, P = 0.323).
Sweat gland activation. The number of active sweat glands (Table 4) on the upper back was significantly greater in women compared with men at the end of each exercise period ($P < 0.001$). As such, the greater upper back sudomotor output in women was entirely due to a greater sweat gland output ($P < 0.001$). Similarly, changes over time in the number of active sweat glands on the chest significantly differed between men and women ($P = 0.018$). Although the number of active sweat glands did not differ at the end of the first ($P = 0.871$) and second ($P = 0.770$) exercise periods, it became greater in women at the end of the third exercise period ($P = 0.021$). A similar pattern was observed for sweat gland output on the chest ($P < 0.001$), such that it did not differ between sexes at the end of the first ($P = 0.480$) and second ($P = 0.153$) exercise periods, but became greater in men at the end of the third exercise period ($P = 0.001$). In contrast, the number of active sweat glands on the forearm did not differ between the sexes throughout exercise ($P = 0.456$). Consequently, the greater forearm sweat rate observed in men was entirely due to a greater sweat output per gland ($P = 0.001$, Table 4).

Local skin blood flow. Skin blood flow at each site increased significantly from baseline rest during exercise ($P < 0.001$). Although skin blood flow values at the upper back significantly increased from the first to third exercise period ($P < 0.05$), those at the chest and forearm did not ($P > 0.05$). No significant differences were observed between the sexes in skin blood flow at the back ($P = 0.195$), chest ($P = 0.705$), and forearm ($P = 0.212$). Similarly, no differences were observed in the onset threshold for increases in skin blood flow at each site ($P > 0.1$, Table 2).

Local skin blood flow. Skin blood flow at each site increased significantly from baseline rest during exercise ($P < 0.001$), with no significant changes from the first to the third exercise period ($P = 0.363$). Mean arterial pressure was significantly lower in women at baseline rest ($80 \pm 2$ vs. $86 \pm 3$ mmHg in men, $P = 0.006$), and remained lower at the end of the first ($83 \pm 2$ vs. $90 \pm 5$ mmHg, $P = 0.014$), second ($83 \pm 2$ vs. $91 \pm 5$ mmHg, $P = 0.026$), and third ($84 \pm 3$ vs. $91 \pm 5$ mmHg, women vs. men, $P = 0.038$) exercise periods. Nonetheless, skin vascular conductance at the back ($P = 0.199$, Fig. 2B), chest ($P = 0.643$, Fig. 3B), and forearm ($P = 0.221$, Fig. 4B) did not differ between the sexes. There were also no sex differences in the thermosensitivity of skin vascular conductance ($P > 0.1$, Table 3). The mean of all three local skin vascular conductance measurements against the change in mean body temperature is presented in Fig. 5B.

Whole limb forearm blood flow and vascular conductance. Forearm blood flow and vascular conductance increased from baseline values during exercise ($P < 0.001$), with no significant changes from the first to the third exercise period ($P > 0.1$). Forearm blood flow ($P = 0.721$) and vascular conductance ($P = 0.278$) did not differ between the sexes throughout exercise. Forearm

