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Physiological Responses of Exercised-Fatigued Individuals Exposed to Wet-Cold Conditions

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Physiological responses of exercised-fatigued individuals exposed to wet-cold conditions

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Tikusis, P., M. B. Ducharme, D. Moroz, and I. Jacobs. Physiological responses of exercised-fatigued individuals exposed to wet-cold conditions. *J. Appl. Physiol.* 86(4): 1319–1328, 1999.—Thirteen healthy and fit men [age = 27 ± 8 (SD) yr, height = 177 ± 5 cm, mass = 75 ± 7 kg, body fat = $14 \pm 5\%$, maximal O_2 consumption = 51 ± 4 ml·kg⁻¹·min⁻¹] participated in an experiment designed to test their thermoregulatory response to a challenging cold exposure after 5 h of demanding mixed exercise during which only water was consumed. Subjects expended $7,314 \pm 741$ kJ on cycling, rowing, and treadmill-walking machines, performed $8,403 \pm 1,401$ kg·m of mechanical work during resistance exercises, and completed 120 inclined sit-ups. Subjects then assumed a seated position in a 10°C air environment while wearing shorts, T-shirt, rain hat, and neoprene gloves and boots. After 30 min the subjects were showered continuously with cold water (~ 920 ml/min at 10°C) on their backs accompanied by a 6 km/h wind for up to 4 h. Blood samples were taken from the nondominant arm every 30 min during the exposure and assayed for energy metabolites, hormones, indexes of hydration, and neurotransmitters. Counterbalanced control trials without prior exercise were also conducted. Blood insulin was higher during the control trial, whereas values of glycerol, nonesterified fatty acids, β -hydroxybutyrate, lactate, cortisol, free triiodothyronine, and thyroxine were lower. Three subjects lasted the maximum duration of 4.5 h for control and fatigue trials, with final rectal temperatures of 36.43 ± 0.21 and $36.08 \pm 0.49^\circ\text{C}$, respectively. Overall, the duration of 172 ± 68 (SD) min for the fatigue trial was not significantly different from that of the control trial (197 ± 72 min) and, therefore, was not affected by the preexposure exercise. Although duration was positively correlated to body fatness and shivering intensity, the latter was not correlated to any physical characteristic or the fitness level of the individual.

shivering; hypothermia; thermoregulation; heat debt; rectal temperature

THE PRIMARY PHYSIOLOGICAL responses to cold exposure in defense against hypothermia are vasoconstriction to reduce heat loss and shivering to generate heat. The latter is especially important with regard to the prediction of survival time (25, 26), particularly if the individual's ability to generate additional heat through exercise is limited. The metabolic substrates that fuel shivering have been estimated (12), but it is not known at what point their availability limits shivering. Shivering exhaustion has been implicated as a probable factor in several hypothermic deaths of individuals (e.g., hikers) caught unprepared for wet-cold exposures. Pugh (22)

and, more recently, Weller et al. (30) showed that when exercise metabolism is reduced, the increase in shivering may be insufficient to prevent a decrease in deep body temperature.

Another recent study involving wet-cold exposure was reported by Thompson and Hayward (24). Subjects walked outdoors at an air temperature of 5°C under a dry condition for the 1st h and were exposed to cold rain for up to an additional 4 h. Of the 18 subjects who participated, 5 lasted the full duration, and they experienced a mean drop of $\sim 1.2^\circ\text{C}$ in rectal temperature (T_{re}) over a period of 2 h after the rain began. The initial period of deep body cooling was followed by 1 h of stabilization and a subsequent drop in T_{re} over the last hour of $\sim 0.4^\circ\text{C}$. Interestingly, the metabolic rate (MR) during the last hour did not rise as expected because of further decreases in body temperatures (25, 26). Whether this indicates a degradation in shivering response is uncertain. One subject who failed to complete the full duration experienced an abrupt cessation of shivering after 2.5 h in the rain followed by a rapid drop in T_{re} . The investigators termed this event "shivering fatigue." It is not known whether this event would have occurred with other subjects had they been tired at the start of the wet-cold exposure and, if so, at what level of tiredness.

Pugh (22) reported a very rapid drop in T_{re} in one cold-exposed subject who had exercised to the point of exhaustion and then rested. Unfortunately, there is insufficient evidence to quantify the influence of the exercise with this drop in T_{re} . Furthermore, Pugh did not ascertain any relationship between T_{re} and shivering metabolism in the wet-cold condition.

The above studies suggest that exercise fatigue might impair shivering response. What is not known is the extent of this impairment, if it indeed exists, in terms of shivering intensity and endurance. There are ample studies that characterize the shivering response of well-rested individuals exposed to cold (9, 27, 29), but only very recently has one involved exercise-fatigued individuals. In that study (31) the cold stress (limbs and torso cooling via a liquid-conditioned suit) evoked a modest 1.9-fold increase in total metabolism, which was unaffected by prolonged exercise (arm and leg ergometry at 60 and 75% of maximum effort to exhaustion) before the exposure. It is not known whether differences in shivering response would have been observed with a more stressful cold exposure [auditory canal temperature dropped by only $\sim 0.1^\circ\text{C}$, and mean-weighted skin temperatures (T_{sk}) remained above 28°C over the 90 min of exposure].

In addition to the above uncertainties, an important component not measured in any of the wet-cold studies

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cited earlier is the actual heat loss experienced by the subjects. Without this information, it is not possible to ascertain the subject's heat debt, except indirectly through changes in body temperature, as attempted by Weller et al. (30). Although heat loss was measured in the subsequent study of Weller et al. (31), no heat debt analysis was conducted. To address these uncertainties, thorough thermoregulatory measurements should be made on individuals exposed to a stressful wet-cold condition after a fatiguing exercise. A sedentary vs. exercise condition during the cold exposure would also facilitate the isolation of shivering metabolic heat production from the total heat production.

The primary purpose of this study was to determine the effects of exercise fatigue on shivering response (intensity and endurance) and the resultant heat debt during a very stressful sedentary wet-cold exposure. Although no effect was found in the study of Weller et al. (31), where the cold stress was moderate, it was hypothesized that an effect would be found with a much higher level of cold stress designed to evoke near-maximal shivering intensities. A second objective was to examine the variability of shivering responses between subjects in an attempt to understand the diverse outcomes of accidental cold exposure victims.

The prolonged aerobic and resistance exercises used in this study were chosen to approximate demanding outdoor activities involving several different muscle groups (e.g., hill walking, climbing, cycling, rowing). It is recognized that muscle recruitment during these exercises differs from that during shivering; however, the focus is on the type of exercise fatigue that outdoor enthusiasts might experience. No attempt is made to identify the mechanism of fatigue or the contribution of muscle fatigue vs. muscle damage toward any measured effect on shivering response. Shivering fatigue is defined here as a progressively decreasing rate of

metabolic heat production during continuous exposure to cold. Finally, postexercise exposure conditions were chosen to simulate the potential for lethal hypothermia.

