TITLE: The Effects of Exhaustive Exercise on Thermoregulatory Fatigue During Cold Exposure

TITLE: Blowing Hot and Cold: Protecting Against Climatic Extremes [Souffler le chaud et le froid: comment se proteger contre les conditions climstiques extremes]

The Effects of Exhaustive Exercise on Thermoregulatory Fatigue During Cold Exposure

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Summary

Two experiments were conducted to examine whether acute (one-hour) or chronic exertional fatigue (3-7 days) would impair the thermoregulatory response during subsequent cold exposure thereby leading to an accentuated core temperature reduction compared to when the same individual was exposed to cold in a rested condition. In Study 1, ten men rested for 2 hours during a standardized cold air test (CAT, 4.6°C) following 2 treatments: 1) 60 min of cycle exercise (EX) at 55% $VO_{2\ peak}$ and 2) passive heating (HEAT). EX was performed during a 35°C water immersion (WI) and HEAT was conducted during a 38.2°C WI. The duration of HEAT was individually adjusted (mean = 53 min) so that rectal temperature (T_{re}) was similar at the end of WI in both EX (38.2°C) and HEAT (38.1°C). During CAT following EX, relative to HEAT: 1) T_{re} was lower ($P < 0.05$) from min 40-120, 2) mean weighted heat flow was higher ($P < 0.05$), 3) insulation was lower ($P < 0.05$), and 4) metabolic heat production was not different. In Study 2, thirteen men (10 experimental and 3 Control subjects) performed a cold-wet walk (CW) for up to 6-h (6 rest-work cycles, each cycle one h in duration) in 5°C air on three occasions. One cycle of CW consisted of 10 min standing in the rain (5.4 $cm \cdot hr^{-1}$) followed by 45 min walking (1.34 $m \cdot s^{-1}$, 5.4 $m \cdot s^{-1}$ wind). Clothing was saturated at the start of each walking period (0.75 clo vs. 1.1 clo when dry). The initial CW trial (Day 0, D0) was performed (afternoon) with subjects rested before initiating exercise-cold exposure. During the next 7 days, 4-h of exhaustive exercise (aerobic, anaerobic, resistive) was performed each morning. The subsequent two CW trials were performed on the afternoon of days 3 (D3) and 7 (D7), ~ 2.5-h after the cessation of fatiguing exercise. For the Control group, no exhaustive exercise was performed on any day. Thermoregulatory responses and body temperature during CW were not different on D0, D3, and D7 in the Control group. In the experimental group, mean skin temperature was higher ($P<0.05$) during CW on D7 and D3, than D0. Rectal temperature (T_{re}) was lower ($P<0.05$) and the ΔT_{re} was greater ($P<0.05$) during the 6^{th} hour of CW on D3. Metabolic heat production during CW was similar among trials. These results suggest that prior physical exercise may predispose a person to greater heat loss and to experience a larger decline in core temperature when subsequently exposed to cold air. The combination of exercise intensity and duration studied in these experiments did not fatigue the shivering response to cold exposure.

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Introduction

Exercise has been conjectured to increase an individual's risk of hypothermia during cold exposure (2, 15). However, experimental and clinical evidence for this is largely anecdotal. Over 30 years ago, Pugh (7, 8) concluded that exercise-induced fatigue was an etiologic factor predisposing hikers, climbers, and outdoorsman to hypothermia, but he provided no data demonstrating this belief with a physiological mechanism for this predisposition. Recently, Thompson and Hayward (12) suggested that exercise during cold-wet exposure may fatigue shivering thermogenesis, but their findings did not definitively support their speculation. Others (4, 16) have reported that exercise performed before subsequent cold water immersion exacerbates the fall in core temperature, but these results were inconclusive because pre-immersion core temperature differed between the experiments (4), or a cross-sectional methodology was employed (16). Furthermore, because water has such a high thermal conductivity, peripheral heat loss during cold water immersion may be too pronounced for exercise effects on thermal balance and thermoregulatory effector responses to be detected.

Exercise could increase the risk of hypothermia during subsequent cold exposure due to several reasons. First, exercise might mediate "thermoregulatory fatigue" which would blunt shivering responses and reduce vasoconstriction during subsequent cold exposure. For example, we (17) have observed that a prolonged period of physical exertion coupled with sleep deprivation and negative energy balance resulted in a lowered threshold for shivering despite normal plasma glucose concentrations. Those findings, however, did not allow isolation of the effects of previous exercise from sleep deprivation and negative energy balance. Second, cold exposure immediately after performing leg exercise might result in accentuated heat loss from "thermoregulatory lag". Thermoregulatory responses are aimed at facilitating heat dissipation during exercise in temperate conditions (10) and subsequent cold exposure might mediate a "lag" in switching from heat loss to conservation. Evidence for this might include increased heat loss from areas of active cutaneous vasodilation such as the torso and arms. Third, exercise might mediate greater heat loss during subsequent cold exposure due to "heat redistribution" to active limbs. During exercise, active skeletal muscle increases perfusion and perfusion can remain elevated for extended durations (11) facilitating regional heat loss over these active limbs during exercise (9). Evidence for a "heat redistribution" might include greater regional heat loss over the active limbs (legs) during subsequent cold exposure .

These studies examined whether exercise impairs the body's capability to maintain thermal balance during subsequent cold exposure. It was hypothesized that a greater decrease in core temperature (T_{core}) would occur during cold exposure following either acute (Study 1) or chronic (Study 2) exercise compared to cold exposure preceded by resting. We hypothesized that exercise would mediate some combination of "thermoregulatory fatigue", "thermoregulatory lag", and/or "heat redistribution" which would be manifested as a more rapid cooling rate during cold exposure.

Methods

Study 1

Subjects. Ten, healthy men volunteered to participate in this study as test subjects. Physical characteristics were age, 24.7 ± 1.7 (SE) yr; height, 176.8 ± 2.1 cm; mass, 78.1 ± 3.5 kg; body surface area, 1.93 ± 0.05 m^2; peak oxygen uptake (VO_{2peak}), 46.1 ± 1.3 $ml \cdot kg^{-1} \cdot min^{-1}$; percent body fat, 15.0 ± 1.2 %; and skinfold thickness, 3.2 ± 0.4 mm.

