Menstrual cycle and oral contraceptive use do not modify postexercise heat loss responses

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Recent reports suggest that the attenuated postexercise vaso- motor and sudomotor heat loss responses, despite sustained elevations in core and muscle temperatures (29, 30), are attributable to nonthermal factors thought to be associated with postexercise blood pressure regulation (25, 29, 30). It is thought that a greater postexercise hypotension elicits a more pronounced decline in both skin blood flow and sweating (25, 31). Some studies demonstrate that postexercise hemodynam-
hormones appear to be similar to those seen in the normal menstrual cycle during rest and exercise (6, 7, 14, 18, 24, 36, 47), their influence on the activation of heat loss responses remains undetermined for the postexercise period. OC agents are often prescribed for the female athlete for contraceptive purposes, cycle regulation, or the treatment of dysmenorrhea (cramping and pain). More recently, birth control pills have been prescribed in athletes with amenorrhea (absence of periods for more than 3 mo) to avoid a decrease in bone density (the cause of skipped periods). Any hormonal differences in thermoregulatory control following exercise may potentially have a pronounced effect on the magnitude of change in body heat content and core temperature during a subsequent thermal challenge.

Thus the purpose of this study was to determine whether differences in female sex hormones during the menstrual cycle contribute to the diminished heat loss responses secondary to postexertional hypotension as measured during a passively induced hyperthermia. We used an exercise paradigm that is known to elicit a postexercise decrease in MAP (31) to evaluate the hypothesis that, in parallel to a postexercise decrease in MAP, the onset of skin vasodilation and sweating would be delayed during a passive heating performed in the postexercise period compared with preexercise but would be similar between menstrual cycle phases.

MATERIALS AND METHODS

Participants

Subsequent to approval of the experimental protocol by the University of Ottawa Human Research Ethics Committee, 16 healthy, recreationally active, non-heat acclimated, nonsmoking, normotensive women volunteered for the study. This sample size was determined using a power calculation on the basis of the 90% power to detect a 10% within-group change with SD of 5%, $\alpha$ of 0.05. Six subjects were required per group. The effect size and standard deviations for this calculation were estimated from previous literature undertaking similar protocols (26, 29). We recruited eight women taking OC and eight women not taking OC so that we would have the desired power within each of the two groups, even if two subjects dropped out.

The subjects were divided into two equal-size groups on the basis of the use (OC) or non-use (non-OC) of OC. Subjects were matched for age, body composition, and physical fitness. Subject characteristics for the two groups are presented in Table 1. All subjects in the OC group were voluntarily taking OC agents for contraceptive purpose only. Participants were on a monophasic contraceptive regimen that provided for 21 days of consumption of 20 to 30 $\mu$g of ethinyl estradiol and a progestogen derivate (Table 2) and a 7-day withdrawal (placebo pill) phase. None of the female participants in the non-OC group had used OC in the past year.

Table 1. Physical characteristics of the subjects

<table>
<thead>
<tr>
<th>Non-OC</th>
<th>OC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yr</td>
<td>29±2</td>
</tr>
<tr>
<td>Height, m</td>
<td>1.66±0.01</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>65.0±1.6</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>22.9±0.6</td>
</tr>
<tr>
<td>Body fat, %</td>
<td>19.7±1.8</td>
</tr>
<tr>
<td>$V_{\text{O2peak}}$, ml·min⁻¹·kg⁻¹</td>
<td>44.2±2.4</td>
</tr>
</tbody>
</table>

Values are means ± SE. Non-OC, non-oral contraceptive users; OC, oral contraceptive users; BMI, body mass index. No differences were observed between groups.

Table 2. OC details for individual contraceptive users

<table>
<thead>
<tr>
<th>OC Subject</th>
<th>Brand Name</th>
<th>Estrogen, mg</th>
<th>Progestin, mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Minovral</td>
<td>0.030</td>
<td>0.15 levonorgestrel</td>
</tr>
<tr>
<td>2</td>
<td>Evra</td>
<td>0.020</td>
<td>0.20 norelgestromin</td>
</tr>
<tr>
<td>3</td>
<td>Alesse</td>
<td>0.020</td>
<td>0.10 levonorgestrel</td>
</tr>
<tr>
<td>4</td>
<td>Cycless</td>
<td>0.020</td>
<td>0.30 levonorgestrel</td>
</tr>
<tr>
<td>5</td>
<td>Alesse</td>
<td>0.030</td>
<td>0.100 levonorgestrel</td>
</tr>
<tr>
<td>6</td>
<td>Marvelon</td>
<td>0.030</td>
<td>0.150 desogestrel</td>
</tr>
<tr>
<td>7</td>
<td>Marvelon</td>
<td>0.030</td>
<td>0.150 desogestrel</td>
</tr>
<tr>
<td>8</td>
<td>Minovral</td>
<td>0.030</td>
<td>0.150 levonorgestrel</td>
</tr>
</tbody>
</table>