Two trials are involved, one with preexposure exercise (Fatigue) and the other without (Control), so that shivering responses can be compared using a repeated-measures design. This represents a departure from most studies (except Ref. 31), where the main effect tested between trials was the exposure condition vs. the preexposure status of the individual.

METHODS

Subjects. Thirteen fit, nonsmoking men were recruited to participate in the experiment. Subjects were fully informed about the procedures and risks according to institute human experimentation ethics guidelines and signed a volunteer consent form. The first visit to the laboratory began with a medical examination and proceeded with baseline measurements. These included physical characteristics such as mass (Wt), height (Ht), percent body fat [BF via hydrostatic weighing (4)], and maximum aerobic power ($\dot{V}O_{2max}$) and heart rate (HR_{max}) with use of a standard exercise test to exhaustion on a treadmill and one repetition maximum (1 RM; i.e., maximum weight lifted in 1 continuous movement) on five different weight-lifting apparatuses. The physical characteristics of the subjects are summarized in Table 1.

During the second visit to the laboratory, the subjects underwent a familiarization trial with the laboratory setting and test procedures (see below). Subsequent visits were the Control and Fatigue trials counterbalanced to avoid any ordering effects. All trials were spaced 1 wk apart, and subjects were required to observe the following restrictions: abstain from alcohol for 48 h before a trial, not exercise within 24 h of a trial, consume a normal dinner the night before, have a normal sleep, consume an unrestricted but typical breakfast before arrival at the laboratory for each trial, and avoid donating blood for 30 days before a trial. The contents of the breakfast foods were recorded, and their caloric values

Table 1. Physical characteristics of subjects listed individually and by group

Subject No./Group	Age, yr	Wt, kg	Ht, m	SA, m ²	BF, %	HR _{max} , beats/min	$\dot{V}O_{2max}$, ml·kg ⁻¹ ·min ⁻¹
01	31	74.5	1.70	1.89	15.9	213	55.9
02	29	75.4	1.75	1.93	13.3	203	57.0
03	38	81.1	1.85	2.05	18.5	183	49.0
04	35	91.0	1.76	2.13	21.3	190	42.0
05	21	72.7	1.83	1.93	10.8	195	53.5
06	43	83.0	1.69	1.99	22.0	181	47.4
07	19	65.7	1.72	1.78	13.7	216	51.3
08	20	77.3	1.78	1.96	13.7	204	48.5
09	29	68.0	1.76	1.83	12.3	175	54.0
10	19	73.6	1.79	1.92	9.2	204	48.5
11	20	69.0	1.78	1.85	12.1	198	54.9
12	19	68.9	1.80	1.86	14.1	205	49.7
13	32	70.3	1.83	1.89	5.7	185	55.7
G60 (13)	27.3 ± 8.2	74.7 ± 7.1	1.77 ± 0.05	1.92 ± 0.09	14.0 ± 4.6	196 ± 13	51.3 ± 4.3
G90 (11)	27.6 ± 8.5	75.6 ± 7.3	1.76 ± 0.05	1.93 ± 0.10	14.8 ± 4.2	197 ± 13	51.1 ± 4.5
G120 (10)	28.4 ± 8.6	76.2 ± 7.4	1.76 ± 0.05	1.94 ± 0.10	15.1 ± 4.3	196 ± 14	50.7 ± 4.5
G150 (7)	30.9 ± 8.7	77.6 ± 8.2	1.76 ± 0.06	1.96 ± 0.11	16.5 ± 4.3	197 ± 14	50.8 ± 5.2
G180 (6)	32.8 ± 7.7	79.6 ± 6.9	1.76 ± 0.07	1.98 ± 0.09	17.0 ± 4.5	194 ± 12	50.8 ± 5.7
G210 (4)	33.3 ± 4.0	80.5 ± 7.6	1.77 ± 0.06	2.00 ± 0.11	17.3 ± 3.4	197 ± 13	51.0 ± 7.0
G270 (3)	32.7 ± 4.7	77.0 ± 3.6	1.77 ± 0.07	1.95 ± 0.08	15.9 ± 2.6	200 ± 15	54.0 ± 4.3

Values are means ± SD. SA, body surface area; BF, body fat; HR_{max}, maximum heart rate; $\dot{V}O_{2max}$, maximum O₂ consumption. Group designations are G_m(n), where m is exposure time (in min) and n is number of subjects.

were subsequently estimated (18). Subjects were also instructed to conduct the same routine before each trial and to inform the investigators of any change in their routine or health status.

Exercise phase. Aerobic exercises were conducted on cycling, rowing, and treadmill-walking machines for 1 h each but were separated by additional 1-h sessions of resistance exercises for a total of ~5 h of demanding exercise. The aerobic exercises began with a warm-up, and work rates were raised within 5 min to a steady-state level requiring 80% of the subject's HR_{max} . Heart rate was monitored (Polar Vantage NV, Polar Electro, Port Washington, NY) and recorded every 5 min, and, if necessary, the work rate was adjusted to maintain consistency. The subject was given water to drink ad libitum; if at the end of each exercise their body mass was still less than their initial value, they were required to consume an amount of water equivalent to this difference to maintain hydration. No other drink or food was consumed during the entire trial (including the cold exposure phase).

The two sessions of the resistance exercises each consisted of three rotations of five standardized weight lift stations plus sit-ups. Leg extension, bench press, lat pull downs, leg flexions, and arm curls were performed at ~70% of the subject's 1 RM (80% for leg extension) to fatigue. If necessary, weight adjustments were made so that the number of repetitions was close to 10 at each station. After each rotation of the five lifts, the subject performed 20 sit-ups on a 6° inclined board. The subject also rested for at least 90 s between exercise stations.

Exercise during the familiarization trial involved 15-min periods on each of the aerobic machines at the work rates and order specified above, including two sessions of single rotations of resistance exercises (one to reestablish the subject's 1 RM and another at protocol intensities outlined above). Subjects were then fully instrumented for the cold exposure familiarization. This involved 30 min each of dry-cold and wet-cold exposures.