### Table 2. Onset threshold of thermoeffector responses

<table>
<thead>
<tr>
<th></th>
<th>200 W/m²</th>
<th></th>
<th>250 W/m²</th>
<th></th>
<th>300 W/m²</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Men</td>
<td>Women</td>
<td>Men</td>
<td>Women</td>
<td>Men</td>
<td>Women</td>
</tr>
<tr>
<td><strong>Sudomotor activity, Δ°C</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Whole body</td>
<td>0.01 ± 0.01</td>
<td>0.01 ± 0.01</td>
<td>0.02 ± 0.02</td>
<td>0.02 ± 0.02</td>
<td>0.04 ± 0.02</td>
<td>0.02 ± 0.02</td>
</tr>
<tr>
<td>Back</td>
<td>0.02 ± 0.02</td>
<td>0.02 ± 0.01</td>
<td>0.02 ± 0.01</td>
<td>0.01 ± 0.01</td>
<td>0.06 ± 0.06</td>
<td>0.02 ± 0.01</td>
</tr>
<tr>
<td>Chest</td>
<td>0.02 ± 0.02</td>
<td>0.01 ± 0.00</td>
<td>0.02 ± 0.01</td>
<td>0.01 ± 0.01</td>
<td>0.02 ± 0.01</td>
<td>0.01 ± 0.01</td>
</tr>
<tr>
<td>Forearm</td>
<td>0.03 ± 0.02</td>
<td>0.02 ± 0.02</td>
<td>0.02 ± 0.01</td>
<td>0.01 ± 0.01</td>
<td>0.02 ± 0.01</td>
<td>0.03 ± 0.02</td>
</tr>
<tr>
<td><strong>Skin blood flow, Δ°C</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Back</td>
<td>0.06 ± 0.02</td>
<td>0.07 ± 0.02</td>
<td>n/a</td>
<td>n/a</td>
<td>n/a</td>
<td>n/a</td>
</tr>
<tr>
<td>Chest</td>
<td>0.04 ± 0.02</td>
<td>0.07 ± 0.02</td>
<td>n/a</td>
<td>n/a</td>
<td>n/a</td>
<td>n/a</td>
</tr>
<tr>
<td>Forearm</td>
<td>0.06 ± 0.01</td>
<td>0.08 ± 0.02</td>
<td>n/a</td>
<td>n/a</td>
<td>n/a</td>
<td>n/a</td>
</tr>
</tbody>
</table>

Values are means ± 95% confidence intervals. Whole body sudomotor activity was measured by direct calorimetry. n/a, Not applicable as the thermosensitivity of skin vascular conductance was not measured at each exercise period. *Significantly different from men ($P < 0.05$).

### Table 3. Thermosensitivity of thermoeffector responses

<table>
<thead>
<tr>
<th></th>
<th>200 W/m²</th>
<th></th>
<th>250 W/m²</th>
<th></th>
<th>300 W/m²</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Men</td>
<td>Women</td>
<td>Men</td>
<td>Women</td>
<td>Men</td>
<td>Women</td>
</tr>
<tr>
<td><strong>Sudomotor activity</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Whole body</td>
<td>496 ± 139</td>
<td>483 ± 185</td>
<td>283 ± 70</td>
<td>211 ± 66</td>
<td>197 ± 61</td>
<td>82 ± 27*</td>
</tr>
<tr>
<td>Back</td>
<td>1.79 ± 0.61</td>
<td>1.38 ± 0.22</td>
<td>1.51 ± 0.17</td>
<td>0.91 ± 0.35</td>
<td>0.90 ± 0.19</td>
<td>0.34 ± 0.08*</td>
</tr>
<tr>
<td>Chest</td>
<td>1.35 ± 0.54</td>
<td>1.14 ± 0.23</td>
<td>1.21 ± 0.26</td>
<td>0.92 ± 0.36</td>
<td>0.67 ± 0.14</td>
<td>0.30 ± 0.10*</td>
</tr>
<tr>
<td>Forearm</td>
<td>1.86 ± 0.58</td>
<td>1.53 ± 0.29</td>
<td>1.30 ± 0.23</td>
<td>1.02 ± 0.49</td>
<td>0.60 ± 0.19</td>
<td>0.29 ± 0.09*</td>
</tr>
<tr>
<td><strong>Skin vascular conductance</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Back, %max/°C</td>
<td>21 ± 5</td>
<td>19 ± 5</td>
<td>n/a</td>
<td>n/a</td>
<td>n/a</td>
<td>n/a</td>
</tr>
<tr>
<td>Chest, %max/°C</td>
<td>21 ± 6</td>
<td>18 ± 5</td>
<td>n/a</td>
<td>n/a</td>
<td>n/a</td>
<td>n/a</td>
</tr>
<tr>
<td>Forearm, %max/°C</td>
<td>18 ± 5</td>
<td>18 ± 5</td>
<td>n/a</td>
<td>n/a</td>
<td>n/a</td>
<td>n/a</td>
</tr>
<tr>
<td>Whole limb, ml·100 ml⁻¹·min⁻¹·mmHg⁻¹·°C⁻¹</td>
<td>3.92 ± 0.58</td>
<td>3.32 ± 1.25</td>
<td>n/a</td>
<td>n/a</td>
<td>n/a</td>
<td>n/a</td>
</tr>
</tbody>
</table>

