

# Prolonged head-down tilt exposure reduces maximal cutaneous vasodilator and sweating capacity in humans

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**Crandall, C. G., M. Shibasaki, T. E. Wilson, J. Cui, and B. D. Levine.** Prolonged head-down tilt exposure reduces maximal cutaneous vasodilator and sweating capacity in humans. *J Appl Physiol* 94: 2330–2336, 2003. First published February 21, 2003; 10.1152/jappphysiol.00790.2002.—Cutaneous vasodilation and sweat rate are reduced during a thermal challenge after simulated and actual microgravity exposure. The effects of microgravity exposure on cutaneous vasodilator capacity and on sweat gland function are unknown. The purpose of this study was to test the hypothesis that simulated microgravity exposure, using the 6° head-down tilt (HDT) bed rest model, reduces maximal forearm cutaneous vascular conductance (FVC) and sweat gland function and that exercise during HDT preserves these responses. To test these hypotheses, 20 subjects were exposed to 14 days of strict HDT bed rest. Twelve of those subjects exercised (supine cycle ergometry) at 75% of pre-bed rest heart rate maximum for 90 min/day throughout HDT bed rest. Before and after HDT bed rest, maximal FVC was measured, via plethysmography, by heating the entire forearm to 42°C for 45 min. Sweat gland function was assessed by administering  $1 \times 10^{-6}$  to 2 M acetylcholine (9 doses) via intradermal microdialysis while simultaneously monitoring sweat rate over the microdialysis membranes. In the nonexercise group, maximal FVC and maximal stimulated sweat rate were significantly reduced after HDT bed rest. In contrast, these responses were unchanged in the exercise group. These data suggest that 14 days of simulated microgravity exposure, using the HDT bed rest model, reduces cutaneous vasodilator and sweating capacity, whereas aerobic exercise training during HDT bed rest preserves these responses.

thermoregulation; spaceflight; microdialysis; skin blood flow; deconditioning

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CUTANEOUS VASODILATION AND sweating are critical responses necessary for appropriate thermoregulation during a heat stress in humans. These responses are altered by a variety of factors, including pathological conditions, heat acclimation, as well as exposure to simulated and actual spaceflight. Regarding the latter condition, our laboratory and others have shown that simulated microgravity exposure, using the 6° head-down tilt (HDT) model, significantly reduces cutaneous vasodilation during passive heating (7) and during exercise (23), whereas Greenleaf and Reese (13) sug-

gested that sweating responses were impaired during dynamic exercise after 14 days of supine bed rest. These ground-based findings were confirmed in an assessment of thermoregulatory function after 115 days of spaceflight, in which two astronauts exhibited pronounced reductions in cutaneous vasodilation and sweating during exercise on returning to Earth (11). However, in both the ground-based and spaceflight studies, mechanisms responsible for impaired thermoregulatory responses were not investigated.

Previous studies have shown that, at the postsynaptic level, cutaneous vasodilator responses (via local heating) and sweating responses (via exogenous administration of sudorific drugs) are modifiable (4, 21, 25, 28, 33, 34). Given these observations, a viable mechanism leading to the aforementioned impaired cutaneous vasodilatory and sweating responses after simulated and actual microgravity exposure may alter postsynaptic responsiveness, such that for a given level of neural drive cutaneous vasodilation and sweating responses are impaired. Thus the purpose of this project was to test the hypothesis that prolonged HDT bed rest impairs cutaneous vasodilator capacity and sweat gland function at the postsynaptic level. Furthermore, because detraining has been implicated in impairing thermoregulatory responses (30), and significant detraining occurs during bed rest (5, 35), a secondary purpose of this project was to test the hypothesis that exercise during HDT bed rest preserves cutaneous vasodilator capacity and sweat gland function.

## METHODS

**Subjects.** Twenty subjects (17 men and 3 women) participated in the protocols outlined in this study. Twelve of these subjects were randomly assigned to an exercise group, while the remaining eight subjects underwent the same bed rest procedure but did not exercise. The subjects' average age was  $34 \pm 2$  yr, and all were of normal height ( $180 \pm 2$  cm), weight ( $82 \pm 4$  kg), and health. A written informed consent from each subject was obtained before participation in the institutionally approved study.