Subject preparation/instrumentation for cold exposure. Immediately after the exercise phase or beginning in a well-rested state for the Control trial, subjects dressed down to standardized dry T-shirts and shorts provided by the laboratory. After self-insertion of a rectal probe (400 series, Baxter Healthcare, Valencia, CA) 15 cm past the anal sphincter, the subjects were instrumented with 12 heat-flow transducers [Concept Engineering, Old Saybrook, NJ; see Eq. 2 for locations and Ducharme et al. (6) regarding recalibration], bipolar electrocardiogram electrodes (Quinton Instrument, Bothell, WA) over the chest for electrocardiogram measurements, and electromyogram (EMG) electrodes (Neuro Supplies, Waterford, CT) 4 cm apart over the vastus lateralis and pectoralis majoris muscles for EMG activity. All EMG signals were amplified, full-wave rectified, smoothed with a 20-ms time constant (MBS 4P-AX Electromyography System, Moroz Biomeasurement Systems, Dundas, ON, Canada), and continuously recorded. Subjects then performed three maximum voluntary isometric contractions (MVC) of each muscle using standard testing procedures described in detail elsewhere (2) to establish the maximum EMG signal. This and the lowest resting value were used to normalize the EMG activity measured during shivering. Finally, an intravenous catheter was inserted into the antecubical vein of the nondominant arm for multiple blood sampling. The elapsed time between the end of exercise and the end of instrumentation was ~1 h.

Subjects then sat quietly for 30 min in a thermoneutral condition (~22°C room air), their O_2 consumption ($\dot{V}O_2$) and CO_2 production ($\dot{V}CO_2$) were measured during the final 10 min by means of open-circuit indirect calorimetry with a meta-

bolic cart (model OCM-2, Ametek, Pittsburg, PA), and a 10-ml venous blood sample was drawn. To avoid unnecessarily cold extremities and excessive discomfort during the wet-cold exposure, the subjects were given neoprene gloves and boots and a rain hat following the example of Pugh (22). Any resultant decrease in total body heat loss due to the added insulation would be minimal because of vasoconstriction of the extremities; the benefit would be an expected increase in subject tolerance time. Subjects were then covered with a blanket, walked into the cold chamber, and took a seated position on a webbed chair. After the sensors were connected to the data-acquisition system for monitoring and recording measurements every minute (28), the blanket was removed and the cold exposure began.

Cold exposure phase. If differences in shivering intensity between rested and fatigued individuals were to occur, then the fatigue level before exposure or the shivering stimulus must be higher and/or longer than that applied in the study of Weller et al. (31), where no effect was found. Hence, in choosing the latter option, the key challenge was to evoke a high shivering response without incurring too rapid a rate of heat debt to cause early termination of the trial in all subjects. Consequently, the subject was first exposed to calm air at 10°C for 30 min, and then his back was exposed to a 6 km/h wind and a 10°C water shower at ~920 ml/min for the remainder of the trial lasting up to an additional 4 h. The initial 30-min dry-cold exposure provided a smoother transition between thermal comfort and the more stressful wet-cold exposure and an opportunity to compare responses.

During each 0.5 h (including the initial dry-cold exposure), the following measurements were taken: hand-grip strength with a dynamometer (Takei Kiki Kogyo) at 5 min and between 20 and 30 min and a blood sample at 25 min. In addition, cognitive performance tasks were conducted between 5 and 18 min (unpublished observations). The trial ended if requested by the subject, if 4 h of the wet portion of the exposure elapsed, or if T_{re} reached 35.0°C. No peripheral temperature withdrawal criterion was considered, given that the ambient temperature was 10°C and the subject's hands and feet were protected. On termination of the trial, the subject was rewarmed in a hot bath of circulating 40°C water, and normal body temperature was usually recovered within 30 min with no untoward effects aside from tiredness.

Blood samples. The blood samples (10 ml) drawn from a venous catheter in the antecubical vein were assayed for energy metabolites [glucose, lactate, nonesterified fatty acid (NEFA), glycerol, and β -hydroxybutyrate (β -OH)], hormones (insulin, glucagon, epinephrine, norepinephrine, and cortisol), indexes of hydration (Hb and hematocrit), neurotransmitters (dopamine and serotonin), and thyroid hormones [thyroid-stimulating hormone, triiodothyronine (T_3 and free T_3), and thyroxine (T_4 and free T_4)]. The subject was continuously infused through the catheter with a slow warm drip saline solution to maintain the ability to draw blood from the forearm vein.

Calculations and statistical analyses. Body surface area (SA, m^2) was estimated using the regression formula based on mass (kg) and height (m) derived by Gehan and George (8)

$$SA = 0.1644 \cdot Wt^{0.51456} \cdot Ht^{0.42246} \quad (1)$$

The aerobic energy expenditures on the cycle and rowing machines were estimated according to the conversion

$$MR \text{ (kcal/min)} = 1.714 + 0.01036 \cdot \text{mechanical work (kpm/min)} \quad (2)$$

regressed from Astrand and Rodahl (1), where the mechanical rate of work was recorded every 5 min. Energy expenditure on the treadmill was calculated using the formula of Pandolf et al. (19). The mechanical work performed during the resistance exercises (in kg·m) was estimated by multiplying the weight lifted by its displacement.

The mean-weighted heat flux (HF) from the body was based on the 12-point Hardy-DuBois formula (11)

$$HF = \sum_{i=1}^{12} a_i \cdot HF_i \quad (3)$$

where a = 0.07 (forehead), 0.0875 (scapula, chest, abdomen, lower back), 0.14 (lower upper arm), 0.05 (hand), 0.095 (front thigh, back thigh), 0.065 (shin, calf), and 0.07 (foot). Respiratory heat losses (Q_r) were based on the subject's minute ventilation (\dot{V}) (5)

$$Q_r = \rho \cdot \dot{V} \cdot (c_a + \gamma_i \cdot c_v) \cdot (T_e - T_i) + \rho \cdot \dot{V} \cdot \lambda \cdot (\gamma_e - \gamma_i) \quad (4)$$

where ρ is the density of air, λ is the latent heat of vaporization, c is the specific heat (subscripts a and v refer to the air and vapor, respectively), T is temperature (subscripts e and i refer to the expired and inspired air, respectively), and γ is the humidity ratio. The MR (in W) was computed from $\dot{V}O_2$ and $\dot{V}CO_2$ according to Peronnet and Massicotte (20)

$$MR = (281.65 + 80.65 \cdot RER) \cdot \dot{V}O_2 \quad (5)$$

where RER is the respiratory exchange ratio ($\dot{V}CO_2/\dot{V}O_2$) and \dot{V} is in l/min STPD. The average value measured during the last 10 min of each 30-min period of cold exposure is assumed to represent the entire 30-min period.

The rate of heat storage (S) was determined from the difference between heat production and heat loss

$$S = MR - HF - Q_r \quad (6)$$

Negative values imply a heat debt. Finally, the normalized EMG activity due to shivering was obtained from (2)

$$\%EMG_{shiv} = 100 \cdot \frac{EMG - EMG_{rest}}{EMG_{MVC} - EMG_{rest}} \quad (7)$$

where the unsubscripted EMG is a 30-min average of the integrated value during the cold exposure and the subscripts rest and MVC refer to the resting and MVC values measured before the exposure, respectively. Values represent the average activity of the two muscle sites, vastus lateralis and pectoralis majoris.