Values are means ± 95% confidence intervals. Whole body sudomotor activity was measured by direct calorimetry. n/a, Not applicable as the thermosensitivity of skin vascular conductance was not measured at each exercise period. *Significantly different from men ($P < 0.05$).
vascular conductance averaged 0.05 ± 0.01, 0.09 ± 0.03, 0.09 ± 0.02, and 0.09 ± 0.01 ml·100 ml tissue⁻¹·min⁻¹·mmHg⁻¹ in men vs. 0.06 ± 0.01, 0.10 ± 0.01, 0.10 ± 0.01, and 0.10 ± 0.02 ml·100 ml tissue⁻¹·min⁻¹·mmHg⁻¹ in women during baseline rest, and the first, second, and third exercise period, respectively. Furthermore, the thermosensitivity of forearm vascular conductance (P = 0.651, Table 3) did not differ between groups.

**Esophageal and mean skin temperatures and heart rate.** At the end of the 30-min baseline period, esophageal temperature averaged 36.97 ± 0.17°C in men and 37.42 ± 0.13°C in women (P = 0.01). The change in esophageal temperature during the first (0.28 ± 0.15 vs. 0.43 ± 0.13°C, P = 0.184) and second (0.32 ± 0.07°C vs. 0.37 ± 0.13°C, men vs. women, P = 0.500) exercise periods did not significantly differ between the sexes. However, it was significantly greater in women (0.72 ± 0.16°C compared with men (0.53 ± 0.09°C, P = 0.052) during the last exercise period. Mean skin temperature was statistically greater in women at the end of the first (36.80 ± 0.15 vs. 36.33 ± 0.12°C, P=0.001), second (36.97 ± 0.27 vs. 36.46 ± 0.18°C, P = 0.008), and third (37.05 ± 0.22 vs. 36.72 ± 0.18°C, P = 0.006) exercise periods, respectively. Furthermore, the thermosensitivity of forearm vascular conductance (P = 0.651, Table 3) did not differ between groups.

**Fig. 2.** Sex differences in upper back sweat rate (A) and skin vascular conductance presented as a percentage of maximum (B) during exercise performed at increasing rates of metabolic heat production (200, 250, 300 W/m²). Dashed lines represent the beginning of each exercise period. Values are means ± 95% confidence intervals. *Significantly different sweat rate between men and women (P < 0.05).

**Fig. 3.** Sex differences in chest sweat rate (A) and skin vascular conductance presented as a percentage of maximum (B) during exercise performed at increasing rates of metabolic heat production (200, 250, 300 W/m²). Dashed lines represent the beginning of each exercise period. Values are means ± 95% confidence intervals. *Significantly different sweat rate between men and women (P < 0.05).
and third (37.30 ± 0.24 vs. 36.83 ± 0.23°C, women vs. men, \( P = 0.015 \)) exercise period. In contrast, no sex differences in heart rate were observed at the end of the first (103 ± 6 vs. 114 ± 9 beats/min, \( P = 0.063 \)), second (123 ± 9 vs. 134 ± 12 beats/min, \( P = 0.136 \)), and third (146 ± 8 vs. 151 ± 13 beats/min, men vs. women, \( P = 0.546 \)) exercise periods.