**Bed rest and exercise.** Strict bed rest was maintained in the 6° HDT position for 14 days. Subjects remained in this

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position at all times, although they were allowed to elevate on one elbow for meals but were horizontal for exercise, transport, and bathing. Subjects were housed in a hospital-based General Clinical Research Center and given a controlled diet, and fluids were allowed ad libitum. Pre-bed rest data were obtained within 1 wk of the onset of bed rest. Post-bed rest data were collected on *day 14* of bed rest. For the exercise group, exercise was performed at 75% of pre-bed rest heart rate maximum for 90 min/day using a supine cycle ergometer. Subjects chose to exercise for this duration either in two bouts of 45 min/day or three bouts of 30 min/day.

**Maximal cutaneous vasodilation.** Assessment of maximal cutaneous vasodilation was accomplished by exposing the subject's left forearm to 42°C for 45 min by using a cylindrical water spray device that encircled the subject's forearm (4, 26). A thermocouple was attached to forearm skin within the water spray device to verify that skin temperature was held at 42°C. Before and after the 45-min heating protocol, the average of six forearm blood flow measurements was obtained by using venous occlusion plethysmography (41). Arterial blood pressure was obtained under both conditions via R-wave-triggered auscultation of the brachial artery (Sun-Tech Medical Instruments, Raleigh, NC), and forearm vascular conductance (FVC) was calculated from the ratio of forearm blood flow to mean arterial blood pressure. The units for FVC are milliliters per 100 ml per minute per 100 mmHg; however, for clarity, these units will be reported as FVC units. Because local heating of the forearm does not alter muscle blood flow (1, 18), elevations in total forearm blood flow and FVC are due solely to elevations in forearm skin blood flow and forearm cutaneous vascular conductance, respectively.

**Assessment of sweat gland function.** Two intradermal microdialysis membranes were placed in dorsal forearm skin. Probes were placed a minimum of 3 cm apart and at the same location for both pre- and post-HDT trials. This technique involved placing a small (200- $\mu$ m outer diameter, 10-mm length) sterile, semipermeable membrane intradermally by using a 25-gauge needle. Construction and insertion of the microdialysis probe and assembly system are reported elsewhere (6, 20). The depth of probe placement was not identified, although Kellogg et al. (20), who used the same procedure, reported that these probes were placed at a depth of 0.3–1.0 mm. Both microdialysis membranes were perfused with Ringer solution at a rate of 2  $\mu$ l/min via an infusion pump (Harvard Apparatus, Holliston, MA). The protocol commenced once skin blood flow returned to normal levels after needle insertion trauma (~60–120 min). Chambers having a small window (10  $\times$  5 mm; i.e., surface area of 0.5 cm<sup>2</sup>) were positioned over each membrane to measure sweat rate by the ventilated capsule method with compressed nitrogen as the perfusion gas. The gas was delivered at a rate of 150 ml/min. Location of capsule placement was aided through the use of markings on the tubing that indicated the center of the membrane portion of the microdialysis probe. Humidity of the effluent gas was measured via a humidity and temperature probe (Vaisala, Woburn, MA) that was positioned 1 m from the capsule on the skin. The humidity and temperature probe connected to a humidity data processor (Vaisala) that calculated absolute humidity from the measurement of relative humidity and temperature. Local skin temperature around the microdialysis membranes was maintained at 40°C through the use of a lamp and a thermocouple. This temperature was selected on the basis of prior studies by us and others showing that local temperature is an important component in the modulation of the sweating response (30, 38), coupled with the observation that without

