

Exercise throughout 6° head-down tilt bed rest preserves thermoregulatory responses

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Shibasaki, Manabu, Thad E. Wilson, Jian Cui, Benjamin D. Levine, and Craig G. Crandall. Exercise throughout 6° head-down tilt bed rest preserves thermoregulatory responses. *J Appl Physiol* 95: 1817–1823, 2003. First published July 25, 2003; 10.1152/jappphysiol.00188.2003.—Spaceflight and its bed rest analog [6° head-down tilt (HDT)] decrease plasma and blood volume and aerobic capacity. These responses may be associated with impaired thermoregulatory responses observed during exercise and passive heating after HDT exposure. This project tested the hypothesis that dynamic exercise during 13 days of HDT bed rest preserves thermoregulatory responses. Throughout HDT bed rest, 10 subjects exercised for 90 min/day (75% of pre-HDT maximum heart rate; supine). Before and after HDT bed rest, each subject exercised in the supine position at the same workload in a 28°C room. The internal temperature (T_{core}) threshold for the onset of sweating and cutaneous vasodilation, as well as the slope of the relationship between the elevation in T_{core} relative to the elevation in sweat rate (SR) and cutaneous vascular conductance (CVC; normalized to local heating maximum), were quantified pre- and post-HDT. T_{core} thresholds for the onset of cutaneous vasodilation on the chest and forearm (chest: 36.79 ± 0.12 to $36.94 \pm 0.13^\circ\text{C}$, $P = 0.28$; forearm: 36.76 ± 0.12 to $36.91 \pm 0.11^\circ\text{C}$, $P = 0.16$) and slope of the elevation in CVC relative to T_{core} (chest: 77.9 ± 14.2 to $80.6 \pm 17.2\% \text{max}/^\circ\text{C}$; $P = 0.75$; forearm: 76.3 ± 11.8 to $67.5 \pm 14.3\% \text{max}/^\circ\text{C}$, $P = 0.39$) were preserved post-HDT. Moreover, the T_{core} threshold for the onset of SR (36.66 ± 0.12 to $36.74 \pm 0.10^\circ\text{C}$; $P = 0.36$) and the slope of the relationship between the elevation in SR and the elevation in T_{core} (1.23 ± 0.19 to $1.01 \pm 0.14 \text{ mg} \cdot \text{cm}^{-2} \cdot \text{min}^{-1} \cdot ^\circ\text{C}^{-1}$; $P = 0.16$) were also maintained. Finally, after HDT bed rest, peak oxygen uptake and plasma and blood volumes were not different relative to pre-HDT bed rest values. These data suggest that dynamic exercise during this short period of HDT bed rest preserves thermoregulatory responses.

temperature regulation; skin blood flow; sweating

SPACEFLIGHT AND GROUND-BASED analogs of microgravity [i.e., 6° head-down tilt (HDT) bed rest] reduce physical performance, orthostatic tolerance, and plasma and blood volume (4, 10, 12, 14, 21). Thermoregulatory responses are also impaired after these exposures, resulting in greater increases in internal temperature (T_{core}) during exercise (20), a shift in T_{core} threshold for

the onset of cutaneous vasodilation and sweating to higher T_{core} (5, 20), and a reduced slope of the relationship between the elevation in skin blood flow (SkBF) and sweat rate (SR) relative to the increase in T_{core} (5, 8). Elevated T_{core} and/or reduced heat-dissipating responses impair physical performance (13, 25) and increase the risk for a heat-related illness (18). Preservation or restoration of crews' thermoregulatory responses during spaceflight, or on returning to a normal gravity (1 G_z) environment, is critical for the well-being of the astronaut. The mechanism(s) by which actual and simulated microgravity alter the control of SkBF and SR remain unknown. However, these exposures alter fluid homeostasis, resulting in a relative hypovolemic state (3, 7, 12, 15, 21), and hypovolemia impairs thermoregulatory responses (9, 11, 22, 24, 30) as observed after simulated and actual microgravity exposure (5, 8, 16, 20). Thus it seems feasible that hypovolemia associated with microgravity exposure may contribute to altered thermoregulatory responses. If a countermeasure could be implemented that preserves hydration, thermoregulatory responses associated with prolonged HDT bed rest or spaceflight may also be preserved.

One such countermeasure may be aerobic exercise training given the proposed effects of exercise training on increasing plasma volume (2, 27), coupled with observations that exercise training improves thermoregulatory responses (23, 26, 28, 29, 31). The stimulus by which aerobic exercise training improves thermoregulatory responses is likely related to sustained elevations in T_{core} during exercise, which may result in a form of heat acclimation. In support of this possibility, improvements in thermoregulatory responsiveness are more effective if the exercise is performed in the heat, but even in a cooler environment, exercise training sufficient to increase T_{core} improved thermoregulatory responses (23). Thus it is possible that aerobic exercise training during thermoneutral HDT bed rest may preserve thermoregulatory responses. In support of this hypothesis, in a few (15, 17), but not all (16), of their studies, Greenleaf et al. showed that exercise during bed rest either preserved plasma volume or attenuated

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the reduction in plasma volume relative to bed rest exposure without exercise. However, in those studies (15–17), the effects of exercise training during bed rest on thermoregulatory responses that contribute to body temperature regulation (e.g., T_{core} threshold for cutaneous vasodilation and sweating as well as the slope of the relationship between the elevation in T_{core} and SkBF or SR) were not investigated. Thus the purpose of this study was to test the hypothesis that aerobic exercise training throughout HDT bed rest preserves the aforementioned thermoregulatory responses during an exercise thermal challenge.