Experimental Procedure

**Screening visit.** Subjects visited the laboratory on three separate occasions. The purpose of the first visit was to measure peak oxygen uptake ($V_{\text{O2peak}}$) and body adiposity. Peak oxygen consumption was measured during a progressive incremental cycling protocol performed on a Monark cycle ergometer. Subjects were asked to cycle continuously at 80 revolution/min, at a starting work rate of 40 W. Every 2 min thereafter, the work rate was increased by 20–40 W increments until the subject could not maintain the pedaling cadence. Selection of the workload increment was subjective, with the goal of producing exhaustion within 8–12 min. Whole body oxygen uptake ($V_{\text{O2}}$) was measured by open circuit technique using expired gas samples drawn from a 6-l fluted mixing box. Expired gas was analyzed for $V_{\text{O2}}$ and $V_{\text{CO2}}$ using Ametek gas analyzers (Ametek, model nos. S-3A/1 and CD 3A; Applied Electrochemistry, Pittsburgh, PA). The $V_{\text{O2peak}}$ data were used to select the submaximal workload for the experimental exercise phase of the study. The hydrostatic weighing technique was used to determine body density. Calculation of the percentage of body fat was based on the Siri equation (52). During this session, the subjects were familiarized with all procedures to be performed during the investigation period. At the end of the screening visit, subjects gave a history of their menstrual cycle and were instructed how to document the start of a menstrual cycle.

**Study visits.** Normally menstruating subjects participated in two testing sessions that differed only by the phase of the menstrual cycle. These were 1) the early follicular phase (FP: 3–5 days after the start of the menstruation, when estrogen and progesterone are low) and 2) midluteal phase (LP: days 19–22, when estrogen and progesterone are elevated). All subjects followed a normal OC routine. The first day of placebo pill consumption was identified as day 1 of the cycle. Menstruation occurs during this period, which corresponds most closely with the FP of eumenorrheic non-OC users and represents a phase of low exogenous hormone availability [low-hormone status (LH)] (11). Testing was performed between days 3 and 5 (2). During the active pill consumption period, testing was performed between days 19 and 22 to allow time for a hormonal steady state to be achieved (2). This period most closely resembles the LP of eumenorrheic non-OC users and represents a phase of high exogenous hormone availability [high-hormone status (HH)] (11). All study sessions were carried out in a random order.

Before each experimental session began, venous blood samples were collected on each study visit for measurement of 17β-estradiol and progesterone to confirm menstrual cycle phase (Table 3). Samples were immediately placed on ice, separated, and stored at −70°C for subsequent analysis. Progesterone and 17β-estradiol concentrations were quantitated using automated chemiluminescent microparticle immunoassays (ARCHITECT system; Abbott Diagnostics, Abbots Park, IL) at Gamma-Dynacare Medical Laboratories (Ottawa, ON, Canada) using appropriate monoclonal antibody-coated microparticles and acridinium-labeled conjugates. Chemiluminescent reactions were measured using the ARCHITECT i-optical system. The ARCHITECT Estradiol assay precision is ±5 pg/ml (total SD) for concentrations in the range of the low control (target 45 pg/ml) and
Plasma progesterone and plasma estradiol in OC and non-OC before the start of the experimental trial

<table>
<thead>
<tr>
<th>Subject #</th>
<th>Estradiol, nmol·l⁻¹</th>
<th>Progesterone, nmol·l⁻¹</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>FP</td>
<td>LP</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>n/a</td>
<td>0.299</td>
</tr>
<tr>
<td>2</td>
<td>0.081</td>
<td>0.231</td>
</tr>
<tr>
<td>3</td>
<td>0.089</td>
<td>0.385</td>
</tr>
<tr>
<td>4</td>
<td>0.096</td>
<td>0.269</td>
</tr>
<tr>
<td>5</td>
<td>&lt;0.060</td>
<td>0.618</td>
</tr>
<tr>
<td>6</td>
<td>0.099</td>
<td>0.494</td>
</tr>
<tr>
<td>7</td>
<td>0.172</td>
<td>0.441</td>
</tr>
<tr>
<td>8</td>
<td>0.079</td>
<td>0.334</td>
</tr>
</tbody>
</table>

Plasma progesterone and plasma estradiol in OC and non-OC measured before the start of the experimental trial for the early follicular (FP) and midluteal phases (LP) of the menstrual cycle and during the active pill consumption (high exogenous hormone phase; HH) and placebo (low exogenous hormone phase; LH) weeks for the OC group. n/a, not available.

≤7% [total coefficient of variation (CV)] for concentrations in the range of the medium control (target 190 pg/ml) and the high control (target 600 pg/ml). The ARCHITECT progesterone assay precision is ≤10% total CV for concentrations in the range of the ARCHITECT progesterone low control (target 0.8 ng/ml) and ≤7% total CV for concentrations in the ranges of the ARCHITECT progesterone medium and high controls (target 4.7 and 21.1 ng/ml for medium and high, respectively).

On the basis of the laboratory test results, data were discarded and experimental sessions repeated under the following conditions: 1) progesterone levels were not elevated during the LP for the non-OC, indicating that ovulation had not occurred (range: 5.3–86.0 nmol/l); 2) progesterone levels were elevated during the HH phase for the OC group, indicating that ovulation had occurred (>5.3 nmol/l).