this level of local warming sweating responses to exogenous acetylcholine are attenuated (unpublished observation). Sweat gland function was assessed by perfusing nine doses (1  $\times$  10<sup>-6</sup> to 2 M) of acetylcholine through the microdialysis membranes. Each dose of acetylcholine was administered for 5 min, while sweat rate over the microdialysis membranes was continuously recorded. Sweat rate during the final minute of each 5-min period was averaged and used for the statistical analysis. Sweat rates from both sites were averaged and are reported as a single value for each dose of acetylcholine. Previously, we reported the validity and reproducibility of this technique in assessing sweat gland function in humans (38). After the acetylcholine challenge, with the sites continuing to be perfused with the highest dose of acetylcholine, the number of activated sweat glands was assessed over both microdialysis membranes by using the starch-iodine technique (22). This procedure was performed by first wiping away residual sweat from the skin, followed by placing a small amount of iodine on the skin over the microdialysis membrane. Excess iodine was removed by blotting the area with tissue paper. Paper containing starch was then placed over the area for a brief period of time. At the location of activated sweat glands, iodine is transferred from the skin to the paper, leaving a small dot on the paper for each activated sweat gland. The dots within a defined area were then counted. This procedure was performed in triplicate over each microdialysis membrane, and these triplicate values were averaged.

**Data analysis.** Data were recorded at a minimum of 20 Hz by using a commercially available data acquisition system (Biopac, Santa Barbara, CA). For both groups, the effects of HDT bed rest on the increase in FVC with local heating were statistically analyzed via paired *t*-test. For the sweat gland function analysis, dose-response curves were mathematically modeled via nonlinear regression curve fitting (GraphPad Software, San Diego, CA). The effective concentration causing 50% of maximal sweating responses (i.e., EC<sub>50</sub>) and maximum sweat rates were obtained via the nonlinear regression model. For each group, the effects of HDT bed rest on the modeled variables were statistically analyzed via a paired *t*-test. All values are reported as means  $\pm$  SE. The  $\alpha$ -level for all statistical analyses was set at 0.05.

## RESULTS

After HDT, upright maximal aerobic capacity was significantly reduced in the nonexercise group but was preserved in the exercise group. These values were previously reported in abstract format (31).

In the nonexercise group, both maximal FVC (pre-bed rest: 21.5  $\pm$  1.3, post-bed rest: 18.7  $\pm$  1.7 FVC units; *P* = 0.01) and the change in FVC with local heating [( $\Delta$ FVC) pre-bed rest: 18.1  $\pm$  1.2, post-bed rest: 15.9  $\pm$  1.7 FVC units; *P* = 0.01] were significantly attenuated after HDT bed rest (Fig. 1 and Table 1). In contrast, in the exercise group when reported either as maximal FVC (pre-bed rest: 21.8  $\pm$  2.0, post-bed rest: 21.4  $\pm$  2.5 FVC units; *P* = 0.39) or as the increase in FVC due to local heating (pre-bed rest: 17.7  $\pm$  1.9, post-bed rest: 18.4  $\pm$  2.4 FVC units; *P* = 0.32), these responses were not significantly different between pre- and post-HDT trials.

In both the exercise and nonexercise groups, the EC<sub>50</sub> of the sweating response was unaffected by HDT bed rest (Table 2 and Fig. 2). However, maximal stim-