**Changes in Plasma Volume and Osmolality**

Decreases in plasma volume became greater with each exercise period (\( P = 0.001 \)), with no significant differences between sexes (\( P = 0.767 \)). Changes from baseline in plasma volume averaged -2.5 ± 4.3, -5.7 ± 3.9, and -10.4 ± 4.2% for men and 0.1 ± 3.7, -7.0 ± 4.0, and -9.2 ± 2.6% for women at the end of the first, second, and third exercise period, respectively. Baseline values of plasma osmolality did not significantly differ between sexes (men: 295 ± 1 mosmol/kgH_2O vs. women: 296 ± 3 mosmol/kgH_2O, \( P = 0.659 \)). Plasma osmolality levels significantly increased with each exercise period (\( P = 0.001 \)). However, there were no significant differences in plasma osmolality between the sexes at the end of each exercise period (\( P = 0.805 \)), averaging 297 ± 2, 300 ± 2, and 302 ± 2 mosmol/kgH_2O for men and 297 ± 3, 300 ± 3, and 302 ± 3 mosmol/kgH_2O for women at the end of the first, second, and third exercise period, respectively.
DISCUSSION

The present study examined sex differences in sudomotor function (local and whole body) and skin blood flow during exercise performed at increasing requirements for heat loss. The main findings demonstrate that women exhibit a lower whole body evaporative heat loss and local sweat rate that is only evidenced beyond a certain requirement for heat loss. These differences are paralleled by a lower thermosensitivity of both responses, without any differences in the onset threshold. The lower local sweat rate in women is attributed to a lower sweat output per gland, as opposed to differences in the number of active sweat glands. In contrast, no sex differences in skin blood flow, as well as in the onset threshold and thermosensitivity of the skin blood flow response, were observed at all requirements for heat loss.

Although a number of studies have examined differences in sweat rate between men and women during exercise, the majority employed experimental protocols that resulted in men exercising at greater rates of metabolic heat production compared with women, making it difficult to determine if sex differences in sweat rate were truly due to physiological differences in temperature regulation, or simply associated with differences in metabolic heat production. An important consideration of the present study is the use of fixed rates of metabolic heat production expressed per unit of body surface area, which, combined with fixed environmental conditions, resulted in the same Ereq for both sexes during exercise. This experimental approach is essential to ascribe the observed differences in local sweat rate and whole body evaporative heat loss to physiological sex differences (rather than physical), as previous studies have shown that the level of local and whole body sweat rate achieved during exercise is determined by the ratio of Ereq and Emax possible in a given environment.

To differentiate between a central and peripheral modulation of sudomotor function, the present study examined the onset threshold and thermosensitivity of local sweat rate and whole body evaporative heat loss during progressive increases in the requirement for heat loss. In theory, differences in neural activity between men and women would expect to yield differences in sweat production, as well as in the onset threshold of the response, at all requirements for heat loss. For example, central adaptations associated with acclimation, sex hormones, and hyperosmolality consistently result in a shift in the onset threshold of both sweating and skin blood flow, with little to no change in thermosensitivity. Furthermore, these shifts are apparent whether the requirement for heat loss is high, such as during exercise, or whether it is relatively low, such as during passive heat stress. In the present study, the onset threshold of both local sweat rate and whole body evaporative heat loss, as well as for increases in skin blood flow, did not differ between the sexes. Furthermore, sex differences in sudomotor thermosensitivity were not observed at lower exercise intensities, only becoming evident at the greatest requirement for heat loss employed. It should be noted that the greater local sweat rate on the back and forearm observed in men during the first and second exercise bouts is likely the result of regional differences in sweat rate between the sexes, as whole body evaporative heat loss did not differ at these two requirements for heat loss.

Measurements of sweat gland activation have also been used to determine whether differences in sweat rate between conditions and/or populations are mediated centrally or peripherally. While sweat gland activation must result from thermoefferent neural activity, the sweat output per gland reflects the peripheral properties of the sweat gland itself. As such, differences in central sudomotor function between the sexes would be expected to result in varying levels of sweat gland activation. In the present study, sweat gland activation was greater in women compared with men. These results are consistent with previous observations during passive heat stress and exercise. Consequently, the observed sex differences in local sweat rate were solely the result of a lower sweat gland output in women. The sweat gland’s maximal capacity to produce sweat has been used as an indicator of peripheral modulation. Interestingly, we observed a clear leveling off in women of whole body evaporative heat loss at the highest requirement for heat loss, whereas it continued to increase in men. This observation is particularly evident when examining evaporative heat loss in relation to Ereq (see Fig. 1A). During the first two exercise periods, evaporative heat loss accounted for a similar proportion of the evaporation needed for heat balance in men and women. However, the lack of increase in evaporative heat loss during the last 10 min of the third exercise period in women resulted in evaporative heat loss values that accounted for a significantly lower proportion of Ereq. In contrast, the greater and continued increase in whole body evaporative heat loss in men maintained evaporative heat loss values that accounted for >90% of the required value for heat balance. Although a true test of concept would require an additional rise in the requirement for heat loss combined with