All data analyzed represent values during or at the end of each 30-min period of the exposure. Because the durations of exposure varied due to early termination, data were grouped according to these durations. For example, the first group includes all the subjects' data up to the earliest termination point, and the second group includes data from only those subjects who lasted until the next termination point. The last group includes data from subjects who completed the 4.5 h of total cold exposure. Note that data in any one group are contained in all previous groups. Also, the data entry for each subject only extends as long as the interval for which there were data from Control and Fatigue trials.

Values are means \pm SD unless otherwise noted. A one-factor (trial) paired t -test and a two-factor (trial \times duration) ANOVA for repeated measures (Control vs. Fatigue) were used to analyze the data (SuperANOVA, Abacus Concepts, Berkeley, CA). The significance of differences is $P \leq 0.05$ (Greenhouse-Geisser adjustment). Regression analyses were

also applied to test for significant correlations among various variables.

RESULTS

Preexposure. Subjects consumed $\sim 2,433 \pm 682$ kJ of food during breakfast before the experiment. The targeted heart rate of 80% of maximum was achieved in the cycle and treadmill-walking exercises during the Fatigue trial, with corresponding mean energy expenditures of $2,654 \pm 406$ and $3,065 \pm 452$ kJ, respectively. These correspond to ~ 67 and 69% of maximum effort if it is assumed that $\dot{V}O_{2,max}$ achieved with cycle exercise is 90% of that achieved with running (18). Subjects had a more difficult time maintaining the same exercise intensity on the rowing machine, achieving 74.4% of HR_{max} and $1,629 \pm 251$ kJ. The total aerobic expenditure was $7,314 \pm 741$ kJ.

There was a significant decrease in the resistance exercises performed during the second session compared with the first, except for sit-ups, where every subject completed 20 on each rotation. The total amounts of mechanical work performed during the two sessions were $4,051 \pm 1,385$, 974 ± 316 , $1,468 \pm 294$, $1,287 \pm 291$, and 623 ± 203 kg·m for the leg press, bench press, lat pull, leg flexion, and biceps curl, respectively. Although the energy expenditure associated with resistance exercise is small compared with the aerobic work, the main impact of the resistance exercises was muscle fatigue and possibly muscle damage.

Duration, thermal, and metabolic variables. Subject complaints were greater during the Fatigue exposure, and terminations by subject request occurred sooner in some cases, although there was no overall significant difference ($P = 0.071$) in the duration of the exposure for the subjects between Control (197 ± 72 min) and Fatigue (172 ± 68) trials. Figure 1 shows the duration of the subjects in both trials; note that T_{re} reached the

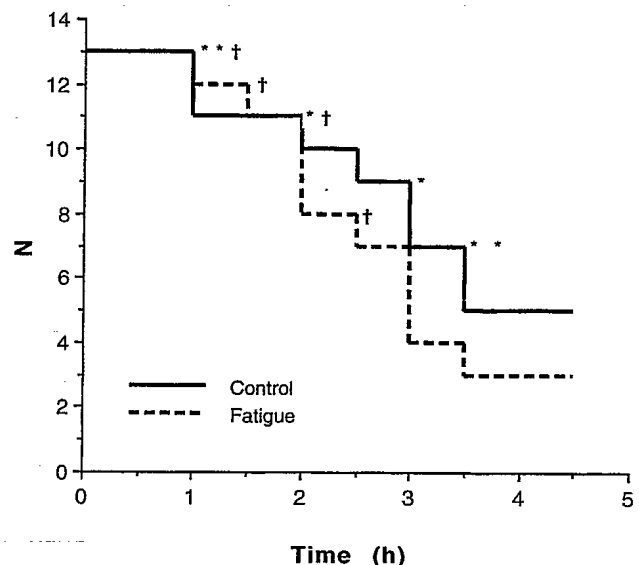


Fig. 1. Number of subjects (n) plotted against duration of exposure. * and † Termination of Control and Fatigue trials, respectively, when rectal temperature (T_{re}) reached $35.0^{\circ}C$.

termination point of 35°C in six subjects during Control and in four during Fatigue. A total of eight trials (6 during Fatigue) were terminated early because of subject request due to intolerable discomfort (cramping and/or headache). The resultant number of subjects (n) in the various data groups (e.g., G60 denotes subjects that completed 60 min of total exposure) for subsequent statistical analyses were as follows: 13 for G60, 11 for G90, 10 for G120, 7 for G150, 6 for G180, 4 for G210, and 3 for G270. The trend of increases in age, mass, SA, and BF from G60 through G210 indicates a shift away from leanness with increasing duration.

Regression analyses indicated that duration was correlated positively to body fatness ($r = 0.716$) and to the MR during exposure ($r = 0.653$), but not to $\dot{V}O_{2\max}$. The multiple regression [duration = $-79.5 + 9.96 \cdot \%BF + 0.859 \cdot MR$ (W/m^2), $r = 0.862$] was also significant. Duration was also found to be correlated to body mass index ($BMI = Wt/Ht^2$) and SA/Vol (where Vol = $Wt/body\ density$); however, because each of these variables is closely correlated to body fatness ($r = 0.839$ and 0.862 , respectively), they provide no additional information. Also no significant differences between trials were found in the overall rate of change in T_{re} or the steepest drop in T_{re} over a 15-min period.

Figure 2 shows T_{re} over time for each subject during the Control trial. The rapid drop in T_{re} observed in subjects 12 and 13 is attributed to a combination of moderate-to-low body fatness (14.1 and 5.7%) and a low MR (average 91.4 and 67.2 W/m^2 , respectively). The resultant rates of heat debt (-123 and -142 W/m^2) were the highest among the subjects. In contrast, four of the five subjects who completed 4.5 h of total cold exposure had higher body fatness (15.9 vs. 22%) and much higher MR (147.1 vs. 216.4 W/m^2). The one exception was subject 02, whose body fatness was 13.3%; however, his MR was also high (180.3 W/m^2). The highest individual average MR (232.1 W/m^2) was

observed in subject 05, but this was insufficient to prevent his core temperature from reaching 35°C, which is attributed to a low BF content (10.8%). With a slightly lower BF content (9.2%) and lower but still relatively high MR (188.5 W/m^2), subject 10 reached the termination point of 35°C even earlier.