METHODS

Subjects. Ten healthy subjects (9 men and 1 woman), who were nonsmokers and passed a comprehensive medical evaluation, participated in this study. The subjects' average age was 31 ± 3 yr, and all were of normal height (182 ± 2 cm) and weight (81 ± 4 kg) and were free of cardiovascular, metabolic, and neurological disorders. A written, informed consent from each subject was obtained before participation in the institutionally approved study.

Bed rest and exercise training. Subjects were housed in the General Clinical Research Center at Parkland Memorial Hospital. Strict bed rest was maintained in the 6° HDT position for 18 days in a hospital-based room. Subjects remained in the HDT position at all times, except that they were allowed to elevate on one elbow for meals and were horizontal during exercise, transport, and bathing. They were given a controlled diet, whereas fluids were allowed ad libitum. The temperature of this room was controlled at 20–23°C by the hospital-based temperature control. Nevertheless, this temperature was reported to be comfortable to the subjects. Daily supine exercise training was performed in the same room where the subject lived, and thus at the aforementioned temperature, at 75% of pre-bed rest heart rate (HR) maximum for 90 min/day, 7 days/wk. Subjects chose to exercise for this duration either in two bouts of 45 min or three bouts of 30 min. HR was monitored (Polar) during these exercise bouts to confirm exercise intensity. Throughout bed rest, subjects adjusted the workload of the cycle ergometer to keep HR at the prescribed level. Subject typically wore only shorts or shorts and a T-shirt for these exercise sessions.

Thermal exercise test. Immediately before beginning bed rest, and on the 13th day of bed rest, each subject exercised for 25 min on a supine cycle ergometer in a 28°C room. For the female subject, the pre-HDT thermoregulatory exercise test was performed 28 days before the post-HDT exercise test such that both tests were conducted at a similar phase of her menstrual cycle. Regular daily exercise was not performed before the post-HDT thermal exercise test. Each subject exercised at the same absolute workload for both pre- and post-HDT trials. The workload was selected to elicit ~75% of pre-bed rest upright maximum HR, and it averaged 122 ± 7 W. In consideration of the effect of circadian rhythms on thermoregulatory responses (1), both pre- and post-HDT thermal exercise tests were performed at the same time of the day in the morning. On entering the laboratory, each subject was instrumented for the measurement of mean skin temperature (T_{sk}) from the weighted average of six thermocouples attached to the skin. T_{core} was measured by thermistor inserted in the esophagus at a distance equal to one-quarter of the subject's height or by telemetry pill. The telemetry pill was used for a subject who chose to not insert

the esophageal temperature probe. HR was monitored by using an ECG. Arterial blood pressure was obtained via R-wave-triggered auscultation of the brachial artery (Sun-Tech Medical Instruments, Raleigh, NC). Mean arterial blood pressure (MAP) was calculated as one-third pulse pressure plus diastolic pressure. Forearm and chest SkBF values were measured by laser-Doppler flowmetry (Perimed). Cutaneous vascular conductance (CVC) was indexed from the ratio of SkBF to MAP. CVC was normalized relative to maximum CVC obtained via local heating of the skin to 42°C for 30 min, which was performed immediately after the thermal exercise test. Forearm SR was measured by the ventilated capsule method with compressed nitrogen (flow rate: 500 ml/min) as the perfusion gas. Relative humidity of the effluent gas was measured via a humidity-temperature probe (Vaisala, Woburn, MA) that was positioned 1 m from the capsule on the skin. This value, as well as gas temperature, flow rate, and the capsule surface area on the skin, was used to calculate SR on-line.

Blood and plasma volumes and peak oxygen uptake. Plasma volume was measured by the Evans blue dye dilution technique (6) both before bed rest and on bed rest *day 15*. Blood volume was calculated on the basis of Evans blue-derived plasma volume and hematocrit. Before and on the last day of HDT bed rest (*day 18*), peak oxygen uptake ($\dot{V}_{\text{O}_2 \text{ peak}}$) was measured by indirect calorimetry with the subject exercising in the upright position on a cycle ergometer. As part of a separate protocol, a subset of these subjects ($n = 5$) received 294 ± 58 ml of a 10% dextran solution before this maximal graded exercise test (HDT *day 18*). However, all thermal exercise tests were completed 5 days before this dextran infusion. Daily exercise was not performed before the measurement of plasma and blood volume or before the $\dot{V}_{\text{O}_2 \text{ peak}}$ test.