Preliminary testing. Body composition was measured using dual energy x-ray absorbitometry (Model DPX-L, Lunar Corp., Madison, WI). All subjects completed an incremental cycle ergometer test for determination of $VO_{2\ peak}$. Briefly, subjects pedaled at 70 watts for 2 min with the resistance increased by 35 watts every 2 minutes until the subject was exhausted and could no longer maintain the exercise intensity.

Experimental Design. Subjects completed two experimental trials, on separate days, spaced by one week. Subjects refrained from smoking, taking medication, and exercising 12 hours before any testing session. Each trial consisted of a standardized cold air test (CAT) preceded by one of two manipulations: A) exercise (EX), or B) passive heating (HEAT). The EX trial consisted of 60 min semi-recumbent cycle ergometer exercise (EX), immersed to shoulder level in a water immersion pool at 35.0 ± 0.1°C followed by

the CAT. The immersion pool holds ~ 36,000 liters and is controlled within 0.5°C by a temperature control system. Mean exercise intensity was 55.4 ± 2.3 % $VO_{2\ peak}$ for EX. The HEAT trial consisted of sitting in the immersion pool at 38.2 ± 0.0°C until rectal temperature rose to match that at the completion of EX followed by the CAT. This approach precluded using a randomized design and the HEAT trial always followed the EX trial. Immediately following EX or HEAT, subjects toweled off, changed into dry shorts and socks, and were taken to the anteroom of the cold chamber for baseline measurements. This took approximately 20 minutes. Five minutes of baseline data (body temperatures, HR, metabolic rate) were collected outside the cold air chamber (22.8 ± 0.8°C) while the subject sat quietly, and then they rose and walked into the cold air chamber (4.6 ± 0.1°C) and reclined for up to 120 min in a nylon mesh lounge chair. While reclining, the subjects sat quietly and were not allowed to employ behavioral thermoregulation. The trials were all conducted at the same time of day to control for the potential influence of circadian rhythmicity.

Measurements and Calculations. Rectal temperature (T_{re}) was measured by a thermistor inserted 10 cm past the anal sphincter. Integrated heat flow and skin temperature disks (Concept Enginnering, Old Saybrook, CT) were secured at 5 (in water) and 8 (CAT) sites (right side of the body). Mean weighted skin temperature ($\bar{T}_{sk}$) during water immersion was calculated as follows: $\bar{T}_{sk} = 0.28T_{subscapular} + 0.14T_{forearm} + 0.08T_{triceps} + 0.22T_{calf} + 0.28T_{lateral\ thigh}$. During CAT, $\bar{T}_{sk}$ (°C) was calculated as follows: $0.06T_{foot} + 0.17T_{calf} + 0.28T_{lateral\ thigh} + 0.14T_{chest} + 0.07T_{tricep} + 0.07T_{forearm} + 0.14T_{subscapular} + 0.07T_{hand}$. Mean weighted heat flow (HF, $W \cdot m^{-2}$) was calculated as follows: $0.06HF_{foot} + 0.17HF_{calf} + 0.28HF_{lateral\ thigh} + 0.14HF_{chest} + 0.07HF_{tricep} + 0.07HF_{forearm} + 0.14HF_{subscapular} + 0.07HF_{hand}$. Tissue insulation was calculated as follows: $I_T = (T_{re}-\bar{T}_{sk})/HF$ (10). Mean body temperature ($\bar{T}_b$) was calculated as follows: pre-CAT, $\bar{T}_b = 0.8T_{re} + 0.2\ \bar{T}_{sk}$, during CAT, $\bar{T}_b = 0.67T_{re} + 0.33\ \bar{T}_{sk}$ (26). Temperature and heat flow measurements were made continuously using an automated data acquisition system.

Oxygen uptake (VO_2) was measured using an automated metabolic measurement and analysis system (Model 2900, Sensormedics, Yorba Linda, CA) at minutes 0 (baseline) and 30 during the water immersion. During CAT, VO_2 was measured at minutes 0 (baseline), 15, 35, 55, 75, 95, and 115. Metabolic heat production (M, $W \cdot m^{-2}$) was estimated from the VO_2 and respiratory exchange ratio (RER) using the following equation: $M = (0.23[RER] + 0.77) \bullet (5.873)(V\ O_2) \bullet (60/A_D)$ where A_D is body surface area (m^2).

Blood was drawn from an indwelling venous catheter (antecubital) in the left arm before beginning the CAT (min 0) and at minutes 15, 30, 60, 90, and 120 during CAT. Catheter patency was maintained between blood draws by injecting heparinized saline into the catheter. Blood samples were analyzed to determine plasma glucose concentration using an auto analyzer (Model 2300, Yellow Springs Instrument, Inc.) to ensure that subjects maintained euglycemia. Plasma norepinephrine (NE) was determined by gas chromatography.

Statistical Analyses. Data were analyzed using a 2-way repeated measures analysis of variance. When significant F-ratios were calculated, paired comparisons were made post-hoc using Newman-Keuls tests. The slope and threshold of each individuals $\bar{T}_b$ vs. ΔM relationship was determined by least squares linear regression. Paired t-tests were used to determine if differences in slope or intercept data existed between EX and HEAT for $\bar{T}_b$ vs. ΔM. Data are reported as means $\pm$ S.E. Significance was accepted at $p < 0.05$.

Study 2

Subjects. Thirteen subjects participated in this study which was approved by the appropriate Institutional Review Boards. The subjects volunteered after being fully informed of the requirements and risks associated with participating in the research. Ten subjects performed exhaustive exercise (EX group) between cold-wet exposures whereas three volunteers did not (Control group). Subject characteristics were age, 24 ± 1 yr; height, 177 ± 2 cm; weight, 82.8 ± 3.6 kg; % fat, 16.4 ± 1.9%; $\dot{V}O_{2peak}$, 56.0 ± 1.8 $ml \cdot kg^{-1} \cdot min^{-1}$; and body surface area 1.99 ± 0.05 m^2 for the EX group and age, 28 ± 4 yr; height, 170 ± 5 cm; weight, 80.5 ± 8.0 kg; % fat, 20.0 ± 2.0%; $\dot{V}O_{2peak}$, 53.6 ± 3.2 $ml \cdot kg^{-1} \cdot min^{-1}$; and body surface area 1.91 ± 0.10 m^2 for the Control group.