**Table 4. Sex differences in the number of active sweat glands and the sweat output per gland during exercise performed at increasing rates of metabolic heat production**

<table>
<thead>
<tr>
<th>Heat Production, W/m²</th>
<th>Sex</th>
<th>No. Active Glands per cm²</th>
<th>SGO, µg/gland</th>
<th>No. Active Glands per cm²</th>
<th>SGO, µg/gland</th>
<th>No. Active Glands per cm²</th>
<th>SGO, µg/gland</th>
</tr>
</thead>
<tbody>
<tr>
<td>a200</td>
<td>Men</td>
<td>56 ± 8</td>
<td>15.97 ± 1.79</td>
<td>57 ± 6</td>
<td>13.56 ± 2.76</td>
<td>92 ± 12</td>
<td>10.99 ± 1.53</td>
</tr>
<tr>
<td></td>
<td>Women</td>
<td>82 ± 13*</td>
<td>9.95 ± 1.06*</td>
<td>56 ± 8</td>
<td>12.22 ± 2.20</td>
<td>106 ± 27</td>
<td>7.46 ± 1.54*</td>
</tr>
<tr>
<td>250</td>
<td>Men</td>
<td>58 ± 6</td>
<td>22.30 ± 1.83</td>
<td>64 ± 9</td>
<td>16.87 ± 3.34</td>
<td>112 ± 12</td>
<td>11.89 ± 1.64</td>
</tr>
<tr>
<td></td>
<td>Women</td>
<td>92 ± 9*</td>
<td>11.23 ± 1.38*</td>
<td>66 ± 7</td>
<td>13.60 ± 2.38</td>
<td>119 ± 18</td>
<td>8.61 ± 1.06*</td>
</tr>
<tr>
<td>300</td>
<td>Men</td>
<td>58 ± 8</td>
<td>28.01 ± 3.28</td>
<td>59 ± 7</td>
<td>22.71 ± 3.28</td>
<td>101 ± 7</td>
<td>15.30 ± 2.00</td>
</tr>
<tr>
<td></td>
<td>Women</td>
<td>93 ± 6*</td>
<td>13.04 ± 1.91*</td>
<td>73 ± 8*</td>
<td>13.82 ± 1.69*</td>
<td>123 ± 23</td>
<td>9.83 ± 1.65*</td>
</tr>
</tbody>
</table>

Values are means ± 95% confidence intervals. SGO, sweat gland output. *Significantly different from men (P ≤ 0.05).
a total absence of increases in evaporative heat loss, these observations provide evidence of a lower maximal evaporative capacity, and therefore maximal sweat production, in women.

In contrast to sudomotor function, sex-related differences in skin blood flow during heat stress have been less examined. Inoue et al. (26) did not observe any sex differences in back, chest, and forearm skin blood flow during passive heating of the lower limbs, while Kolka et al. (31) reported a similar onset threshold and thermosensitivity of forearm skin blood flow between sexes during exercise in a warm (30°C) environment. It should be noted, however, that Inoue et al. (26) did report a greater thermosensitivity of skin blood flow on the thigh in women, which led them to speculate that women may rely to a greater extent on increases in skin blood flow compared with men for effective heat dissipation. In contrast, our results do not support a greater reliance on skin blood flow in women for heat loss during exercise in the heat, as we did not observe any differences in both local and whole limb skin blood flow at all requirements for heat loss. Furthermore, recent evidence suggests that skin blood flow can independently modulate the thermosensitivity of local sweat rate, without affecting the onset threshold of the response (52). As such, the similar local and whole limb skin blood flow between men and women in the present study rule out the possibility that the lower thermosensitivity of local sweat rate in women is associated with differences in skin blood flow.