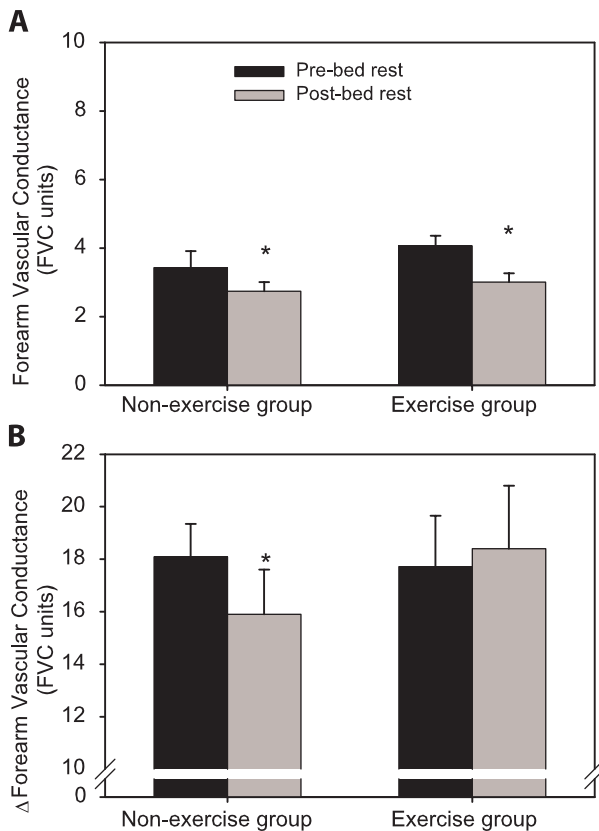


Fig. 1. Forearm vascular conductance (FVC) from the nonexercise and exercise groups before and after 14 days of head-down tilt (HDT) bed rest. In both groups, before local heating (A), FVC was significantly reduced after bed rest relative to pre-bed rest baseline. B: effects of HDT bed rest on the change in FVC ( $\Delta$ FVC) due to local heating. The increase in FVC due to local heating was significantly attenuated in the nonexercise group. In contrast, in the group of subjects who exercised throughout bed rest, there was no difference in  $\Delta$ FVC with local heating between pre- and post-HDT conditions. Values are means  $\pm$  SE. \* $P < 0.05$  vs. pre-HDT bed rest values.

ulated sweat rate for the nonexercise group was significantly attenuated after HDT bed rest (pre-bed rest:  $0.63 \pm 0.06$ , post-bed rest:  $0.42 \pm 0.03$   $\text{mg}\cdot\text{cm}^{-2}\cdot\text{min}^{-1}$ ;  $P = 0.001$ ), whereas no significant difference was observed for the exercise group (pre-bed rest:  $0.81 \pm 0.15$ , post-bed rest:  $0.77 \pm 0.10$   $\text{mg}\cdot\text{cm}^{-2}\cdot\text{min}^{-1}$ ;  $P = 0.31$ ). Regardless of the group, HDT bed rest did not significantly change the number of activated sweat glands during administration of the highest dose of acetylcholine (see Table 2).

## DISCUSSION

The primary novel findings from this investigation are that 14 days of HDT bed rest reduces maximal cutaneous vasodilation and maximal acetylcholine-induced sweat rate. Moreover, chronic aerobic exercise during HDT preserved both of these responses. In contrast, sweat gland sensitivity (defined as the  $\text{EC}_{50}$  of the sweating response) and the number of activated sweat glands during exogenous administration of acetylcholine were unaffected by HDT bed rest regardless of whether the subjects exercised during HDT. These

data indicate that HDT bed rest alters postsynaptic responses associated with the cutaneous vasculature and sweating and that these responses are normalized when subjects perform aerobic exercise training throughout bed rest.

A number of studies report greater increases in internal temperature during exercise after bed rest deconditioning relative to pre-bed rest conditions (10, 12, 13). Reduced cutaneous vasodilation (7, 23) and/or reduced sweating responsiveness (12, 13) during the thermal challenge could lead to elevated internal temperatures after bed rest. Consistent with this observation, Fortney et al. (11) identified pronounced reductions in sweat rate and cutaneous vasodilation during exercise in two astronauts after 115 days in space. Thus there is strong evidence to support the hypothesis that thermoregulation is altered after spaceflight and its bed rest analogs and that impaired thermoregulatory responsiveness is likely due to reduced cutaneous vasodilation and sweating during a thermal challenge. However, before the present study, the mechanism(s) by which HDT bed rest alters cutaneous vasodilation and sweating responsiveness was not investigated.

*Cutaneous vasodilator responses.* In both groups, baseline FVC was significantly reduced after HDT bed rest, which is a consistent finding relative to some (2, 7) but not all (39) HDT studies. The mechanism by which baseline FVC was reduced as a result of HDT bed rest in both the control and exercise groups remains unknown. This response could be due to altered muscle and/or skin vascular conductances. Prior studies have shown that muscle sympathetic nerve activity is elevated after actual and simulated spaceflight (19, 24, 32). Thus it is possible that reduced baseline FVC after HDT bed rest is due to increased sympathetic vasoconstrictor tone to muscle. It remains unknown whether HDT bed rest alters skin sympathetic nerve activity, and thus it is unclear whether reduced cutaneous vascular conductance contributes to reduced baseline FVC after HDT bed rest. Finally, it is possible that the observed response is due to the effects of HDT bed rest on vascular morphology given findings that simulated microgravity exposure in rats can cause vascular remodeling (8). However, such remodeling would be expected to have less of an influence on baseline vascular conductance relative to vasodilator responses. Regardless of the mechanism responsible for altering baseline FVC after HDT bed rest, exercise during HDT is ineffective in preserving this response.