Preliminary testing. Body composition was measured using dual energy x-ray absorbitometry (Model DPX-L, Lunar Corp., Madison, WI). An incremental treadmill test was used for determination of peak oxygen uptake ($\dot{V}O_{2peak}$). Briefly, subjects ran at 9.7-11.3 $km \cdot hr^{-1}$ at a 0% grade for 1.5 min. Thereafter, the grade increased 2% every 1.5 minutes until the subject became exhausted. The one repetition maximum (1-RM) of the upright row, chest press, latissimus dorsi pull-down, and biceps curl was determined for members of the exhaustive exercise group but not the control group. Subjects completed a series of no more than 6, single repetitions as resistance was increased incrementally until the subject could no longer lift the weight correctly. Approximately one minute elapsed between successive 1-RM attempts.

Experimental design. The subjects' body composition, peak oxygen uptake ($\dot{V}O_{2peak}$), and muscle strength were assessed before beginning the experiment. The subjects then completed three experimental cold, wet walks (CW) from ~ 1330-2000 hours when they were well-rested before beginning the heavy exercise regimen (D0), and after 3 (D3) and 7 (D7) consecutive days of exhaustive exercise (EX group) or at the same between trial intervals for the Control group. The purpose of including the Control group was to assess the possibility that three, repeated exposures to cold completed over a one week period would induce habituation or acclimatization to cold, separate from effects of the exhaustive exercise, although their small sample number limits statistical inferences. The Control group refrained from exercising for 24 hours before each CW. On D3 and D7, ~ 2.5 hours (140-170 min) elapsed between the end of the last daily exercise session and the subsequent CW. The CW was modified from an experimental protocol described by Weller et al. (14). Briefly, CW consisted of 360-min intermittent treadmill walking (six cycles of 10-min standing rest in the rain, 45-min walking, 5-min for transition between rest and walking) in an environmental chamber with air temperature set at 5°C. During the rain, the subjects stood still for 10 min (except for the initial cycle of rain, during which they sat) and were wetted at a rate of 5.41 $cm \cdot hr^{-1}$ under a sprinkler designed to simulate rainfall. Following each rest/rain period, subjects walked at 1.34 $m \cdot s^{-1}$ (3 mph) at 0% grade on a motor-driven treadmill. Wind velocity was 1.1 $m \cdot s^{-1}$ (2.5 mph) during the 10-min rain and 5.4 $m \cdot s^{-1}$ (12 mph) while walking. The CW for each subject was terminated if the rectal temperature was < 35°C, or if the subject asked to stop.

Each subject consumed one US Army Meal-Ready-to-Eat (1260 ± 29 kcals) 1.5 hr before each CW. During the rest/rain portion of each cycle (not including the first cycle), 250 ml of a commercial carbohydrate drink (Gatorade®, Quaker Oats, Barrington, IL) was consumed to help subjects maintain normal plasma glucose concentrations throughout CW. Before beginning CW, baseline measurements of temperature, oxygen uptake and thermal sensation were obtained in an anteroom outside the environmental chamber (22°C) for 20-min. Volunteers were tested in groups of 3-4 people. Clothing for each subject consisted of a US Army Battle Dress Uniform (cotton shirt, cotton-nylon jacket, cotton-nylon pants, cotton-nylon hat with ear flaps, socks, gloves, leather boots; clo = ~1.1). Additionally, during the rain, the subjects wore a 100% nylon rain hat and nylon boot gaiters. The clo value, following the rain, for a completely wetted uniform was 0.75 clo.

The exhaustive exercise routine for days 1-7 consisted of the following activities each day: running & sprinting (hiking substituted on D3 & D7), weightlifting, ergometry, and an anaerobic power test. Subjects ran 4.8 km at their personal best and sprinted 800 m three consecutive times. Weightlifting consisted of one set of repetitions to exhaustion on four different resistance exercises (row, chest press, lat pull-down, biceps curl), each at 70% of the one repetition maximum. Aerobic exercise consisted of four consecutive 20 min sets of stair-stepping (Stepmill, Stairmaster Corp., Seattle, WA), rowing (Concept II, Concept II Inc., Morrisville, VT), treadmill walking (substituted for rowing on D3 and D7), upright cycling (Model HRT-2000A, Preference), and semi-recumbent cycling (Model HRT-2000R, Preference), all at ~ 65% $\dot{V}O_{2peak}$. This percentage was estimated from the VO_2-HR relationship derived during the determination of $\dot{V}O_{2peak}$. A 5-min rest was allowed between bouts. One 30-sec anaerobic test (Wingate test) was performed on a cycle ergometer (CardioO_2, Ergometrix Corp., Minneapolis, MN) and concluded each exhaustive exercise session. Subjects' pedaled as fast as they could for 30-sec with resistance set at 5.8 $J \cdot rev^{-1} \cdot kg^{-1}$. Hiking (substituted for running and sprinting on D3 and D7) consisted of a 9.7 km hike over varied terrain at ~6.4 $km \cdot hr^{-1}$, carrying a 9.1 kg backpack. Exhaustive exercise was performed from 0900-1300 h (D1, D2, D5, D6) or 0700-1100 h (D3, D4, D7). Subjects were provided a carbohydrate-electrolyte beverage to drink *ad libitum* during the exhaustive exercise regimen.