Table 3. Plasma progesterone and plasma estradiol in OC and non-OC before the start of the experimental trial

Fig. 1. Experimental protocol time line. \( V\text{O}_2\text{peak} \) peak oxygen consumption; LCS, liquid conditioned suit; CVC, cutaneous vascular conductance. Note: During preexercisepostexercise warming mean skin temperature was gradually increased as the water circulating through the suit was progressively increased to 48°C. Local skin temperature was clamped at 34°C throughout the experimental protocol except for the final 30 min for the measurement of peak CVC.

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temperature was raised to 43°C until skin blood flow achieved an elevated and sustained plateau (30 ± 3 min).

Measurements

Thermal response. Esophageal temperature (T es) was measured by placing a pediatric thermocouple probe of ~2 mm in diameter (Mon-a-therm nasopharyngeal temperature probe; Mallinckrodt Medical, St-Louis, MO) through the participant’s nostril while she was asked to sip water through a straw. The location of the probe tip in the esophagus was estimated to be in the region bounded by the left ventricle and aorta, corresponding to the level of the eighth and ninth thoracic vertebrae (41). Skin temperature was measured at 12 points over the body surface using 0.3-mm diameter T-type (copper-constantan) thermocouples integrated into heat-flow sensors (Concept Engineering, Old Saybrook, CT). Thermocouples were attached using surgical tape (Blenderm; 3M, St. Paul, MN). Mean skin temperature (T sk) was calculated using the 12 skin temperatures weighted to the regional proportions as determined by Hardy and DuBois (19): head 7%, hand 4%, upper back 9.5%, chest 9.5%, lower back 9.5%, abdomen 9.5%, bicep 9%, forearm 7%, quadriceps 9.5%, hamstring 9.5%, front calf 8.5%, and back calf 7.5%.

Sweating response. Local sweat rate was measured using a 5.0-cm² ventilated capsule placed over the medial inferior aspect of the trapezius muscle. Anhydrous compressed air was passed through the capsule and over the skin surface (Brooks 5850, Mass Flow Controller; Emerson Electric, Hetfield, PA). The vapor density of the effluent air was calculated from the relative humidity and temperature measured using the Omega HX93 humidity and temperature sensor (Omega Engineering, Stamford, CT). Local sweat rate was calculated as the average over a 30-s interval using the difference in water content between effluent and influent air and the flow rate. The flow rate through the capsule was 0.5 l/min. The sweat rate value was adjusted for skin surface area under the capsule and expressed in mg·min⁻¹·cm⁻² (28, 33).

Index of skin blood flow. An index of skin blood flow was derived from measuring red blood cell flux values by laser-Doppler flowmetry (PeriFlux System 5000, main control unit; PF5010 LDPM, operating unit; Perimed, Stockholm, Sweden) at the right midanterior forearm. The laser-Doppler flow probe D was affixed with adhesive rings to the ventral forearm in a site without superficial veins that demonstrated high flux values and pulsatile activity (38). Skin blood flow measures were expressed as cutaneous vascular conductance (CVC), calculated throughout the experimental protocol by using the ratio of 30-s averages of laser-Doppler flow and MAP and normalized to the maximal values achieved during local heating at 43°C at the end of the protocol (31). Local skin temperature at the forearm skin measurement site was controlled using a heating element (PF 5020 temperature unit, Perimed), housing the laser-Doppler flow probe.

Heart rate and MAP. Heart rate (HR) was monitored using a Polar Advantage interface and Polar Precision Performance software (Polar Electro, Oulu, Finland). MAP was estimated from the integration of a noninvasive recording of blood pressure at the middle digit of the left hand (Finapres 2300; Ohmeda, Madison, WI) fixed at heart level (the third intercostal space). MAP was verified periodically throughout the protocol by auscultation.

Thermal data and local sweat rate data were collected using an HP Agilent data acquisition module (model 3497A) at a sampling rate of 10 s and simultaneously displayed and recorded in spreadsheet format on a personal computer (IBM ThinkCentre M50) with LabVIEW software (Version 7.0; National Instruments, Austin, TX).

Statistical Analysis

The onset threshold for cutaneous vasodilation (Th os) was taken to be the esophageal temperature at which there was a sustained increase in CVC measured on the ventral surface of the forearm, observed in three consecutive 30-s measurement intervals (31, 39). The esophageal temperature at the onset threshold for sweating (Th sw) was identified when a rapid sustained increase in sweat rate was observed in at least three consecutive 30-s measurement intervals (31). Th os and Th sw were assessed by an investigator blinded to the conditions and subjects involved. The sensitivity of the thermal reflex of both skin blood flow and sweating were estimated from the slope of the linear relationship between heat loss response and esophageal temperature for both CVC (CVC sens) and sweat rate (Sw sens). The linear portion of this curve was selected by visual inspection, and the slopes were determined by least squares linear regression analysis (39). For statistical analysis, a three-way mixed ANOVA was employed with the repeated factors of menstrual cycle phase (levels: LP/HH and FP/LH) and exercise (levels: preexercise and postexercise) and the nonrepeated factor of OC pill (levels: OC and non-OC). The dependent variables were the absolute Te s and Th a at Th os and Th sw and the values derived for CVC sens and Sw sens. For ANOVA main effects, Huynh-Feldt corrected statistics are reported where the assumption of sphericity was not met. Post hoc within-subject comparisons were performed using paired sample t-tests, and post hoc between-subject comparisons were performed using independent sample t-tests. The changes in Te s, MAP, and HR data from preexercise rest were analyzed using paired sample t-tests within each cycle phase and pill group at predetermined points throughout the experimental protocol (start of preexercise warming, end of exercise, 15 min postexercise, and start of postexercise warming). Absolute Te s, MAP, and HR data were also compared using between FP and LP (non-OC group) and LH and HH (OC group) with paired sample t-tests, as well as between pill groups (i.e., FP and LH; LP and HH), at baseline resting, and the predetermined points described above using independent sample t-tests. All analyses were performed using the statistical software package SPSS 15.0 for Windows (SPSS, Chicago, IL). The level of significance was set at 0.05, and the α level was adjusted during multiple comparisons so as to maintain the rate of type I error at 5% using Holm-Bonferroni correction.