The two-factor ANOVA indicated a significant main effect of duration in all cases except for T_{re} (G60), RER (G60 and G90), and grip strength (G60, G210, and G270). The initial transient rise in T_{re} is a common characteristic of the response to cold and is responsible for approximately no net change over the 1st h. A significant main effect of trial was found for RER and HR in all groups and in the following cases: EMG (G150, G180, and G210), T_{re} (G60), T_{sk} (G60, G90, G150, and G180), and grip strength (G60 and G120). The significant increase in HR for the Fatigue trial is attributed to postexercise recovery (15). In the case of T_{sk} , values were higher during Fatigue, likely because of a postexercise increase in blood flow concomitant with the increased HR. The resultant increased blood flow to muscle tissue combined with the likelihood of greater muscle heat content would enhance the dissipation of heat to the skin. The reduced grip strength during Fatigue was expected, and although it was significant for only two groups, the tendency for a reduction was consistent throughout and concurs with the findings of Thompson and Hayward (24). EMG activity correlated with the MR during the Fatigue trial ($r = 0.744$), but not during Control, where an unexplained decrease in EMG activity occurred between 2.5 and 4 h of exposure.

No trial differences were found for $\dot{H}F$, $\dot{V}O_2$, MR, and S . Figure 3 shows all the thermal variables plus grip strength plotted against time. A small but insignificant difference in T_{re} appears in some of the subject groups; however, this difference was present at the start of the exposure (significant for G60) and was essentially

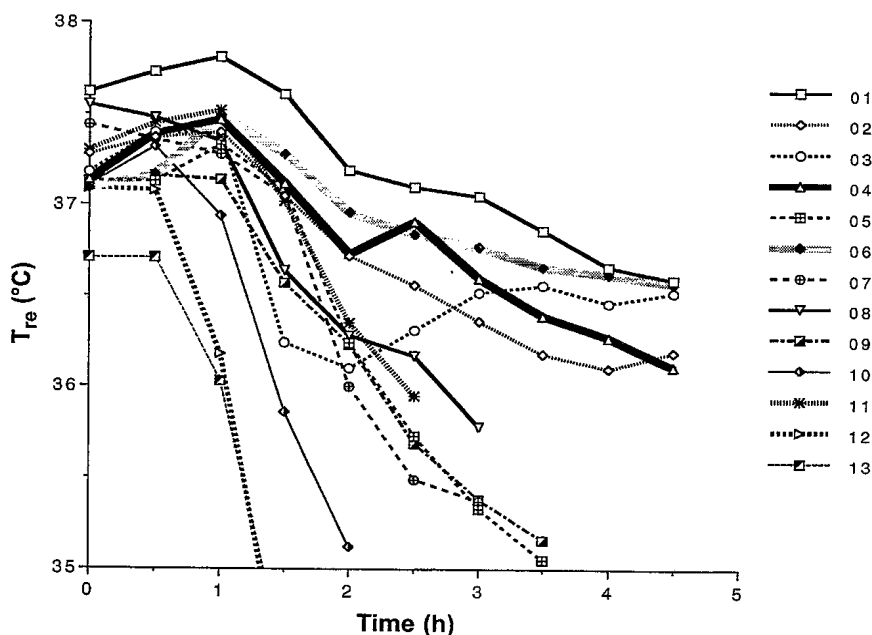


Fig. 2. T_{re} plotted against time of exposure for each subject (01-13, see Table 1) during Control trial. Thin, medium, and thick lines refer to different levels of body fatness (<10%, 10-20%, and >20%, respectively).

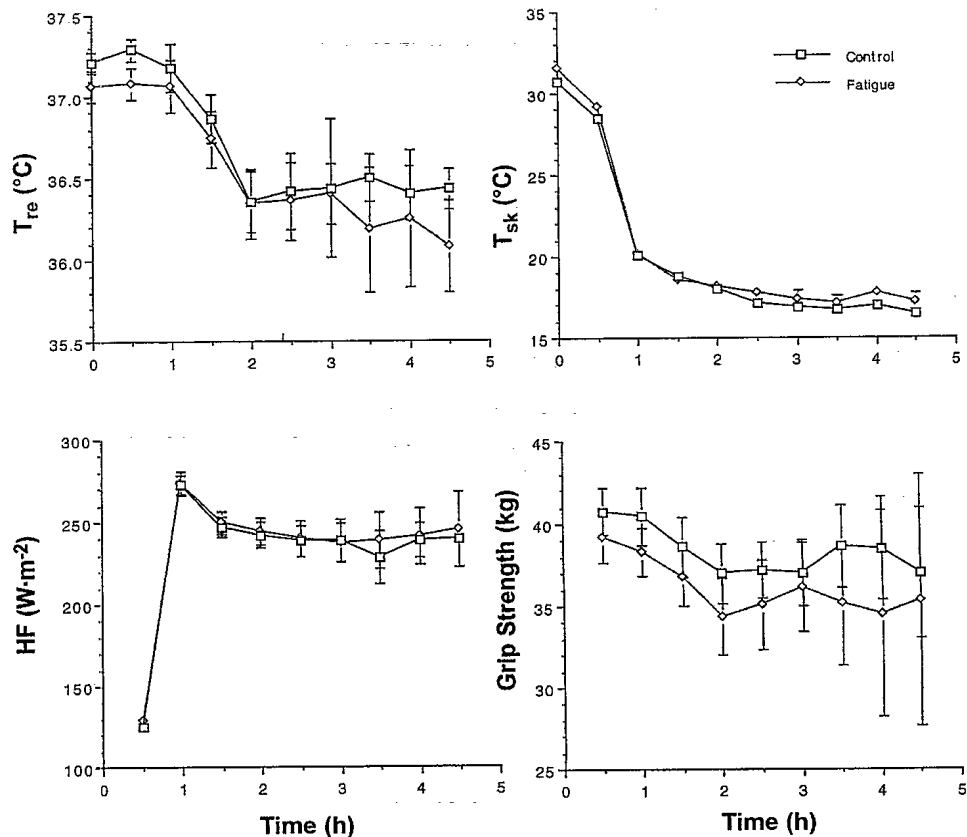


Fig. 3. Thermal variables and grip strength plotted against time of exposure for each trial. Points correspond to different data groups (G) depending on duration as follows: G60 ($n = 13$) for 0, 0.5, and 1.0 h; G90 ($n = 11$) for 1.5 h; G120 ($n = 10$) for 2.0 h; G150 ($n = 7$) for 2.5 h; G180 ($n = 6$) for 3.0 h; G210 ($n = 4$) for 3.5 h; and G270 ($n = 3$) for 4.0 and 4.5 h. Values are means \pm SE. HF, heat flux; T_{sk} , skin temperature.

carried throughout. Figure 4 shows all the metabolic-related variables plotted against time. \dot{V} is not shown but was matched with $\dot{V}O_2$. Clearly, the dry-cold exposure during the first 0.5 h was not nearly as stressful as the subsequent wet-cold exposure, as indicated by the marked increases in $\dot{V}O_2$ and MR and decrease in S . The differences in RER between the trials were not sufficient to cause differences in MR, which are attributed to the relative insensitivity of MR to the value of RER (i.e., a change of ± 0.1 from a reference value of 0.85 causes a change of only $\pm 2.3\%$ in MR; see Eq. 4).