Measurements and calculations. Rectal temperature (T_{re}) was measured every minute using a thermistor inserted 10 cm past the anal sphincter. Skin temperature (T_{sk}) was measured using thermistor disk sensors (Concept Engineering, Old Saybrook, CT) attached on the skin surface at five sites (ventral aspect of forearm, tricep, subscapula, anterior thigh, and calf). Mean weighted skin temperature (T_{sk}) was calculated as: $T_{sk} = 0.28T_{subscapular} + 0.14T_{forearm} + 0.08T_{triceps} + 0.22T_{calf} + 0.28T_{thigh}$. Heart rate (HR) was measured near the end of each walking portion of the CW from three chest electrodes (CM-5 configuration) and radiotelemetered to an oscilloscope-cardiotachometer (Hewlett-Packard). Oxygen uptake ($\dot{V}O_2$), carbon dioxide output, and minute ventilation were measured by open-circuit spirometry before CW (sitting) and during the 25-27th min of walking during each exercise portion of the rest-walking cycle. Additionally, in four subjects from the EX group and the three Control group subjects, expired air was collected immediately following the rain portion of each cycle to evaluate shivering thermogenesis during rest. Percent oxygen (Applied Electrochemistry S-3A), carbon dioxide (Beckman LB-2), and volume (Tissot Spirometer, Collins) were measured from a 1.5-min collection of the subjects' expired air into a Douglas Bag. Metabolic heat production ($\dot{M}$, $W \cdot m^{-2}$) was estimated from the $\dot{V}O_2$ and respiratory exchange ratio (RER) using the following equation: $\dot{M} = (0.23[RER] + 0.77) \bullet (5.873)(\dot{V}O_2) \bullet (60/A_D)$ where A_D is body surface area (m^2). Whole body insulation (I) was calculated using the following equation: $I = (T_{re}-T_{sk})/\dot{M}$. Self-reported dietary and sleep records were kept each day beginning the day before the first CW and continuing through day 7.

Blood samples for determination of serum glucose and plasma catecholamines were collected after the subject sat quietly for 20 min on D0, D3, and D7 at 0700-h, before CW (~1315-h, glucose only), and 20-min following CW (post-CW) from an indwelling cannula in an antecubital vein. Plasma and serum were separated using a refrigerated centrifuge. Serum glucose was measured on an auto-analyzer (Model 2300, Yellow Springs Instrument, Inc., Yellow Springs, OH). Plasma catecholamine concentrations were measured with mass spectroscopy-gas chromatography. Plasma volume changes were determined from hemoglobin and hematocrit measurements.

Statistical analyses. Data were analyzed using a 2-factor (time X experimental trial) repeated measures analysis of variance. When significant F-ratios were calculated, paired comparisons were made post-hoc using Fisher's least significant difference test. Because exposure duration varied for each subject among the 3 trials, statistical analysis was performed on complete data sets for all three trials. For the EX group, data from 10 subjects were analyzed from 0-180 min and data from 4 subjects were analyzed for 360 min. For the Control group, data from the 3 subjects were analyzed for 240 min. There were missing data points at various points due to difficulty drawing blood samples from subjects during cold exposure. Therefore, catecholamine data were analyzed with t-tests between D0 and D3 and between D0 and D7. Unless otherwise specified, the level of significance for differences reported is $P < 0.05$. Data are presented as mean ± S.E.

Results

Study 1

Water Immersion. All subjects completed 60 min of cycling during EX. The mean immersion time required during HEAT to match the T_{re} rise observed during EX was 53.4 ± 5.0 min. The mean T_{re} at the end of the immersion periods were 38.19 ± 0.14°C and 38.08 ± 0.10°C, during EX and HEAT, respectively ($P > 0.05$). The average VO_2 ($L \cdot min^{-1}$) during immersions were 1.97 ± 0.12 and 0.34 ± 0.02, for EX and HEAT, respectively ($P < 0.05$). For EX, this VO_2 corresponded to 55.4 ± 2.3% of the measured $VO_{2\ peak}$. Final heart rates ($beats \cdot min^{-1}$) during immersion were 149.3 ± 6.1 and 102.1 ± 3.1, for EX and HEAT, respectively ($P < 0.05$). Weight loss (kg) from sweat was 1.07 ± 0.15 and 1.06 ± 0.18 during EX and HEAT, respectively ($P > 0.05$).

Rectal temperature (CAT). During the transition from the immersion pool to the cold air chamber, T_{re} fell during HEAT. Therefore, T_{re} at min 0 was slightly, but significantly higher (0.14°C, $P < 0.05$) in EX vs. HEAT (Figure 1). By the 10th min of cold air exposure, differences between trials were no longer apparent. However, by the 40th min of CAT, T_{re} had fallen lower ($P < 0.05$) during EX compared to HEAT and the difference between trials grew larger as exposure continued to the 120th min. The cooling rate ($°C \cdot h^{-1}$) from min 10 to the end of the exposure was faster ($P < 0.05$) for EX (-0.64 ± 0.07) than HEAT (-0.57 ± 0.04).

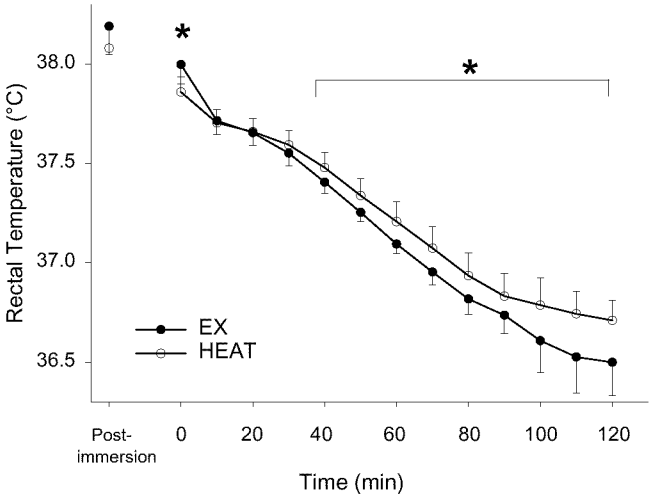

Figure 1. Rectal temperature vs. time for Exercise (●, EX) and Passive Heating (○, HEAT) experiments during cold air exposure. Values are mean ± SE. * Exercise significantly different than Control at specified times. Post-immersion denotes temperature at the end of the water immersion.