RESULTS

Baseline resting. Baseline resting Te s was greater (P < 0.05) by 0.18°C (SD 0.08) in the LP relative to the FP in the non-OC group and by 0.17°C (SD 0.06) in the HH phase relative to the LH phase in the OC group (Table 4). However, the magnitude of this Te s difference between phases remained similar throughout the entire protocol in both OC and non-OC groups. No difference was observed in baseline Th a between menstrual cycle phase (P = 0.883) or pill group (P = 0.532). In addition, there was no effect of menstrual cycle phase on CVC (P = 0.747), sweat rate (P = 0.407), MAP (P = 0.214), or HR (P = 0.219), nor was there an effect of pill group on CVC (P = 0.478), sweat rate (P = 0.928), MAP (P = 0.680), or HR (P = 0.111).

Start of preexercise warming phase. Similar to the baseline resting period, Te s was greater (P < 0.05) by 0.16°C (SD 0.13) in the LP relative to the FP in the non-OC group and by 0.19°C (SD 0.06) in the HH relative to the LH phase in the OC group before the warming phase that preceded exercise (Table 4). No difference was observed in Th a between menstrual cycle phase (P = 0.805) or pill group (P = 0.405). No difference was observed in MAP between menstrual cycle phase (P = 0.267) or pill group (P = 0.621) or in HR between menstrual cycle phase (P = 0.255) or pill group (P = 0.161). In addition, CVC and sweat rate were also not different between FP/LH and LP/HH (P > 0.05) (Table 4). Once the preexercise warming phase began, thresholds for the onset of cutaneous vasodilation and sweating and the subsequent thermal sensitivities for these
heat loss responses were measured. These data are provided in later sections.

Exercise followed by 15-min postexercise. We employed a 30-min cycling bout at 75% of each participant’s predetermined V̇O₂peak to produce a postexercise decrease in MAP. At the end of exercise, MAP was elevated in all conditions (P < 0.05). However, as soon as the postexercise period began, MAP reduced rapidly such that it was below baseline resting (P < 0.05) after 2-min recovery (Fig. 2). After 15-min postexercise, MAP was below baseline resting by 8 mmHg (SD 2) and 10 mmHg (SD 2) in the FP and LP, respectively, for the non-OC group and by 9 mmHg (SD 2) in both the LH and HH phases for the OC group. In parallel to these changes in MAP, at the end of exercise Tes, sweat rate, CVC, and HR were all elevated above baseline resting levels (P < 0.05). However, Tes, sweat rate, CVC, and HR (all P < 0.001) rapidly declined as postexercise recovery progressed (Fig. 2). At the end of 15-min recovery, sweat rate and CVC declined to levels approximately one-quarter of the value observed at the end of exercise, despite Tes remaining elevated above baseline resting by 0.45°C (SD 0.11) and 0.53°C (SD 0.07) in the FP and LP, respectively, in the non-OC group and by 0.51°C (SD 0.05) and 0.41°C (SD 0.07) in the HH and LH phases, respectively, in the OC group (all P < 0.001). All variables at all postexercise time points were similar between FP/LH and LP/HH (Fig. 2).

Start of postexercise warming phase. Following the 15-min postexercise recovery period and before the start of the postexercise warming phase, each participant underwent a 15-min bout of clamping mean skin temperature to once again establish baseline resting esophageal and skin temperatures. At the start of the postexercise warming phase, Tes was no longer elevated above baseline resting in any condition, but Tes remained greater by 0.12°C (SD 0.06) in the LP relative to the FP in the non-OC group and by 0.12°C (SD 0.06) in the HH phase relative to the LH phase in the OC group (Table 4). Before postexercise warming, Tsk returned to levels not different to baseline resting values, and no difference was observed in Tsk between menstrual cycle phase (P = 0.734) or pill group (P = 0.353). By the beginning of the postexercise warming protocol, MAP still remained below baseline resting by 7 mmHg (SD 1) and 9 mmHg (SD 1) in the FP and LP groups and by 8 mmHg (SD 1) and 9 mmHg (SD 1) in the LH and HH groups. However, no differences in MAP were observed between cycle phases in either pill group, nor was there any difference between MAP responses between the OC and non-OC group (all P > 0.05). In addition, HR remained elevated above baseline resting values but was not different between menstrual cycle phase or pill group (both P > 0.05). Finally, CVC and sweat rate were not elevated above baseline resting at the start of the postexercise warming phase and were not different between FP/LH and LP/HH (all P > 0.05) (Table 4).