Data collection and analysis. Data were recorded at 200 Hz (Biopac, Santa Barbara, CA) and were reduced to 1-s averages. Two-way repeated-measures ANOVA was used to identify the effects of HDT bed rest on measured responses during the exercise test (i.e., temperatures, HR, MAP, SR on the forearm, and SkBF on the chest and forearm). Main factors of this ANOVA were bed rest condition (i.e., pre- or post-HDT bed rest) and duration of exercise. Differences in responses for the resting period between pre- and post-HDT thermal exercise tests were compared by using Student's paired *t*-test. T_{core} thresholds for the onset of sweating and cutaneous vasodilation were identified with the investigator blinded as to the bed rest condition (i.e., pre- or post-HDT bed rest). This threshold was identified by the T_{core} at which progress and sustained increases in CVC and SR were observed. These values were statistically compared by using Student's paired *t*-test. The relationship (i.e., slope) between the elevation in T_{core} and the elevation in SR, SkBF, and CVC were obtained by simple linear regression of all points after the T_{core} threshold. These values were statistically compared between bed rest conditions by using Student's paired *t*-test. All data are expressed as means \pm SE. The level of statistical significance was set at $P < 0.05$.

RESULTS

During one of the 30-min daily exercise sessions, around *day 9* of HDT bed rest, oxygen uptake (\dot{V}_{O_2}) was measured and was found to be $66 \pm 15\%$ of pre-bed rest upright $\dot{V}_{\text{O}_2 \text{ peak}}$. Average HR for this exercise bout was 136 ± 9 beats/min, which was 74% of pre-bed rest maximum upright HR.

Table 1. Peak oxygen uptake, blood volume, plasma volume, and body weight before and after HDT bed rest

	Pre-HDT	Post-HDT	P Value
$\dot{V}O_{2\text{ peak}}$			
ml·kg ⁻¹ ·min ⁻¹	37.0 ± 1.8	37.2 ± 1.5	0.89
l/min	3.04 ± 0.25	2.92 ± 0.14	0.44
Blood volume			
liters	5.53 ± 0.35	5.53 ± 0.31	0.99
ml/kg	68.8 ± 4.6	70.3 ± 2.9	0.80
Plasma volume			
liters	3.41 ± 0.20	3.34 ± 0.17	0.80
ml/kg	42.5 ± 2.8	42.6 ± 1.9	0.98
Weight, kg	81.4 ± 4.2	79.1 ± 3.8	<0.001

Values are means ± SE. Peak oxygen uptake ($\dot{V}O_{2\text{ peak}}$) values were obtained before head-down tilt (HDT) bed rest and on the 18th day of HDT bed rest in the upright position. Plasma and blood volumes were measured before HDT bed rest and on the 15th day of HDT bed rest. Body weight was obtained before HDT bed rest and on the 18th day of HDT bed rest.

After HDT bed rest, $\dot{V}O_{2\text{ peak}}$ and blood and plasma volumes were not different relative to pre-HDT bed rest levels (Table 1). When blood and plasma volumes were expressed relative to body mass, these values remained not different between pre- and post-HDT conditions (blood volume: 68.8 ± 4.6 vs. 70.3 ± 2.9 ml/kg, $P = 0.80$; plasma volume: 42.5 ± 2.8 vs. 42.6 ± 1.9 ml/kg, $P = 0.98$).

Figure 1 shows the time course of temperatures, HR, forearm SR, and SkBF on the chest and forearm throughout the thermal exercise test before and after HDT bed rest. All parameters increased during exer-

cise, but no significant differences were identified between pre- and post-HDT bed rest trials.

HR, MAP, T_{core} , and T_{sk} before the thermal exercise test were not different between pre- and post-HDT measures (Table 2). Similarly, at the end of the thermal exercise test, there were no differences in these values. Thus the calculated increases in these values during the thermal exercise test were also not different between pre- and post-HDT trials (Table 2).

Exercise during HDT bed rest preserved the T_{core} threshold for the onset of sweating as well as the slope of the relationship between the elevation in SR and the elevation in T_{core} during the thermal exercise test (Fig. 1, Table 3). Thus the calculated absolute increase in sweating during the thermal exercise test was not different between pre- and post-HDT trials (Table 2).

Before the thermal exercise test, CVC was not different between pre- and post-HDT measures (Table 2). Cutaneous vascular responses during the thermal exercise test, whether expressed as SkBF or CVC, were also preserved by aerobic exercise training throughout HDT bed rest (Tables 2 and 3; Figs. 1 and 2). Specifically, the T_{core} threshold for the onset of cutaneous vasodilation (both expressed as SkBF and CVC) at forearm and chest sites, as well as the slope of the relationship between the elevation in T_{core} and the elevation in SkBF or CVC, was not different between pre- and post-HDT thermal exercise tests. Thus the elevation in SkBF and CVC during the thermal exercise test, as well as CVC and SkBF at the end of the thermal exercise test, was not different between pre- and post-HDT trials (Table 2).