Heat flow (CAT). HF was higher ($P < 0.05$) during CAT in EX vs. HEAT (Figure 2). Also I_T during CAT was lower ($P < 0.05$) in EX compared to HEAT (Figure 2).

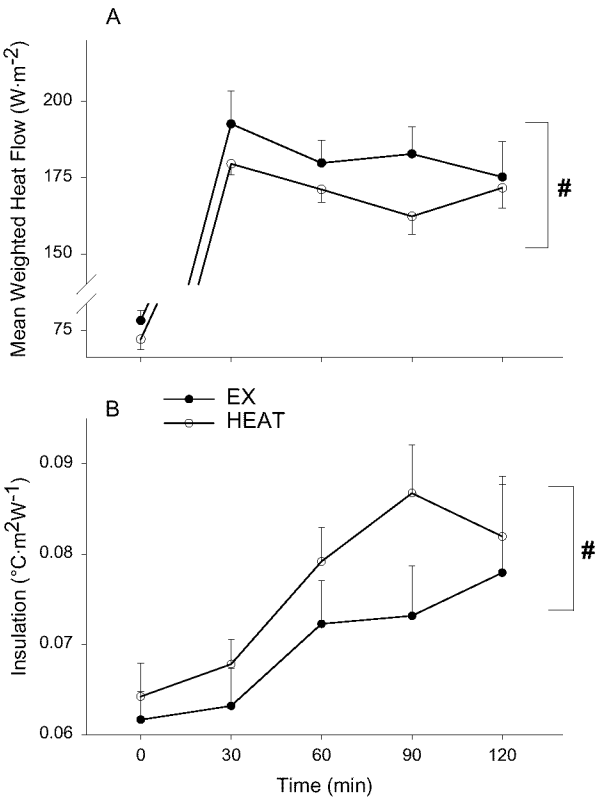

Figure 2. Mean weighted heat flow (A) and insulation (B) vs. time for Exercise (●, EX) and Passive Heating (○, HEAT) experiments during cold air exposure. Values are mean ± SE. #, main effect, Exercise significantly different than Control, P<0.05.

Individual site HF and I_T are presented in Figure 3. Calf HF and I_T demonstrated a significantly ($P < 0.05$) greater HF and lower I_T between EX and HEAT. Hand HF also tended ($p = 0.06$) to be higher in EX.

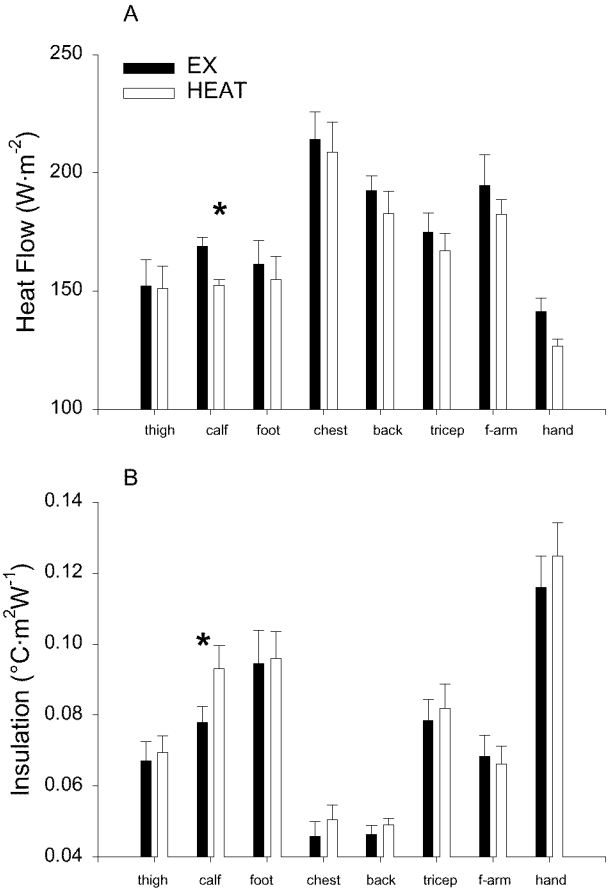

Figure 3. Individual heat flow (A) and insulation (B) for the 8 sites measured. Calf heat flow was higher ($P < 0.05$) and insulation lower ($P < 0.05$) during EX. Values are mean ± SE.

Metabolic heat production & heat debt (CAT). M did not differ between EX and HEAT at any time throughout CAT. The final M at min 115 was 146.6 ± 6.5 and 136.1 ± 3.6 $W \cdot m^{-2}$ for EX and HEAT, respectively. The relationships (slope and intercept) between mean body temperature ($\bar{T}_b$) and the corresponding increment in metabolic heat production over pre-CAT values (Δ M, a measure of shivering thermogenesis) did not differ between trials. Slopes ($W \cdot m^{-2} \cdot °C^{-1}$) were -33.8 ± 3.0 and -32.7 ± 3.4 for EX and HEAT, respectively. Intercepts (°C) were 34.5 ± 0.2 and 34.3 ± 0.1 for EX and HEAT, respectively.

Plasma glucose, norepinephrine (CAT). Plasma glucose concentrations were not affected by CAT in either trial and there were no differences between trials. Glucose values averaged between 4-6 $mmol \cdot L^{-1}$ throughout CAT. Plasma norepinephrine concentrations increased from 2.5 $nmol \cdot L^{-1}$ to 10-15 $nmol \cdot L^{-1}$ during cold air exposure, with no differences between EX and HEAT.

Study 2

Exercise Duration, Cold Tolerance, Food and Sleep Diaries.

Six subjects (4 in EX group; 2 in Control group) completed 360 min in all 3 cold exposure trials. The other 6 subjects in the EX group completed a minimum of 180 min in all three trials and the average time completed for the trials in these subjects was 305 ± 24, 281 ± 23, and 287 ± 25 minutes for D0, D3, and

D7, respectively. The third subject in the Control group completed 240 min in all three trials. One subject sustained a foot injury on Day 5 and did not participate in the Day 7 cold exposure. The main reasons for not completing all 6 hours during CW included hip flexor cramping and/or leg pain and overall body stiffness. Mean daily sleep reported ranged from 6.6-7.8 hours per night for the duration of the study. Mean body mass (kg), for all subjects, at the beginning of D0, D3, and D7, respectively, was 81.6 ± 3.2, 81.6 ± 3.2, and 81.3 ± 3.1. Mean daily caloric intake reported throughout the experiment was 2656 ± 94 kcal·day^{-1}.