Once the postexercise warming phase began, thresholds for the onset of cutaneous vasodilation and sweating and the subsequent thermal sensitivities for these heat loss responses were once again measured. These data are compared with the data obtained during the preexercise warming period below.

Onset for cutaneous vasodilation (Thv0) during preexercise and postexercise warming phases. Esophageal temperature (Fig. 3) at the onset of increased cutaneous vasodilation (Thv0) was greater following exercise compared with preexercise by 0.19°C (SD 0.10) and 0.26°C (SD 0.08) in the FP and LP, respectively, in the non-OC group and by 0.24°C (SD 0.14) and 0.17°C (SD 0.12) in the LH and HH phases, respectively, in the OC group (P < 0.05). However, the magnitude of the effect of exercise upon Thv0 was not different between phases or pill groups. Within the non-OC group, Thv0 was greater in the LP than the FP by 0.18°C (SD 0.11) preexercise and by 0.24°C (SD 0.14) postexercise (P < 0.05). In the OC group, Thv0 was greater in the HH phase than the LH phase by 0.13°C (SD 0.16) preexercise and by 0.06°C (SD 0.08) postexercise (P < 0.05).

Thermal sensitivity for CVC during preexercise and postexercise warming phases. The sensitivity of the thermal reflex estimated from the slope of the linear relationship between

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### Table 4. Esophageal temperature and hemodynamic responses during baseline resting and start of pre- and postexercise warming for all conditions

<table>
<thead>
<tr>
<th>Variable</th>
<th>FP</th>
<th>LP</th>
<th>LH</th>
<th>OC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tes, °C</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline resting</td>
<td>36.89 ± 0.07†</td>
<td>37.07 ± 0.08</td>
<td>36.86 ± 0.02†</td>
<td>37.03 ± 0.06</td>
</tr>
<tr>
<td>Start of PreEx warming</td>
<td>36.87 ± 0.07†</td>
<td>37.03 ± 0.08</td>
<td>36.84 ± 0.07†</td>
<td>37.03 ± 0.06</td>
</tr>
<tr>
<td>Start of PostEx warming</td>
<td>36.95 ± 0.07†</td>
<td>37.07 ± 0.10</td>
<td>37.01 ± 0.06†</td>
<td>37.13 ± 0.05</td>
</tr>
<tr>
<td>Tsk, °C</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline resting</td>
<td>31.72 ± 0.31</td>
<td>31.69 ± 0.44</td>
<td>31.82 ± 0.266</td>
<td>31.95 ± 0.22</td>
</tr>
<tr>
<td>Start of PreEx warming</td>
<td>32.57 ± 0.18*</td>
<td>32.70 ± 0.20*</td>
<td>32.61 ± 0.13*</td>
<td>32.66 ± 0.16*</td>
</tr>
<tr>
<td>Start of PostEx warming</td>
<td>32.87 ± 0.18*</td>
<td>32.68 ± 0.10*</td>
<td>32.71 ± 0.16*</td>
<td>32.73 ± 0.05*</td>
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<tr>
<td>MAP, mmHg</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline resting</td>
<td>88 ± 1</td>
<td>90 ± 2</td>
<td>90 ± 1</td>
<td>90 ± 2</td>
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<tr>
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<td>89 ± 2</td>
<td>90 ± 1</td>
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<tr>
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<td>81 ± 1*</td>
<td>80 ± 1*</td>
<td>82 ± 1*</td>
<td>80 ± 1*</td>
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<tr>
<td>HR, beats/min</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline resting</td>
<td>64 ± 3</td>
<td>68 ± 3</td>
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<tr>
<td>Start of PreEx warming</td>
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<td>67 ± 3</td>
<td>68 ± 3</td>
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<tr>
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<td>78 ± 4*</td>
<td>82 ± 4*</td>
<td>84 ± 2*</td>
<td>90 ± 3*</td>
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</tbody>
</table>

Values are means ± SE. PreEx, preexercise; PostEx, postexercise; Tes, esophageal temperature; Tsk, mean skin temperature; MAP, mean arterial pressure; HR, heart rate. PostEx MAP for the OC and non-OC groups represents values for n = 6 and n = 7, respectively. *Significant difference from baseline resting; †significant difference from LP (non-OC group) and HH (OC group).
CVC and esophageal temperature was 69.9 (SD 20.1) and 94.7 %CVC_peak/°C (SD 21.4) for the pre- and postexercise warming periods in the LP of the non-OC group. The pre- and postexercise thermal sensitivity for CVC (CVC_sens) in the FP of the non-OC group was 93.6 (SD 17.9) and 87.6 %CVC_peak/°C (SD 17.4). For the OC group, CVC_sens was 79.2 (SD 17.1) and 84.8 %CVC_peak/°C (SD 15.3) during the HH phase and 87.0 (SD 32.0) and 87.4 %CVC_peak/°C (SD 26.5) during the LH phase. CVC_sens was not different between cycle phases (P

Onset for sweating (Th_sw) during preexercise and postexercise warming phases. Esophageal temperature (Fig. 4) at the onset of increased sweating (Th_sw) was greater following exercise compared with preexercise by 0.16°C (SD 0.10) and 0.16°C (SD 0.08) in the FP and LP, respectively, in the non-OC group and by 0.11°C (SD 0.12) and 0.13°C (SD 0.14) in the LH and HH phases, respectively, in the OC group (P < 0.05). However, the magnitude of the effect of exercise upon Th_sw was not different between phases or pill groups. Within the non-OC group, Th_sw was greater in the LP than the FP by 0.27°C (SD 0.16) preexercise and by 0.26°C (SD 0.14) postexercise (P < 0.05). In the OC group, Th_sw was greater in the LP than the FP by 0.10°C (SD 0.25) preexercise and by 0.11°C (SD 0.16) postexercise (P < 0.05).