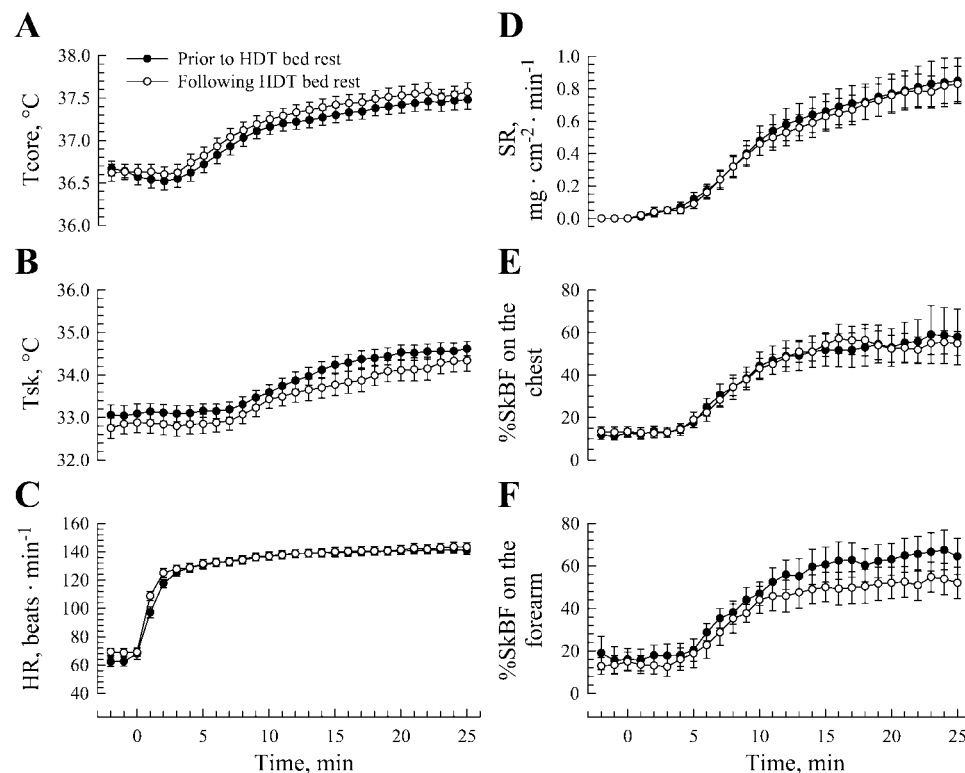


Fig. 1. Time course of the change in internal and skin temperatures [T_{core} (A) and T_{sk} (B), respectively], heart rate (HR; C), sweat rate (SR; D) on the forearm, and percentage of maximum skin blood flow (%SkBF) on the chest (E) and forearm (F) during the exercise thermal challenge before and after 13 days of head-down tilt (HDT) bed rest. No significant differences were observed for any of these variables between pre- and post-HDT thermal exercise tests.

Table 2. Effects of HDT bed rest with an exercise countermeasure on physiological variables at rest (preexercise) and at the end of the thermal exercise test and the increase in responses due to the thermal exercise test

	Preexercise	End of Exercise	Δ Response
T_{core} , °C			
Pre-HDT	36.6 ± 0.1	37.5 ± 0.1	0.9 ± 0.1
Post-HDT	36.6 ± 0.1	37.6 ± 0.1	1.0 ± 0.1
T_{sk} , °C			
Pre-HDT	33.1 ± 0.2	34.6 ± 0.2	1.5 ± 0.2
Post-HDT	32.9 ± 0.2	34.2 ± 0.3	1.3 ± 0.2
HR, beats/min			
Pre-HDT	68.0 ± 4.0	141.7 ± 2.2	73.7 ± 5.1
Post-HDT	69.2 ± 3.0	143.4 ± 2.9	74.2 ± 4.2
MAP, mmHg			
Pre-HDT	83.8 ± 4.6	101.3 ± 5.6	17.5 ± 2.4
Post-HDT	82.2 ± 3.3	97.3 ± 5.6	15.1 ± 2.7
Forearm SR, $\text{mg} \cdot \text{cm}^{-2} \cdot \text{min}^{-1}$			
Pre-HDT		0.85 ± 0.13	0.85 ± 0.12
Post-HDT		0.85 ± 0.11	0.84 ± 0.11
%SkBF			
Chest			
Pre-HDT	12.7 ± 2.1	54.0 ± 9.7	41.3 ± 8.8
Post-HDT	13.4 ± 2.3	51.3 ± 6.2	37.9 ± 6.0
Forearm			
Pre-HDT	16.1 ± 5.2	61.7 ± 7.7	45.6 ± 5.5
Post-HDT	15.0 ± 4.5	50.9 ± 6.8	35.9 ± 2.9
%CVC			
Chest			
Pre-HDT	12.8 ± 2.2	44.7 ± 7.3	31.9 ± 6.5
Post-HDT	13.5 ± 2.4	44.6 ± 6.5	31.1 ± 6.0
Forearm			
Pre-HDT	16.1 ± 5.1	52.5 ± 5.5	36.4 ± 3.6
Post-HDT	14.8 ± 4.9	46.8 ± 7.1	32.1 ± 3.1

Values are means ± SE. T_{core} , internal temperature; T_{sk} , skin temperature; HR, heart rate; MAP, mean arterial blood pressure; SR, sweat rate; %SkBF, skin blood flow expressed as a percentage of maximal flux; %CVC, cutaneous vascular conductance expressed as a percentage of maximum. No significant differences were observed before exercise, at the end of exercise, or the increase in the response due to the thermal exercise test between pre- and post-HDT trials (Δ Response).