Temperature Regulation Responses (EX Group).

Rectal temperature. Rectal temperature was significantly higher during the first 2 hours (n = 10, F = 3.67, P < 0.001) and significantly lower in the 6th hour of cold exposure (n = 4, F = 2.02, P < 0.001) on D3 compared to D0 (Figure 4). T_{re} was also significantly higher in the 2nd and 3rd hours (n = 10) of cold exposure on D7, compared to D0, with no difference between these trials for the last three hours (n = 4) of exposure. The change in T_{re}, relative to the initial T_{re} at time 0 was significantly greater (F = 3.68, P < 0.001) during the 6th hour of cold exposure on D3 compared to D0.

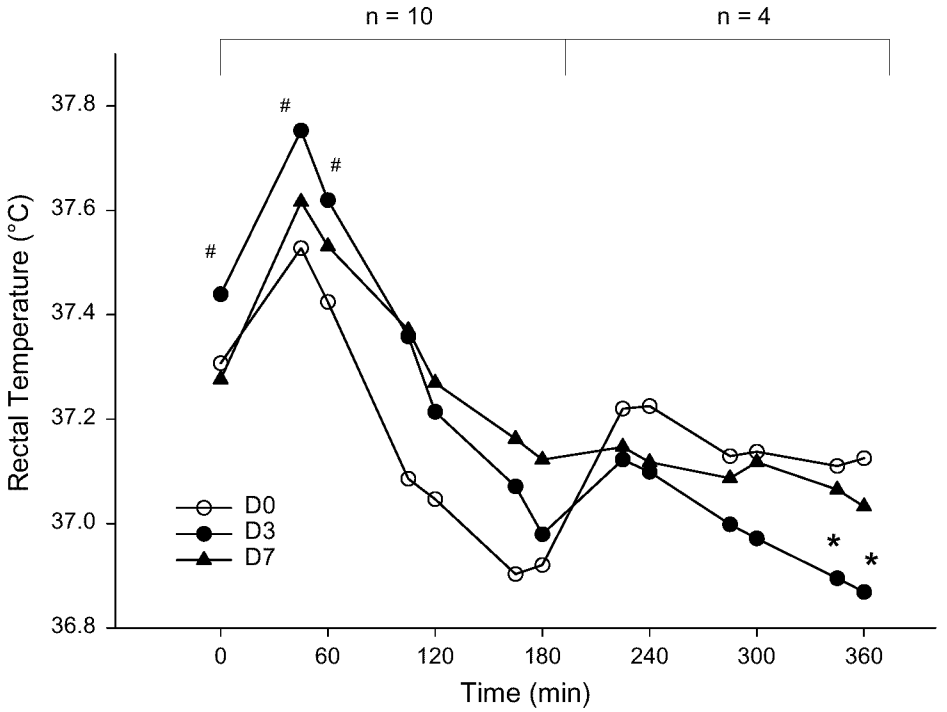

Figure. 4. Rectal temperature vs. time during cold exposure before (D0, ○), after 3 days (D3, ●) and after 7 days (D7, ▲) of physical exertion. Data from min 0 to min 180 are from 10 subjects and data from min 190 to min 360 are from 4 subjects. *, D3 significantly (P < 0.05) different than D0; ‡, D3 and D7 significantly (P < 0.05) different than D0; #, D3 significantly (P < 0.05) different than D0 and D7.

Skin temperature. Mean skin temperatures were significantly higher (F = 3.17, P < 0.001) on D7 and D3, vs. D0, from the 1st to 6th hour of cold exposure (Fig. 5). The change in mean skin temperature (ΔT_{sk}, a quantifier of the magnitude of vasoconstrictor response) was significantly less (F = 3.17, P < 0.001) in the 2nd and 3rd hours (n = 10) on D7, vs. D0 and D3. The ΔT_{sk} for the 3rd through 6th hours was significantly less on both D7 and D3, compared to D0. Forearm skin temperature changes during the first 3 hours of cold exposure demonstrated a significantly smaller fall (F = 1.63, P < 0.05) in forearm skin temperature on D3 and D7, vs. D0, and the fall in calf skin temperature during the same time period was also significantly less (F = 2.35, P < 0.001) on D7, vs. D0 and D3.