Thermal sensitivity for sweat rate (Sw_sens) during preexercise and postexercise warming phases. The sensitivity of the thermal reflex estimated from the slope of the linear relationship between sweat rate and esophageal temperature was 2.3 (SD 1.4) and 2.3 (SD 1.1) mg·min⁻¹·cm⁻²·°C⁻¹ for the pre- and postexercise warming periods in the LP phase of the non-OC group. The pre- and postexercise Sw_sens in the FP phase of the non-OC group was 1.8 (SD 1.4) and 1.6 (SD 1.1) mg·min⁻¹·cm⁻²·°C⁻¹. For the OC group, Sw_sens was 1.2 (SD 0.6) and 1.2 (SD 0.5) mg·min⁻¹·cm⁻²·°C⁻¹ during the HH phase and 1.4 (SD 0.4) and 1.6 (SD 0.8) mg·min⁻¹·cm⁻²·°C⁻¹ during the LH phase. Sw_sens not different between cycle phases (P = 0.158) or between pre-
Our findings confirm an elevation in ThVD and ThSW following exercise, with this being more pronounced in the LP compared with the FP. We observed a decrease in the amplitude of the circadian core temperature rhythm is less during the LP compared with the FP. Furthermore, the temperature (mesor or circadian rhythm-adjusted mean) is the same before and after exercise is higher in the LP compared with the FP. It is well-documented that the resting core temperature is elevated during the LP compared with the FP in women during the FP (28, 31). A novel finding of this study is that the upward shift in ThVD and ThSW pre- and postexercise in the LP is most likely not modulated by differences in peripheral afferent stimuli due to endogenous fluctuations of sex hormones. Together, our findings suggest that any effect of the menstrual cycle on vasomotor and sudomotor activity is primarily of a central origin (18).

A postexercise decrease in MAP was observed in both menstrual cycle phases in the upright seated position. Lynn et al. (37) reported a similar pattern of postexercise hypotension in both the FP and LP with no effects of menstrual cycle on postexercise hemodynamics in the supine position. In contrast, Esformes et al. (12) showed that MAP dropped to significantly lower levels during postexercise recovery in the early FP relative to the late FP or mid LP. They concluded that buffering of postexercise hypotension appears to be enhanced in the late FP and mid LP. However, they did not account for differences in baseline resting MAP. It is therefore likely that their reported differences in MAP with phase of menstrual cycle would be less pronounced when comparing relative changes in MAP over time. Lynn et al. (37) observed a similar elevation of core temperature (measured using an ingestible temperature monitoring pill) and rapid decay in arm vascular conductance (sweating was not measured) to baseline resting values in the mid to late stages of supine recovery (i.e., 30 to 90 min of recovery) in both early FP and mid LP. However, they accounted for differences in baseline resting MAP. It is therefore likely that their reported differences in MAP with phase of menstrual cycle would be less pronounced when comparing relative changes in MAP over time.

Fig. 4. Esophageal temperature (Tes) at onset of increased sweating (Thsw) for pre- (solid bar) and postexercise (open bar) heating during both the FP/LH and LP/LH phases for the non-OC and OC groups, respectively. Values are means ± SE. *Significant difference from preexercise; †significant difference from FP/LH.

and postexercise (P = 0.571). In addition, OC use did not influence Sw_sens (P = 0.110).

DISCUSSION

We evaluated the effects of menstrual cycle phase and OC use on the postexercise onset of heat loss responses during a passive heating exposure. The main finding of this study is that neither menstrual cycle nor OC use modifies the magnitude of the postexercise elevation in the onset of local skin vasodilation and sweating during a passively induced hyperthermia. Following exercise, we observed a similar elevation relative to preexercise in both ThVD and ThSW, following exercise in both cycle phases with and without OC use. However, the absolute temperatures of all postexercise thresholds were greater in both the LP and HH. The upward shift of both thresholds due to exercise was paralleled by decreases in MAP, and this response was consistent across all conditions. The sensitivities (slopes of the heat loss responses vs. Tes) did not differ between conditions.