DISCUSSION

Previously, our laboratory (5) and others (16, 20) showed that ground-based analogs of microgravity impair sweating and cutaneous vascular responses during passive heat stress or exercise. Similar findings have been reported from two astronauts after prolonged spaceflight (8). In the present study, we found

that aerobic exercise training, at workloads equivalent to 75% of upright pre-bed rest maximum HR, throughout strict HDT bed rest preserved thermoregulatory responses during exercise in a moderately warm room (28°C). These findings are supported by the observation that the T_{core} threshold for the onset of sweating and cutaneous vasodilation, and the slope of the relationship between the elevation in T_{core} and the elevation in heat-dissipative responses (i.e., SR, SkBF, and CVC), was not different between pre- and post-HDT trials.

Thermoregulatory responses during exercise are closely related to the workload performed, the individual's aerobic capacity, and body fluid status (9, 19). In the present study, aerobic capacity and blood and plasma volumes were not different between pre- and post-HDT bed rest trials as shown in Table 1. Moreover, the subject exercised at the same absolute workload for both pre- and post-HDT thermal exercise tests. Because, in these exercising subjects, HDT bed rest did not reduce $\dot{V}_{\text{O}_2 \text{ peak}}$, the relative workload performed for the thermal exercise tests was also similar between pre- and post-HDT trials. This observation is supported by the finding that HR during the thermal exercise test was similar between pre- and post-HDT trials. Thus it is possible that the preservation of plasma and blood volumes, as a result of the subjects exercising during HDT bed rest, contributed to the preservation of thermoregulatory responses during the thermal exercise test.

Previously, Greenleaf and Reese (16) used a similar protocol to assess the effects isotonic exercise training (60 min/day of supine cycle ergometry at 68% maximal \dot{V}_{O_2}) during 14 days of horizontal bed rest on thermoregulatory responses. They reported that the increase in rectal temperature after 70 min of supine cycle ergometry (thermal exercise test) in these subjects who exercised throughout bed rest was significantly greater relative to when the subjects were ambulatory (i.e., pre-bed rest). This finding is in contrast to the present findings that T_{core} values at the end of exercise were similar between pre- and post-HDT thermal exercise tests. Moreover, despite rectal temperature being significantly higher during the thermal exercise test after bed rest in the aforementioned study (16), SR was not significantly different relative to the ambulatory control thermal exercise test. These data suggest that

Table 3. T_{core} threshold for the onset of sweating and cutaneous vasodilation and the slope of the relationship between the elevation in T_{core} relative to the elevation in forearm SR, %SkBF, and %CVC

	Forearm SR			Cutaneous Vasodilation on the Chest			Cutaneous Vasodilation on the Forearm		
	Threshold, °C	Slope, $\text{mg} \cdot \text{cm}^{-2} \cdot \text{min}^{-1} \cdot \text{°C}^{-1}$	Threshold, °C	%SkBF slope, %max/°C	%CVC slope, %max/°C	Threshold, °C	%SkBF slope, %max/°C	%CVC slope, %max/°C	
	Pre-HDT	36.66 ± 0.12	1.23 ± 0.19	36.79 ± 0.12	97.63 ± 18.12	77.92 ± 14.20	36.76 ± 0.12	95.47 ± 15.29	76.33 ± 11.78
Post-HDT	36.74 ± 0.10	1.01 ± 0.14	36.94 ± 0.13	94.28 ± 16.80	80.60 ± 17.24	36.91 ± 0.11	79.92 ± 15.56	67.45 ± 14.28	
P value	0.36	0.16	0.28	0.61	0.75	0.16	0.11	0.39	

Values are means ± SE.