Blood samples. Preexposure blood samples were obtained from all subjects in both trials. Blood concentrations for the Control and Fatigue trials were as follows (means \pm SD; * indicates a significant difference; Table 2): hematocrit = 45.0 ± 1.8 and $44.9 \pm 2.1\%$, Hb = 15.8 ± 1.0 and 15.5 ± 0.8 g/dl, insulin* = 11.67 ± 7.38 and 4.68 ± 1.11 μ U/ml, glucagon = 101.4 ± 17.8 and 109.9 ± 27.7 pg/ml, glycerol* = 0.041 ± 0.018 and 0.106 ± 0.051 mmol/l, NEFA* = 0.44 ± 0.27 and 1.63 ± 0.42 mmol/l, β -OH* = 0.14 ± 0.09 and 2.20 ± 1.37 mmol/l, glucose* = 4.01 ± 0.31 and 3.40 ± 0.47 mmol/l, lactate* = 0.772 ± 0.304 and 0.864 ± 0.168 mmol/l, cortisol* = 9.97 ± 4.15 and 15.68 ± 4.39 μ g/dl, T_3 = 1.68 ± 0.17 and 1.62 ± 0.13 ng/ml, free T_3 * = 4.98 ± 0.90 and 6.53 ± 1.67 pg/ml, T_4 * = 6.62 ± 1.36 and 8.00 ± 1.75 μ g/dl, and free T_4 = 1.64 ± 0.26 and 1.57 ± 0.22 ng/dl.

Despite the application of a warm saline solution through the venous catheter, blood sampling during the exposures was incomplete because of the vasoconstrictic-

tion experienced by several subjects, especially those of lower BF. Consequently, the ANOVA of the blood samples does not necessarily include data of all times up to the durations noted in Table 2, which summarizes the results. In addition, the number of the subject samples varies among the different blood components. Where a main effect of time was found, concentrations increased with duration. The plasma volume changes, which are also tabulated, were not applied in the statistical analysis. The only significant differences beyond 180 min were for hematocrit (210 and 270 min), insulin (270 min), and lactate (210 min), consistent with their differences at earlier times shown in Table 2.

Hb and hematocrit concentrations increased with time after 30 and 60 min, respectively, but were not different between trials. Insulin was higher during Control, whereas glycerol, NEFA, and β -OH were higher during Fatigue. Respective increases over time occurred only after 90, 150, and 60 min in these cases. Glucose was higher during Control before the wet portion of the cold exposure, and its concentration increased with time after 60 min. Similar discontinuities were found for lactate, cortisol, T_3 , and free T_3 . T_4 was consistently higher during Fatigue at all times, whereas the only significant finding with free T_4 was an increase with time at 60 min. Not shown in Table 2 is the result for thyroid-stimulating hormone, which indicated no significant differences with time or between trials.

Epinephrine, norepinephrine, dopamine, and serotonin were analyzed only in blood samples taken before

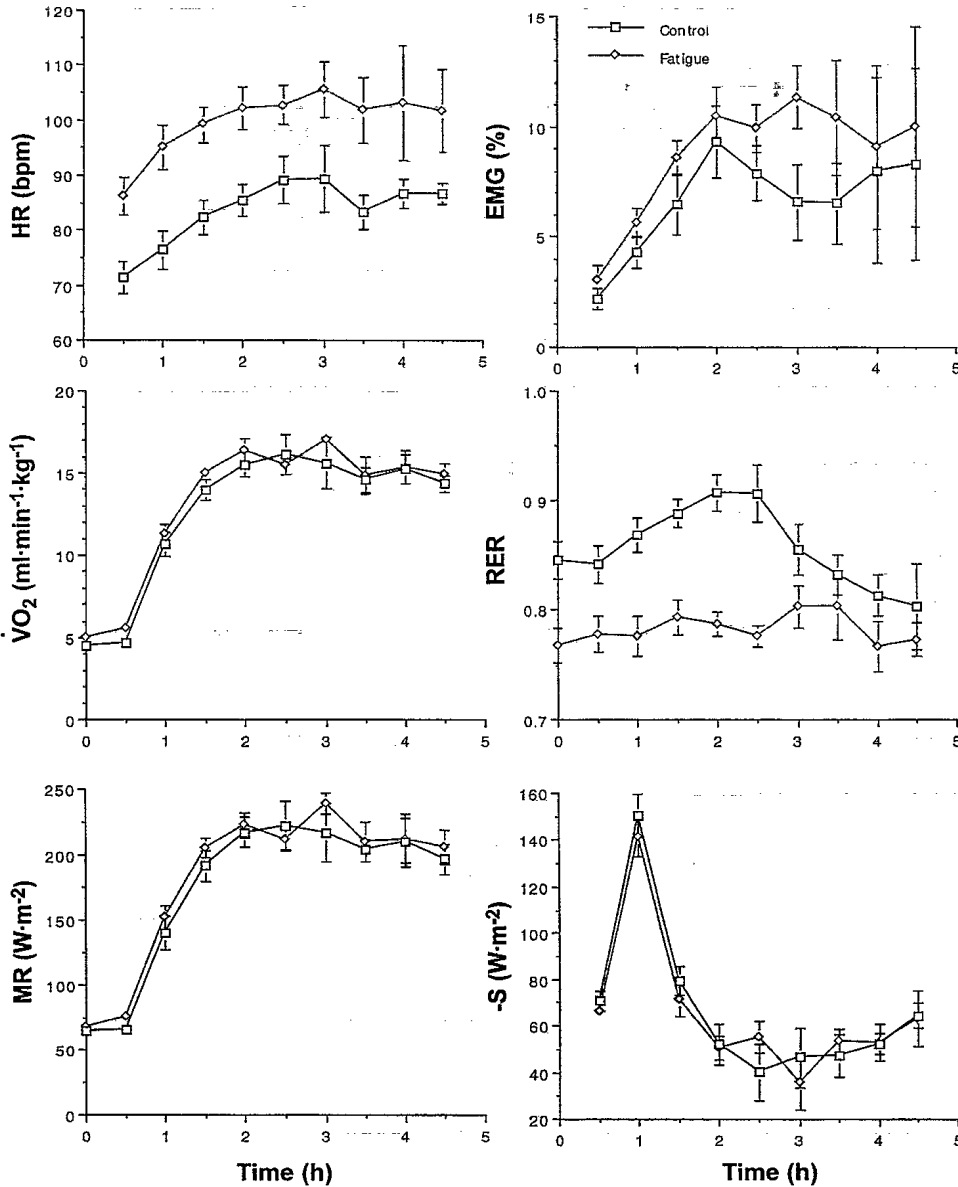


Fig. 4. Metabolic variables plotted against time of exposure for each trial. Points correspond to different data groups (G) depending on duration as follows: G60 ($n = 13$) for 0, 0.5, and 1.0 h; G90 ($n = 11$) for 1.5 h; G120 ($n = 10$) for 2.0 h; G150 ($n = 7$) for 2.5 h; G180 ($n = 6$) for 3.0 h; G210 ($n = 4$) for 3.5 h; and G270 ($n = 3$) for 4.0 and 4.5 h. Values are means \pm SE. HR, heart rate [in beats/min (bpm)]; EMG, electromyogram; $\dot{V}O_2$, O_2 consumption; RER, respiratory exchange ratio; MR, metabolic rate; $-S$, heat loss.