The effect of the normal menstrual cycle (non-OC group). Our findings confirm an elevation in ThVD and ThSW following exercise as previously demonstrated in men (31, 32, 33) and in women during the FP (28, 31). A novel finding of this study is that the postexercise elevation in ThVD and ThSW is similar in both menstrual cycle phases. However, the esophageal temperature at which the onset of skin vasodilation and sweating occurs during passive heating performed before and following exercise is higher in the LP compared with the FP. It is well-documented that the resting core temperature is elevated during the LP compared with the FP in normally menstruating women (10, 14, 27). For example, using an ingestible temperature-sensing pill, Coyne et al. (10), showed that the daily mean core temperature (mesor or circadian rhythm-adjusted mean) is greater during the LP compared with the FP. Furthermore, the amplitude of the circadian core temperature rhythm is less pronounced in the LP compared with the FP. We observed a similar pattern of response. Baseline resting esophageal temperature was ~0.18°C higher in the LP compared with the FP. Although estrogen and progesterone are known to have varying effects on core body temperature response (53, 54), the transient increase in esophageal temperature observed during the LP appears to be related to combined influence of the higher levels of circulating sex hormones, progesterone and estrogen (20, 21).

Some studies have suggested that sweating and skin blood flow are not affected by the phase of the menstrual cycle either in exogenously heated (4, 49) or in exercising women (15). In contrast, others show that the core temperature at which onset of sweating and skin vasodilation occur during rest (7, 16, 20, 22) is higher in the LP compared with the FP when progesterone levels are highest, relative to the late follicular phase when estrogen concentrations are highest (7, 8, 51). It remains unclear, however, if this effect is a sex-steroid-induced change in the J1 central response (action in the brain to change the regulated temperature) (18, 45, 51), 2 locally mediated peripheral response (smooth muscle vascular response) (6), or a combination of both (18, 22). For example, progesterone or one of its metabolites has been shown to decrease the rate of firing of warm-sensitive neurons and increase that of cold-sensitive neurons comparable to a fever-like response (45). In addition to the central modification of body temperature by estrogen and progesterone, estrogen may enhance the vasodilator response to local warming via a nitric oxide-dependent vasodilator response (6, 9). However, in the present study, no differences in thermal sensitivities between FP and LP in the pre- and postexercise periods were observed. This suggests that the upward shift in ThVD and ThSW pre- and postexercise in the LP is most likely not modulated by differences in peripheral afferent stimuli due to endogenous fluctuations of sex hormones. Together, our findings suggest that any effect of the menstrual cycle on vasomotor and sudomotor activity is primarily of a central origin (18).

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women during the early FP (25, 28, 29, 31). Lynn et al. (37) speculated that “exercise appears to reset the threshold for cutaneous vasodilation such that cutaneous blood flow rapidly returns to preexercise levels despite continued elevations in core temperature, thus minimizing the influence of skin blood flow on postexercise hemodynamics”. Our findings support their conclusion in that we demonstrated a postexercise increase in Thvn and Thsw measured during a passively induced hyperthermia. However, we showed that hormonal fluctuations that occur during the menstrual cycle do not affect the magnitude of increase in Thvn and Thsw during a postexercise thermal challenge compared with preexercise. The elevations in Thvn and Thsw observed during the postexercise passive heat stress were therefore likely independent of hormonal changes during a normal menstrual cycle and were possibly the consequence of a nonthermal baroreceptor mechanism as suggested previously (25, 28, 29, 31).

The similar MAP and heart rate response measured during the different menstrual cycle phases suggest that baroreceptor afferent input to the central nervous system may be similar in both menstrual cycle periods. Minson et al. (42) reported a greater sympathetic baroreflex sensitivity and resting muscle sympathetic nerve activity in the LP compared with the FP. However, these observations are based on measurements performed during handgrip exercise to fatigue and 1 min postexercise ischemia in the supine position, whereas our participants performed 30 min of cycle ergometry followed by upright seated recovery. Both exercise type (static vs. dynamic) and postural effects could alter this response (46). Furthermore, whether or not this effect would be maintained in the postexercise period remains to be studied. Enhanced baroreceptor activity could lead to a decrease in cutaneous vascular conductance and a possible influence on blood pressure and heart rate response. Although we did not specifically measure baroreflex activity, we did not see an effect of menstrual cycle phase on postexercise blood pressure response or heart rate during the upright recovery period although we did see a delayed onset of cutaneous vasodilation and sweating during the LP. However, since the magnitude of the upward shift in Thvn and Thsw remained the same between menstrual cycle phases, it appears that baroreceptor function and baroreceptor-mediated influence of postexercise heat loss responses are unaffected by menstrual cycle phase.

**Effect of OC use (OC group).** Our observations are consistent with previous studies indicating that the thermal and hemodynamic responses of OC use are very similar to those of non-OC users. Earlier work by Rothchild et al. (48) demonstrated that endogenous steroids contribute significantly to temperature rhythm during the menstrual cycle. Similar to non-OC users, resting core temperature is higher during the HH phase compared with the LH phase (8, 18, 47). Several studies reveal that fluctuations in exogenous female reproductive hormones estrogen and progesterone during the high (OC pill) and low (placebo) exogenous hormone state alter thermoregulatory effector control (18, 23, 47). For example, it has been reported that the onset for cutaneous vasodilation is elevated during passive heating at rest in the HH compared with the LH (8, 23). The primary mechanism influencing the difference in the skin blood flow response appears to be the result of an altered active vasodilatory response and not an increase in adrenergic vasoconstrictor tone in the HH (8). A similar increase in onset of sweating has been observed during passive heating at rest and during exercise (8, 18, 47). We showed that, during the HH, Thvn and Thsw is elevated compared with the LH. However, the magnitude of this upward displacement was similar during the pre- and postexercise passive heat stress. This indicates that the difference between pre- and postexercise within each phase is independent of exogenous hormone levels.