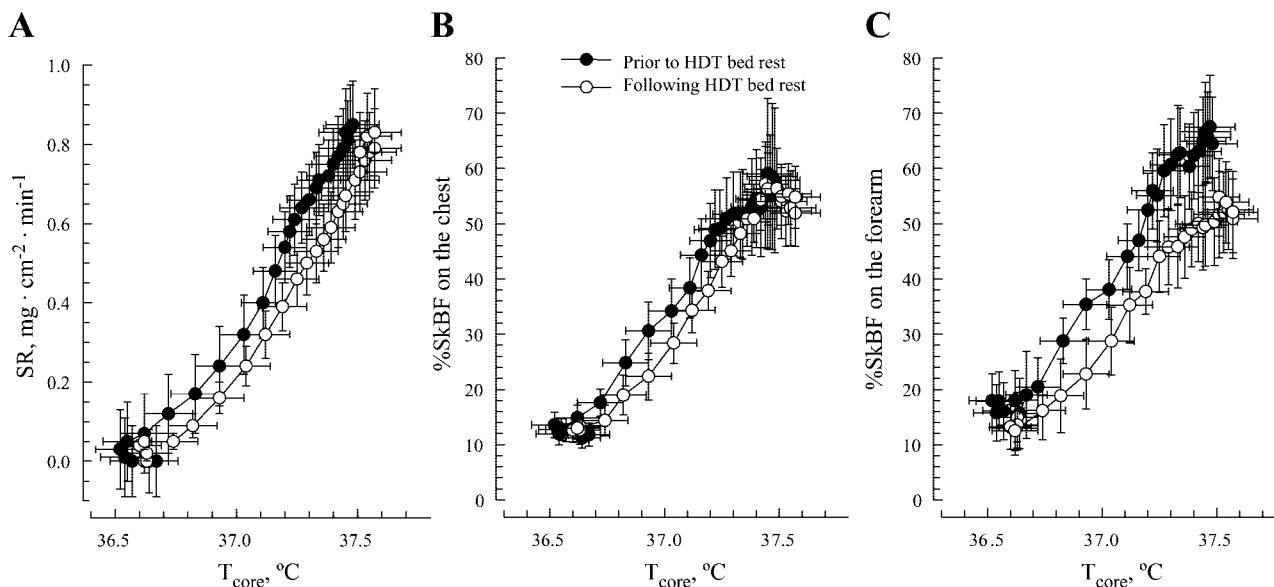


Fig. 2. Effects of a combination of exercise and HDT bed rest on the relationship between the elevation in T_{core} and the elevation in forearm SR (A) as well as the elevation in T_{core} and the relationship in forearm (C) and chest (B) SkBF (expressed relative to maximal skin blood flow; %SkBF). No significant differences were observed for the onset of sweating, the onset of cutaneous vasodilation, or for the slope of the relationship between the elevation in T_{core} and the elevation in SR and SkBF after HDT bed rest.

thermoregulatory responses remained impaired despite the subjects exercising during bed rest. It is interesting to point out that 60 min/day of cycle ergometry exercise also did not maintain maximal \dot{V}_{O_2} or plasma volume (16), which is in contrast to the present findings (see Table 1). Besides obvious differences in exercise duration (90 vs. 60 min/day) and position throughout bed rest (i.e., HDT vs. horizontal), room temperature during the thermal exercise test was lower ($\sim 22^\circ\text{C}$) in the study by Greenleaf and Reese relative to the present study (28.0°C). Thus the thermal challenge was likely greater during the thermal exercise test in the present study. It is not clear which, or whether, these differences in methods are responsible for the contradictory findings between the present study and that of Greenleaf and Reese.

Unique to the present study is the assessment of the effects of aerobic exercise training during HDT bed rest on mechanisms responsible for the regulation of T_{core} . Specifically, we measured the T_{core} threshold for cutaneous vasodilation and sweating as well as the slope of the relationship between the elevation in T_{core} and the elevation in SkBF, CVC, and SR. Prior studies have reported that HDT bed rest and spaceflight increase the T_{core} threshold for cutaneous vasodilation and sweating (5, 8, 20) and/or reduce the slope of the relationship between the elevation in T_{core} relative to the elevation in SkBF, CVC, and SR (5, 8, 20). These data suggest that factors associated with detraining contribute to the impairment of these thermoregulatory responses. In contrast, a number of studies report that aerobic exercise training improves thermoregulatory responses by reducing the T_{core} threshold for the onset of cutaneous vasodilation and sweating (23, 26, 31) as well as increasing the aforementioned slope of

the relationship between the increase in T_{core} relative to the increase in SkBF, CVC, and SR (23, 26, 31). Data from the present study suggest that exercise during HDT bed rest is capable of countering impaired thermoregulatory responses associated with deconditioning, resulting in a preservation of the control of SkBF and sweating responses.

The mechanism(s) by which exercise training during HDT bed rest resulted in the observed responses can only be speculated on. Although heat acclimation greatly improves thermoregulatory capacity, exercise training in a cooler environment also improves thermoregulatory responses (23). In the present study, because room temperature where subjects were housed was between 20 and 23°C , subjects were not exposed to an external thermal challenge during the daily exercise bouts. Nevertheless, the thermal challenge during these exercise bouts was sufficient to cause pronounced sweating in each subject. Thus it is possible that repeated elevations in T_{core} during exercise may have resulted in a form of heat acclimation, which likely contributed to the observed findings.