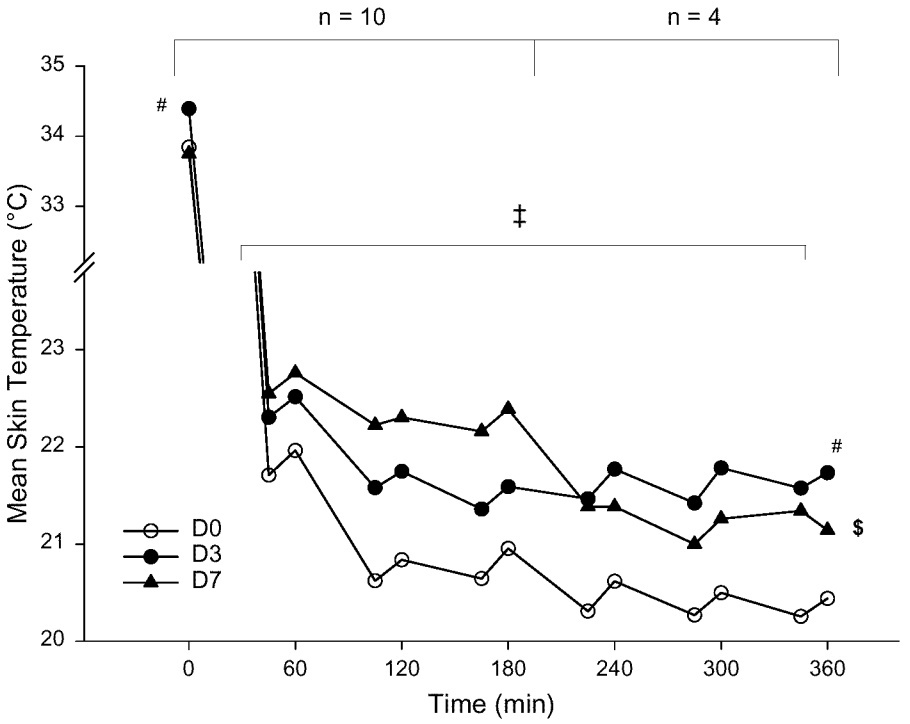

Figure. 5. Mean skin temperature vs. time during cold exposure before (D0, ○), after 3 days (D3, ●) and after 7 days (D7, ▲) of physical exertion. Data from min 0 to min 180 are from 10 subjects and data from min 190 to min 360 are from 4 subjects. ‡, D3 and D7 significantly (P < 0.05) different than D0; #, D3 significantly (P < 0.05) different than D0 and D7; $, D7 significantly (P < 0.05) different than D0.

Metabolic heat production, insulation, heart rate, thermal sensation. Metabolic heat production increased from rest during all 3 cold exposures with no differences among trial days. A higher metabolic heat production was observed during the rest/rain periods through the 3rd rain period on D3, vs. D0 and D7. Whole body insulation was less ($F = 11.62$, $P < 0.01$) on D3 and D7, vs. D0, during the last three hours of cold exposure. Forearm insulation was lower ($F = 8.33$, $P < 0.01$) on D3 and D7, compared to D0, and there were no differences among days for calf insulation. Heart rate was significantly higher (main effect, $F = 4.52$) on D3 compared to D0 during the first 3 hours of cold exposure. Heart rate was similar before and during the first 3 hours of exercise-cold stress. Thermal sensation was similar among trial days during cold exposure.

Blood Responses.

Serum glucose concentrations averaged between 4.5-6 $mmol \cdot L^{-1}$ throughout the study, with no significant differences between groups, trials or measurement times. No hypoglycemia (< 2.7 $mmol \cdot L^{-1}$) was observed. Plasma volume expanded on D3, relative to D0, 15.8 ± 7.1% and on D7, relative to D0, 15.2 ± 5.4%. Plasma catecholamine concentrations measured at 0700-h (basal) and after cold exposure are presented in Fig. 6. Catecholamine concentrations at baseline (0700-h) were corrected for plasma volume changes. Plasma norepinephrine was significantly higher at 0700-h on D3 and D7, compared to D0. Plasma norepinephrine increased significantly ($F = 11.61$, $P < 0.02$) during all three CW, but there were no differences in post-exposure NE concentration among trials. Cold exposure elicited a 3 to 4 fold increase in plasma epinephrine; however there were no differences among trials at 0700-h or post-CW (Fig. 6).

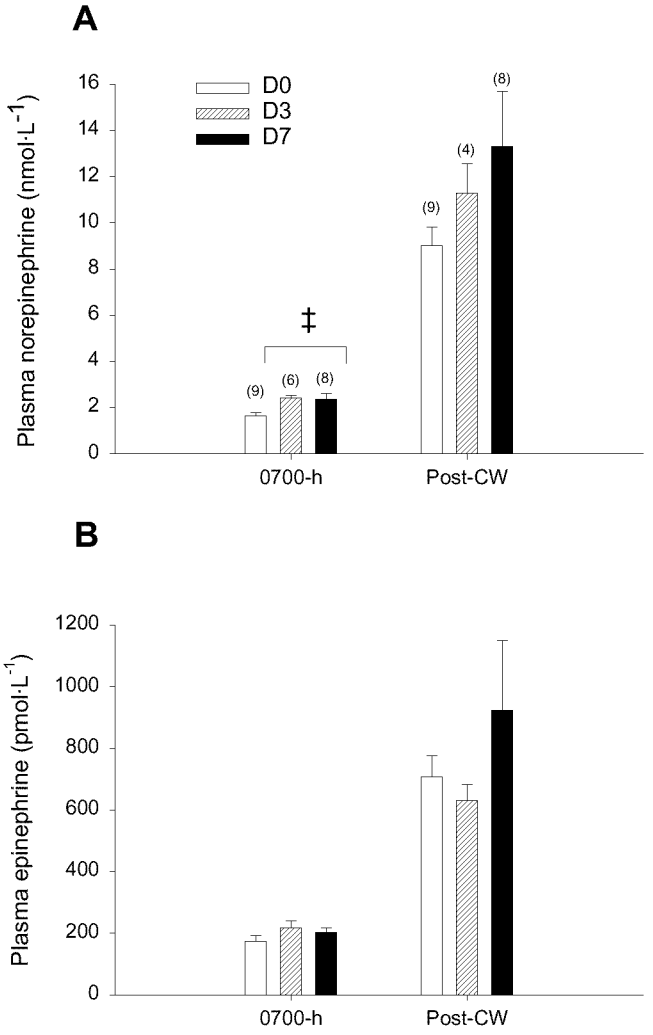

Figure. 6. Plasma norepinephrine (A) and epinephrine (B) concentrations at 0700-h (baseline) and after cold exposure (Post-CW) before (D0), after 3 days (D3) and after 7 days (D7) of exhaustive exercise. Number of subjects for each timepoint for norepinephrine and epinephrine is indicated in parentheses. ‡, D3 and D7 significantly different ($P < 0.05$) than D0.

Discussion

The primary finding from these studies was that when individuals exercised before cold exposure, they cooled faster than when rest preceded cold exposure. However, the data are not consistent with our hypothesis that exercise would lead to "thermoregulatory fatigue" of the shivering response to cold. We had based that hypothesis on our own finding (1) and those reported by others (7, 8, 12) suggesting that shivering can become fatigued. In this study, the shivering response to cold was the same whether or not acute or chronic exercise preceded the cold exposure. In contrast, mean weighted heat flow and skin temperature measurements were higher and, concomitantly, tissue insulation less during cold exposure following exercise. Collectively, these observations indicate that, following either acute or chronic exercise, greater peripheral heat loss from the skin ("thermoregulatory lag" and/or "heat redistribution") was responsible for the greater cooling rates during cold exposure.