and immediately after exposure. No significant differences were found between trials. However, significant increases during exposure occurred in all substances except serotonin; respective P values (Greenhouse-Geisser adjusted) are <0.001 , <0.001 , and 0.006 . Actual pre- vs. postexposure concentrations were 48 ± 17 vs. 179 ± 86 pg/ml (epinephrine), 462 ± 257 vs. $2,449 \pm 841$ pg/ml (norepinephrine), 57 ± 24 vs. 149 ± 87 pg/ml (dopamine), and 37 ± 31 vs. 38 ± 25 ng/ml (serotonin).

DISCUSSION

The significant decrease in mean RER for the Fatigue trial suggests that shivering thermogenesis is more dependent on fat metabolism than during the Control trial. This finding is consistent with other studies that indicate a greater predisposition for fat metabolism after prolonged acute exercise (14, 31). The lower preexposure blood concentrations of insulin, glucose, and lactate and higher exposure concentrations of

glycerol, NEFA, and β -OH for the Fatigue trials are also consistent with the interpretation that the subjects were more predisposed toward fat than carbohydrate metabolism during the Fatigue trials (7, 13). Despite this difference, subjects were able to shiver at the same intensity as measured in the Control trial. Although substrate utilization was not found to be a limiting factor of shivering thermogenesis in a previous study (29), the levels of cold stress and MR were considerably higher in the present study. This study further emphasizes the body's uncompromised ability to utilize available substrates to maintain shivering thermogenesis.

The overwhelming conclusion of this study is that there are no differences in the physiological variables of importance for metabolism and core temperature during a stressful wet-cold exposure between a well-rested condition and one where demanding mixed exercise is performed for 5 h beforehand. This extends the findings

Table 2. Mean plasma volume changes and statistical analyses of blood components

Component	Pre-exposure	Exposure, min				
		30	60	90	120	180
Plasma volume						
<i>n</i>		11	9	8	8	5
% Δ		2.92	-3.47	-7.39	-10.28	-9.62
\pm SD		\pm 3.62	\pm 3.81	\pm 4.69	\pm 3.81	\pm 4.80
Hematocrit						
<i>n</i>	13	12	9	7	5	5
Time			<0.001	<0.001	<0.001	<0.001
Hb						
<i>n</i>	13	12	9	7	5	5
Time		0.010	0.003	0.006	<0.001	0.007
Insulin						
<i>n</i>	13	12	9	6	4	5
C>F	0.004	0.002	0.008	0.015	0.046	0.026
Glucagon						
<i>n</i>	13	12	8	5	4	4
Time					.041	.010
Glycerol						
<i>n</i>	13	12	9	7	5	5
Time				0.038	0.030	0.020
F>C	<0.001	<0.001	<0.001	0.006	0.050	0.011
NEFA						
<i>n</i>	13	12	8	7	5	5
Time						0.002
F>C	<0.001	<0.001	<0.001	0.002	0.019	0.006
β -OH						
<i>n</i>	13	12	9	7	5	5
Time			0.006	0.003	<0.001	0.007
F>C	<0.001	<0.001	<0.001	0.003	0.025	0.024
Glucose						
<i>n</i>	13	12	9	7	5	5
Time			0.024	0.032	0.049	0.022
C>F	0.001	0.002				
Lactate						
<i>n</i>	13	12	9	7	5	5
Time			0.014	0.009	0.010	0.014
F>C		0.043	0.029	0.024		
Cortisol						
<i>n</i>	13	12	9	6	5	4
Time			0.018			
F>C	0.001	0.001	0.007	0.039		
T ₃						
<i>n</i>	13	12	6	5	4	4
Time			0.012	0.019	0.005	0.031
Free T ₃						
<i>n</i>	13	12	8	5	4	4
F>C	0.003	<0.001	0.006	0.043		
T ₄						
<i>n</i>	13	12	8	5	4	4
F>C	0.003	0.001	0.021	0.029	0.041	0.029
Free T ₄						
<i>n</i>	13	12	8	6	4	4
Time			0.015			

n, Number of subjects; NEFA, nonesterified fatty acid; β -OH, β -hydroxybutyrate; T₃, triiodothyronine; T₄, thyroxine. Significance is noted as Greenhouse-Geisser adjusted *P* value; absence of a value indicates no significant effect. Tests are for main effects of time (increase with duration) and trial [Control (C) and Fatigue (F)]. Preexposure values were tested only between trials.

of Weller et al. (31), where the stress and duration of the cold exposure were less. In addition, there was no evidence of shivering fatigue during the exposures. Hence, our hypothesis of an exercise-induced fatigue effect must be rejected. The significant increase in blood cortisol levels for the Fatigue trial before and

during the first 90 min of the cold exposure confirms that strenuous activity was performed. Changes in the other blood components were consistent with the effects of exertional fatigue and/or cold exposure (7, 14, 16, 17; for review see Ref. 12). However, given that shivering fatigue was not observed in this study, it is evident that muscle fatigue and/or muscle damage as a result of the exercise did not attenuate the shivering response.

There were, however, large differences in MR between subjects, but not within subjects (except *subject 12*) and not necessarily associated with body fatness. A high MR is necessary to generate sufficient heat to delay hypothermia, but lack of body fatness severely impedes the body's ability to contain this heat. This conclusion concurs with Pugh et al. (23) and Weller et al. (30), who also found that high heat production without adequate body fatness may be insufficient to prevent core cooling. The variability in MR between subjects may account for subnormal shivering performance sometimes incorrectly attributed to prior exertional fatigue. As noted earlier, the average MR during the Control exposure ranged from as low as 67 to as high as 232 W/m². Yet, no correlation was found between MR and the subjects' level of fitness (V_{O_{2max}}). No measured physical or physiological characteristic, including age, can be traced to the more than threefold difference in MR between the subjects. Insofar as the shivering drive is concerned, higher signals should be expected from individuals with greater core cooling (3), yet low MR values persisted. Acclimative, behavioral, and/or psychological factors remain to be explored.