Perspectives

The observed sex differences in sudomotor thermosensitivity, which only occurred at the highest requirement for heat loss, combined with the lack of sex differences in the onset threshold of the response, as well as in skin blood flow as a whole, are consistent with a peripheral modulation of sudomotor function in women. This is particularly evident when considering that parallel shifts in the onset threshold of both thermoeffector responses are typical of a central modulation of temperature regulation (18). A peripheral modulation of sudomotor function during exercise in women could be mediated through sex differences in either the cholinergic sensitivity of the sweat gland (17, 28, 33), the physical properties (e.g., size) of the sweat gland (40), the concentration of cholinergic agonists released in the sudomotor junction, and/or the concentration of acetylcholinesterase present within the sudomotor junction (44). Further research is, therefore, needed to determine which of these factors is specifically responsible in mediating the lower sudomotor thermosensitivity in women during exercise.

Considerations

It may be argued that the observed differences in sudomotor function are related to differences in the percentage of maximum oxygen consumption elicited by fixed rates of metabolic heat production. However, this would disregard recent findings, which demonstrate that differences in relative exercise intensity and maximum oxygen consumption between independent groups do not modulate local sweat production when exercise is performed at a fixed requirement for heat loss (7, 27). It is also noteworthy that relative exercise intensity differed between men and women during each exercise period, yet consistent differences in local sweat rate and whole body evaporative heat loss were only observed during the last exercise period. Moreover, both sexes in the present study had a similar training history, suggesting that the lower absolute maximum oxygen consumption in women is likely attributed to a lower fat free mass, as opposed to differences in training status. In contrast to local sweat rate (7, 27), increases in skin blood flow during exercise are determined not only by the requirement for heat loss, but also by the competition created by the metabolic requirement of the active musculature (19). In the present study, the similar skin blood flow response in women occurred despite a relatively greater demand for blood flow to the active musculature, particularly at the highest requirement for heat loss. It is unknown whether similar results would have been observed if exercise had been performed at fixed percentages of maximum oxygen consumption. Future studies are required to determine the impact of using fixed requirements for heat loss compared with fixed percentages of maximum oxygen consumption on the skin blood flow response. Finally, it should also be considered that we did not observe any sex differences in changes in plasma volume and osmolality throughout the experimental protocol in a subset of participants. It is, therefore, unlikely that the present results can be attributed to possible differences in either of these variables. However, it is possible that, although changes in plasma volume were similar between men and women, absolute plasma volume would have started at a lower level in women, thus reducing to lower absolute values. Future studies are needed to examine this possibility.

Conclusion

The present study examined sex differences in sudomotor function (local and whole body) and skin blood flow during exercise in the heat performed at increasing requirements for heat loss. Consistent sex differences in local sweat rate and whole body evaporative heat loss were only evidenced at the highest requirement for heat loss employed. A lower local sweat rate and whole body evaporative heat loss was observed in women, which was paralleled by a lower thermosensitivity of each response without any differences in the onset threshold. Furthermore, the lower local sweat rate in women was solely the result of a lower sweat gland output, as opposed to differences in sweat gland activation. We also observed a leveling off of whole body evaporative heat loss at the highest requirement for heat loss in women, which suggests a lower maximal evaporative capacity. In contrast, no sex differences in both the onset threshold and thermosensitivity of skin blood flow were observed throughout the experimental protocol. Taken together, these results provide evidence that sex differences in sudomotor function during exercise are mediated peripherally.

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GRANTS

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DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the author(s).

AUTHOR CONTRIBUTIONS

Author contributions: D.G. performed experiments; D.G. analyzed data; D.G. and G.P.K. interpreted results of experiments; D.G. prepared figures; D.G. drafted manuscript; D.G. and G.P.K. edited and revised manuscript; D.G. and G.P.K. approved final version of manuscript.

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