Several factors might explain why peripheral heat loss and mean skin temperatures during cold exposure were greater when preceded by acute or chronic exercise. One possibility is that post-exercise

hyperemia in the leg muscles persists during cold exposure, increasing convective heat transfer from the body's core to the periphery overlying active muscle relative to cold exposure preceded by rest ("heat redistribution"). The higher heat flow and lower insulation in the calf during cold exposure following exercise in Study 1, compared to passive heating, are consistent with this explanation. However, the higher skin temperatures observed in Study 2 during cold exposures completed after seven days of exhaustive exercise do not likely represent the "heat redistribution" mechanism. In Study 1, resting cold exposures were completed shortly after (20 min) exercise, so effects of a persistent post-exercise hyperemia would be pronounced compared to the other trial in which resting cold exposures were not shortly preceded by exercise. In Study 2, subjects performed standardized exercise of the same intensity during all the cold exposures, so muscle blood flow, and thus heat redistribution, should have been constant among trials. Thus, we believe that our observations indicate that fatigue induced by exhaustive exercise may indeed blunt the vasoconstrictor response during cold exposure, although the possibility that post-exercise hyperemia contributes to higher skin temperatures cannot be ruled out.

Another possibility is that the prior exercise blunted the sympathetic drive for vasoconstriction normally elicited in response to cold ('thermoregulatory lag"). However, in Study 1, the norepinephrine response to cold was the same whether cold exposure was preceded by exercise or passive heating. In contrast, following chronic exercise (Study 2), the blunting of the vasoconstrictor response to cold subsequent to severe physical exertion may be related to concomitant elevations in basal circulating norepinephrine levels. Opstad (5) has observed higher circulating norepinephrine levels in soldiers following multiple days of exhaustive exercise coupled with sleep deprivation, and Young et al. (17) reported similar effects in soldiers who had just completed an 8-week training course that entailed heavy physical exertion throughout coupled with sleep deprivation and negative energy balance. In this study, we observed that basal norepinephrine levels were elevated in our subjects after three and seven consecutive days of exercise. Despite the elevation of basal norepinephrine concentrations, cold exposure elicited similar sympathetic activation during all three cold exposures, as evidenced by the increment in norepinephrine concentrations observed by the end of each of the cold exposures, the magnitude of which did not differ among trials. Stimulation of adrenergic receptors mediates cold-induced vasoconstriction. Since the increment in norepinephrine was similar during all three cold exposure trials, a blunted sympathetic nervous stimulus does not appear to account for the less pronounced vasoconstrictor response. A diminished sensitivity of the adrenergic receptors remains as a viable mechanism to explain blunting of cold-induced vasoconstriction observed in the present experiments. Chronically elevated norepinephrine levels have been shown to decrease adrenergic receptor sensitivity in animal models (13) and similar effects have been suggested to develop in humans in whom circulating norepinephrine levels remain chronically elevated (5).

The absence of an exercise effect on shivering thermogenesis in both experiments suggests that this response to cold is not easily fatiguable. We observed no difference in the $\bar{T}_b$ vs. ΔM relationship between trials suggesting that the differences in T_{re} between trials were not due to a change in central control of shivering thermogenesis. In Study 1, perhaps the exercise intensity and duration were not sufficient to fatigue the shivering mechanism, which is a relatively low intensity activity, at least compared to exercise. In Pugh's case report of the Four Inn's Walk (7), the participants were exercising up to 20-h in cold-wet conditions. Likewise, the subject in Thompson and Hayward's study (12) who developed shivering fatigue was exercising for 4-h in severe cold-wet conditions. We modeled this exposure in Study 2 and still did not observe shivering fatigue. Another possibility is that shivering impairments observed in these earlier studies may not reflect fatigue, but rather hypoglycemia, which is known to impair shivering (3, 6). Plasma glucose levels were not measured in those previous studies (7, 12). In our studies, plasma glucose concentrations remained normal throughout cold exposure. It may be that exhaustive exercise must be coupled with other factors such as sleep deprivation or caloric deprivation before this thermoregulatory effector response is blunted.

Many subjects, during the chronic exercise experiment, were unable to continue walking for 6 hours in the cold-wet conditions due to muscle cramping (n = 4), leg and knee pain (n = 2), and general muscle stiffness (n = 1). If these volunteers were subjected to wet-cold conditions in a scenario where they could not escape the cold after discontinuing exercise, shivering alone would be insufficient to offset heat loss, and core temperature would fall. Weller et al. (14) and Thompson and Hayward (12) demonstrate this elegantly in their studies when exercise intensity decreases during prolonged cold-wet exposure. Thus, physical

exertion affects the ability to maintain normal body temperatures during cold exposure via both direct (i.e. impairing thermoregulatory response-vasoconstriction) and indirect (impairing capacity to increase metabolic heat production) mechanisms.

In conclusion, this series of studies examined the effects of acute (one hour) and multiple days of exhaustive exercise on temperature regulation during prolonged cold exposure. Our findings demonstrate that following either type of physical exertion, the vasoconstrictor response to cold exposure is blunted, perhaps due to a fatigue-related mechanism. In contrast, shivering thermogenesis appears less sensitive to the effects of previous physical exertion. Increases in peripheral heat loss during prolonged cold-wet exposure associated with impaired vasoconstrictor responses to cold would eventually exacerbate the fall in core temperature, if metabolic heat production is unchanged, thereby increasing susceptibility to hypothermia. These findings have implications for individuals, such as hikers, military personnel, and outdoor workers, who are exposed to cold-wet environments and have been engaged in heavy, fatiguing exercise.

Disclaimer

The views, opinions and/or findings in this report are those of the authors and should not be construed as official Department of the Army position, policy, or decision unless so designated by other official designation. Human subjects participated in these studies after giving their free and informed voluntary consent. Investigators adhered to AR 70-25 and USMRDC Regulation 70-25 on Use of Volunteers in Research.

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