An inherent difficulty in extracting significant differences in this study is having sufficient data as the exposure time increased, since the number of subjects diminished. Furthermore, any divergence in response can be expected to occur as the exposure time is increased. For example, Fig. 5 shows T_{re} plotted against time for G210 (*n* = 4). A divergence appears after 2 h of

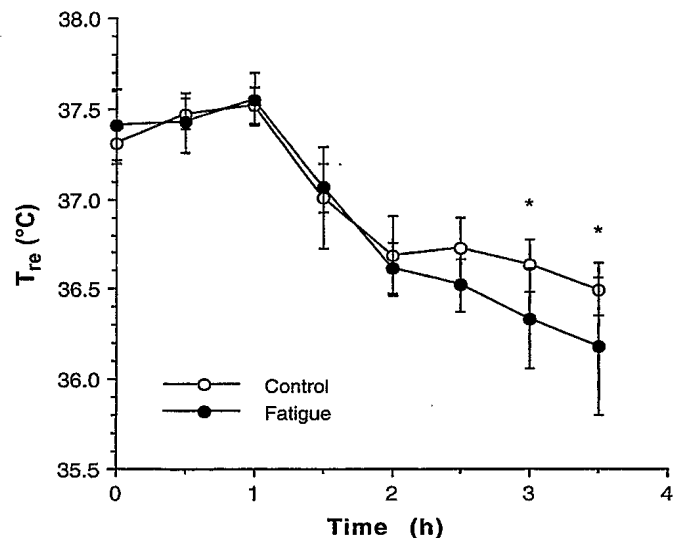


Fig. 5. T_{re} plotted against time of exposure for G210 (*n* = 4) for each trial. Values are means \pm SE. *Significant difference if acceptance criterion is relaxed (Hunyh-Feldt adjustment).

exposure, but no significant effect of trial was found. If the acceptance criterion is relaxed, then a significant trial \times duration interaction occurs (Hunyh-Feldt adjustment, $P = 0.043$). Post hoc testing indeed reveals that the T_{re} values are significantly different late in the exposure, i.e., at 3 and 3.5 h. Interestingly, in the wet-cold study reported by Thompson and Hayward (24) discussed below, there is also the suggestion that core temperature begins to fall in the last hour of exposure. However, considering that the other variables in our study did not indicate a similar "divergence," we are reluctant to conclude that the level of exercise fatigue in this study impacts on shivering response within the duration of the wet-cold exposure.

The recent studies of Thompson and Hayward (24) and Weller et al. (30) involved walking under wet-cold conditions. The respective total amount of work due to exercise alone is calculated to be $\sim 7,540$ and $9,210$ kJ on the basis of the reported measurements in the dry condition. Although these values exceed our aerobic output on the exercise machines ($7,314 \pm 741$ kJ), the additional resistance exercises probably placed our subjects at a higher level of muscular fatigue. Furthermore, the metabolic output during the subsequent sedentary wet-cold exposure in our study was quite high, averaging $1,080$ kJ/h (300 W) and $1,145$ kJ/h (318 W) during the Control and Fatigue trials and $\sim 1,440$ kJ/h (400 W) after 1.5 h, thus surpassing the shivering intensities reported in the other two studies.

In the wet-cold studies of Thompson and Hayward (24) and Weller et al. (30), the subjects were men and similar in their physical characteristics to those in our study. However, they were clothed more than our subjects, which resulted in higher T_{sk} (20 – 24°C) and presumably less heat loss. Shivering fatigue was not observed by Weller et al., and core temperatures remained relatively high ($\sim 37^\circ\text{C}$), probably because the exercise intensity was sufficiently high to offset most of the heat loss. The more recent study of Weller et al. (31) involved exhaustive arm and leg exercise with energy expenditures estimated at $2,330$ and $4,780$ kJ, respectively, for a total of $7,110$ kJ. Although similar to our output level excluding the resistance exercises, the subsequent moderate cold exposure evoked only a modest increase in shivering intensity.

It appears that the exposure conditions reported by Thompson and Hayward (24) resulted in more cold stress than those in the studies of Weller et al. (30, 31) on the basis of a wider separation in core temperature between the cold exposure trials and a high dropout rate in the former study. Two subjects in the study of Thompson and Hayward experienced very high rates of core cooling ($\sim 2.5^\circ\text{C}/\text{h}$), which they attributed to exercise fatigue in one case and shivering fatigue in the other. To what extent exercise contributes to the latter subject's response is not known, since no sedentary wet-cold exposure was conducted. These decreases in T_{re} match very closely the rates shown by *subjects 12* and *13* in our study (Fig. 2). Furthermore, these values occurred during the Control exposure, when the subjects were in a well-rested state. *Subject 13* exhibited

the same rate of drop during Fatigue, but, interestingly, *subject 12* did not, since his MR was considerably higher during Fatigue (final values of 193.0 vs. 142.5 W/m^2), which we cannot explain. This anomalous behavior accounts for the lack of a significant difference in duration between trials.

Pugh (21, 22) suggested that victims of accidental hypothermia in wet-cold conditions are generally lean and, on losing their ability to continue exercising (e.g., hiking) due to exhaustion, succumb to hypothermia. Low BF is clearly implicated in all studies including our own. However, it is also evident from our study that rapid core cooling is not contingent on exercise fatigue, as observed in several of our subjects during their Control trial (*subjects 05, 07, 09, 12, and 13*; Fig. 2). The amount of aerobic activity in Pugh's study (22) was not higher than that in our Fatigue trial, nor was it of longer duration. One of Pugh's subjects was able to stabilize his core temperature above 35°C , and another exhibited a rapid drop during rest after exercise. Because no control trial was conducted, it would be speculative to conclude that exercise fatigue in this case was the main cause of rapid core cooling. Hypoglycemia, which would affect shivering response (10), was not a factor in our study (no individual value was < 2 mmol/l at any time during the cold exposure trials) and seems unlikely in the studies of Pugh and Thompson and Hayward (24) given the amounts of exercise performed.

The above interpretation should not be misconstrued as suggesting that exercise fatigue has no impact on shivering response; it may at some point, but apparently not within the limits of this experiment. Our study establishes the minimum conditions or benchmark that should be exceeded to achieve an effect, i.e., by exceeding the combination of 5 h of demanding mixed exercise and 4 h of a stressful wet-cold exposure without any replenishment of metabolic substrates. Yet, considering the hardship that this experiment imposed on the subjects, continued experimentation beyond the benchmark will prove to be very challenging. The wide subject variability in the rate of core cooling observed under conditions below the benchmark can be mostly explained by low body fatness and a low shivering intensity. However, the latter is not necessarily the result of exercise fatigue, at least at the levels applied in this and the above-cited studies. It appears that certain individuals simply lack the shivering "drive" usually observed in others having the same physical characteristics or within themselves, as in the case of *subject 12*, whose MR during the Fatigue cold exposure was 35% higher than during Control. This might help explain why such individuals might perish while others survive under seemingly similar cold exposure conditions.

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