A related mechanism possibly contributing to the preservation of thermoregulatory responses during HDT bed rest in the present study is the effect of exercise on maintaining plasma volume. It is widely recognized that hypovolemia impairs thermoregulatory responses (9, 11, 22, 24, 30). Given that bed rest without an exercise countermeasure reduces both blood and plasma volumes (10, 21), it is possible that reduced thermoregulatory responses associated with HDT bed rest may be related to the relative hypovolemia that occurs during bed rest. However, in the present study, we found that both plasma and blood volumes were not different between pre- and post-HDT

periods (Table 1). Thus it is possible that similar plasma and blood volumes during the pre- and post-HDT thermal exercise tests contributed to the normalization of thermoregulatory responses.

Limitation of study. We recognize that a limitation of the present study is the absence of a nonexercise bed rest group to serve as control for the responses observed after exercise training throughout HDT bed rest. However, a number of studies have clearly shown that thermoregulatory responses are impaired after 13+ days of HDT bed rest (5, 20) or supine bed rest (16) in subjects who did not exercise during the exposure. Thus given these prior findings (5, 16, 20), coupled with the costs of repeating this study with nonexercising subjects, we chose to study the effects of aerobic exercise training during HDT bed rest only on subjects who exercised during bed rest exposure. However, because the consistency of the observation that thermoregulatory responses are impaired by bed rest (5, 16, 20), we are confident that our data support the hypothesis that aerobic exercise training during relative short-duration HDT bed rest (i.e., 13 days) is capable of preserving thermoregulatory responses during exercise.

This study was a component of a larger study that divided the group of exercising subjects into two groups before the measurement of $\dot{V}O_{2\text{ peak}}$ on bed rest *day 18*. One-half of the studied subjects received 294 ± 58 ml of a dextran solution before the $\dot{V}O_{2\text{ peak}}$ test. Dextran was administered to address an unrelated question and did not affect the thermal exercise test results or blood volume and plasma volume measurements because these data were obtained on days before bed rest *day 18*. However, it is possible that the reported maintenance of $\dot{V}O_{2\text{ peak}}$ after HDT bed rest was confounded by the administration of this plasma volume expander in one-half of the subjects. To investigate this possibility, we separately analyzed $\dot{V}O_{2\text{ peak}}$ in the five subjects who received dextran before the post-HDT $\dot{V}O_{2\text{ peak}}$ exercise test (pre-HDT: 34.4 ± 1.6 ml·kg⁻¹·min⁻¹, post-HDT 35.9 ± 1.8 ml·kg⁻¹·min⁻¹; $P = 0.16$), as well as the five subjects who did not receive dextran before this test (pre-HDT 39.6 ± 3.0 ml·kg⁻¹·min⁻¹, post-HDT: 38.6 ± 2.4 ml·kg⁻¹·min⁻¹; $P = 0.37$), and did not observe differences in $\dot{V}O_{2\text{ peak}}$ in either subgroup. However, we recognize that because we did not measure post-HDT $\dot{V}O_{2\text{ peak}}$ before administering dextran to these five subjects, we cannot conclusively state that dextran administration had no effect on $\dot{V}O_{2\text{ peak}}$ in these subjects. Nevertheless, pre- and post-HDT bed rest $\dot{V}O_{2\text{ peak}}$ was not different in the five subjects who did not receive dextran, suggesting that the exercise training during HDT bed rest maintained their peak aerobic capacity.

Conclusion. The present study indicates that aerobic exercise training throughout HDT bed rest preserves thermoregulatory responses after short-term simulated microgravity exposure. The mechanisms by which this countermeasure preserves thermoregulatory responses may be related to the maintenance of $\dot{V}O_{2\text{ peak}}$ and accompanying maintenance of plasma and blood volumes.