OC use also did not alter the pattern and magnitude of the postexercise hypotension between the HH and LH. Minson et al. (42) reported that sympathetic baroreflex activity was augmented in the LP of the menstrual cycle, whereas the opposite effect was observed in OC users (43). The decrease in sympathetic baroreflex activity measured during the HH was paralleled by a decrease in MAP. In contrast, we did not observe any difference in MAP response between the LH and HH in the upright seated recovery position. Using a comparable exercise protocol (cycling for 30 min at 60% \( \text{VO}_2 \text{peak} \)) to that of the present study, Birch et al. (2) reported similar findings during supine recovery, suggesting that posture does not influence postexercise hypotension under OC use. However, the source of the apparent disparity between these observations remains to be determined.

**Considerations.** A parallel group design was employed to examine the effects of menstrual cycle phase and OC use on the activation of heat loss responses during a passively induced hyperthermia performed pre- and postexercise. Since different subjects were used to examine these responses during non-OC and OC use, between-subject variation may have confounded our findings making our comparisons between non-OC and OC use groups limited. However, much of this between-subject variation can be eliminated by using a crossover study design in which treatment comparisons are entirely with the same subject. For example, Strachenfeld et al. (53) employed a randomized crossover design to examine the effects of progesterone alone and in combination with estrogen on thermoregulatory control. Subjects underwent a heat stress test during the early FP and the mid LP after 4 wk of combined estradiol-norethindrone OC administration and after 4 wk of progesteronly OC use. A 4-wk washout period was employed between the 4-wk treatment periods. However, due to the prolonged nature of the study design (i.e., 3 mo), it is important to consider and (or) control for such factors as differences in the level of acclimation associated with seasonal changes in ambient conditions, level of physical activity, diet, etc., which may potentially influence thermoregulatory responses.

Although the type and dosage of estrogen and progesterone can modify thermoregulatory control, it has also been suggested that differences in bioactivity of these sex steroids may modulate the response (23). Although we did not control for progestational activity in this study, we show a similar pattern of response in all eight of our subjects using OC with different levels of progestins (Table 2).

Core temperature thresholds for heat loss responses have been shown to have a time-dependent decrease with successive warming procedures (3). Kenny et al. (34) made sequential measurements (i.e., subjects remained seated with no exercise for 45 min before start of second warming period) and actually demonstrated a time-dependent decrease in Thsw and no change in Thvn. A similar response was observed in subjects who underwent the passive heating in the early and late...
morning. Brengelmann et al. (3) also observed a time-dependent decrease in Thsw over a 2-h period. If anything, these data may underestimate the magnitude of the exercise-induced increase in heat loss effector response thresholds in the present study.

Subjects were evaluated in the mid morning and early afternoon, albeit each subject was tested at the same time of day for both experimental trials. Hence, it is possible that the circadian effect on set-point shift and therefore time of day at which the tests were conducted may have had some bearing on the observed results. However, studies show that the circadian temperature rhythm is influenced by the waking time and level of arousal with temperature minimums occurring earlier in morning-type subjects compared with late risers (1, 55). Although we did not attempt to classify our subjects as either morning or afternoon types, we show that the results of those experimental trials conducted at zenith in early afternoon were comparable to those conducted in the late morning.

It is possible that differences in hydration status may explain our observations of a postexercise increase in the onset thresholds for cutaneous vascular conductance and local sweating. Montain and Coyle (44) demonstrated that 2 h of dynamic exercise (65% of maximal VO2) in a warm environment (33°C) with no water intake results in a maximum weight loss of 4.2 kg. A 70-kg adult could potentially lose ~2.5% of water content per hour of heavy exercise in the heat owing primarily to water loss from sweating (40). In our study, the short duration of moderate-intensity exercise performed in a cooler environment (26°C) with unrestricted pretrial and preexercise (i.e., following the first passive heating exposure) water intake caused only a ~0.6% weight loss. Under this condition, our subjects could be considered euhydrated (17).

Perspectives and significance. Recent reports suggest that the attenuation of postexercise vasomotor and sudomotor activity, despite sustained elevations in core and muscle temperatures, may be the result of adjustments of the proportional thermal controller due to nonthermal factors thought to be associated with postexercise blood pressure regulation (25, 29, 30). We show that the normal menstrual cycle and OC use do not appear to influence the overall pattern and magnitude of local cutaneous vasodilation and sweating differently during a thermal challenge performed with or without prior exercise. However, the pre- and postexercise onsets occurred at a higher temperature in the LP and HH. This was not associated with a concomitant change in the postexercise hypotension response. This would suggest that nonthermal factors associated with changes in reproductive hormones modulate central thermoregulatory control of heat loss effector responses similarly during both the preexercise and postexercise periods. However, the greater attenuation of the heat loss responses observed in the LP and HH would result in a reduced potential for heat dissipation giving residual body storage (35). This may lead to an increased risk of exertional heat-related stress and/or injury especially during higher intensity exercise performed in hot conditions. This information can be used to develop better heat management strategies and to reduce the risk of heat injury in female athletes and workers.

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