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REFERENCES

1. Aoki K, Stephens DP, and Johnson JM. Diurnal variation in cutaneous vasodilator and vasoconstrictor systems during heat stress. *Am J Physiol Regul Integr Comp Physiol* 281: R591–R595, 2001.
2. Convertino VA. Blood volume: its adaptation to endurance training. *Med Sci Sports Exerc* 23: 1338–1348, 1991.
3. Convertino VA. Clinical aspects of the control of plasma volume at microgravity and during return to one gravity. *Med Sci Sports Exerc* 28: S45–S52, 1996.
4. Convertino VA, Bloomfield SA, and Greenleaf JE. An overview of the issues: physiological effects of bed rest and restricted physical activity. *Med Sci Sports Exerc* 29: 187–190, 1997.
5. Crandall CG, Johnson JM, Convertino VA, Raven PB, and Engelke KA. Altered thermoregulatory responses after 15 days of head-down tilt. *J Appl Physiol* 77: 1863–1867, 1994.
6. Foldager N and Blomqvist CG. Repeated plasma volume determination with the Evans Blue dye dilution technique: the method and a computer program. *Comput Biol Med* 21: 35–41, 1991.
7. Fortney SM, Hyatt KH, Davis JE, and Vogel JM. Changes in body fluid compartments during a 28-day bed rest. *Aviat Space Environ Med* 62: 97–104, 1991.
8. Fortney SM, Mikhaylov V, Lee SMC, Kobzev Y, Gonzalez RR, and Greenleaf JE. Body temperature and thermoregulation during submaximal exercise after 115-day spaceflight. *Aviat Space Environ Med* 69: 137–141, 1998.
9. Fortney SM, Nadel ER, Wenger CB, and Bove JR. Effect of blood volume on sweating rate and body fluids in exercising humans. *J Appl Physiol* 51: 1594–1600, 1981.
10. Fortney SM, Schneider VS, and Greenleaf JE. The physiology of bed rest. In: *Handbook of Physiology. Environmental Physiology*. Bethesda, MD: Am. Physiol. Soc., 1996, sect. 4, vol. II, chapt. 39, p. 889–939.
11. Fortney SM, Wenger CB, Bove JR, and Nadel ER. Effect of hyperosmolality on control of blood flow and sweating. *J Appl Physiol* 57: 1688–1695, 1984.
12. Gerzer R, Heer M, and Drummer C. Body fluid metabolism at actual and simulated microgravity. *Med Sci Sports Exerc* 28: S32–S35, 1996.
13. Gonzalez-Alonso J, Teller C, Andersen SL, Jensen FB, Hyldig T, and Nielsen B. Influence of body temperature on the development of fatigue during prolonged exercise in the heat. *J Appl Physiol* 86: 1032–1039, 1999.
14. Greenleaf JE. Energy and thermal regulation during bed rest and spaceflight. *J Appl Physiol* 67: 507–516, 1989.
15. Greenleaf JE, Bernauer EM, Young HL, Morse JT, Staley RW, Juhos LT, and Van Beaumont W. Fluid and electrolyte shifts during bed rest with isometric and isotonic exercise. *J Appl Physiol* 42: 59–66, 1977.
16. Greenleaf JE and Reese JD. Exercise thermoregulation after 14 days of bed rest. *J Appl Physiol* 48: 72–78, 1980.
17. Greenleaf JE, Vernikos J, Wade CE, and Barnes PR. Effect of leg exercise training on vascular volumes during 30 days of 6° head-down bed rest. *J Appl Physiol* 72: 1887–1894, 1992.
18. Hales JR. Hyperthermia and heat illness. Pathophysiological implications for avoidance and treatment. *Ann NY Acad Sci* 813: 534–544, 1997.
19. Johnson JM and Proppe DW. Cardiovascular adjustments to heat stress. In: *Handbook of Physiology. Environmental Physi-*

- ology. Bethesda, MD: Am. Physiol. Soc., 1996, vol. I, sect. 4, chapt. 11, p. 215–243.
20. **Lee SM, Williams WJ, and Schneider SM.** Role of skin blood flow and sweating rate in exercise thermoregulation after bed rest. *J Appl Physiol* 92: 2026–2034, 2002.
 21. **Levine BD, Zuckerman JH, and Pawelczyk JA.** Cardiac atrophy after bed-rest deconditioning: a nonneural mechanism for orthostatic intolerance. *Circulation* 96: 517–525, 1997.
 22. **Nadel ER, Fortney SM, and Wenger CB.** Effect of hydration state on circulatory and thermal regulations. *J Appl Physiol* 49: 715–721, 1980.
 23. **Nadel ER, Pandolf KB, Roberts MF, and Stolwijk JA.** Mechanisms of thermal acclimation to exercise and heat. *J Appl Physiol* 37: 515–520, 1974.
 24. **Nishiyasu T, Shi X, and Mack GW.** Effect of hypovolemia on forearm vascular resistance control during exercise in the heat. *J Appl Physiol* 71: 1382–1386, 1991.
 25. **Nybo L and Nielsen B.** Hyperthermia and central fatigue during prolonged exercise in humans. *J Appl Physiol* 91: 1055–1060, 2001.
 26. **Roberts MF, Wenger CB, Stolwijk JAJ, and Nadel ER.** Skin blood flow and sweating changes following exercise training and heat acclimation. *J Appl Physiol* 43: 133–137, 1977.
 27. **Sawka MN, Convertino VA, Eichner ER, Schnieder SM, and Young AJ.** Blood volume: importance and adaptation to exercise training, environmental stresses, and trauma/sickness. *Med Sci Sports Exerc* 32: 332–348, 2000.
 28. **Shvartz E, Saar E, Meyerstein N, and Benor D.** A comparison of three methods of acclimatization to dry heat. *J Appl Physiol* 34: 214–219, 1973.
 29. **Strydom NB and Williams CG.** Effect of physical conditioning on state of heat acclimatization of Bantu laborers. *J Appl Physiol* 27: 262–265, 1969.
 30. **Takamata A, Nagashima K, Nose H, and Morimoto T.** Osmoregulatory inhibition of thermally induced cutaneous vasodilation in passively heated humans. *Am J Physiol Regul Integr Comp Physiol* 273: R197–R204, 1997.
 31. **Takeno Y, Kamijo Y, and Nose H.** Thermoregulatory and aerobic changes after endurance training in a hypobaric hypoxic and warm environment. *J Appl Physiol* 91: 1520–1528, 2001.