Given differences in baseline FVC after HDT bed rest, statistical analysis was performed on the elevation in FVC due to local heating to identify whether HDT bed rest alters maximal cutaneous vasodilator responses. Because local heating-induced increases in FVC are due entirely to elevations in forearm skin blood flow (1, 18), findings from this study indicate that detraining associated with HDT bed rest reduces maximal cutaneous vasodilator capacity, whereas maintenance of aerobic capacity with exercise during HDT preserves this response. The mechanism(s) responsible for these responses can only be speculated on at this

Table 1. Effects of HDT bed rest on blood pressure, forearm blood flow, and forearm vascular conductance from both the nonexercise and the exercise groups

	Pre-HDT	Post-HDT	P Value
<i>Nonexercise group (n = 8)</i>			
Baseline			
Mean arterial blood pressure, mmHg	82 ± 4	81 ± 4	0.35
Forearm blood flow, ml · 100 ml <sup>-1</sup> · min <sup>-1</sup>	3.0 ± 0.4	2.2 ± 0.2	0.01
Forearm vascular conductance, ml · 100 ml <sup>-1</sup> · min <sup>-1</sup> · 100 mmHg <sup>-1</sup>	3.4 ± 0.48	2.7 ± 0.27	0.03
Local heating			
Mean arterial blood pressure, mmHg	82 ± 3	82 ± 3	0.39
Forearm blood flow, ml · 100 ml <sup>-1</sup> · min <sup>-1</sup>	17.9 ± 1.2	14.8 ± 1.6	0.02
Forearm vascular conductance, ml · 100 ml <sup>-1</sup> · min <sup>-1</sup> · 100 mmHg <sup>-1</sup>	21.5 ± 1.3	18.6 ± 1.7	0.01
ΔForearm blood flow, ml · 100 ml <sup>-1</sup> · min <sup>-1</sup>	14.9 ± 1.2	12.6 ± 1.6	0.04
ΔForearm vascular conductance, ml · 100 ml <sup>-1</sup> · min <sup>-1</sup> · 100 mmHg <sup>-1</sup>	18.1 ± 1.2	15.9 ± 1.7	0.01
<i>Exercise group (n = 12)</i>			
Baseline			
Mean arterial blood pressure, mmHg	85 ± 3	81 ± 3	0.10
Forearm blood flow, ml · 100 ml <sup>-1</sup> · min <sup>-1</sup>	3.5 ± 0.3	2.6 ± 0.2	<0.01
Forearm vascular conductance, ml · 100 ml <sup>-1</sup> · min <sup>-1</sup> · 100 mmHg <sup>-1</sup>	4.1 ± 0.29	3.0 ± 0.26	<0.01
Local heating			
Mean arterial blood pressure, mmHg	83 ± 3	81 ± 3	0.20
Forearm blood flow, ml · 100 ml <sup>-1</sup> · min <sup>-1</sup>	18.0 ± 1.3	16.9 ± 1.4	0.14
Forearm vascular conductance, ml · 100 ml <sup>-1</sup> · min <sup>-1</sup> · 100 mmHg <sup>-1</sup>	21.8 ± 2.0	21.4 ± 2.5	0.39
ΔForearm blood flow, ml · 100 ml <sup>-1</sup> · min <sup>-1</sup>	14.4 ± 1.2	14.3 ± 1.5	0.46
ΔForearm vascular conductance, ml · 100 ml <sup>-1</sup> · min <sup>-1</sup> · 100 mmHg <sup>-1</sup>	17.7 ± 1.9	18.4 ± 2.4	0.32

Values are means ± SE; n, no. of subjects. HDT, head-down tilt; Δforearm blood flow, increase in forearm blood flow above baseline due to local heating; Δforearm vascular conductance, increase in forearm vascular conductance above baseline due to local heating.

time; possibilities include impaired responsiveness to nitric oxide-dependent vasodilation, impaired nitric oxide release, enhanced cutaneous vasoconstriction, and/or structural alterations.

Recent studies by Kellogg et al. (20) and Minson et al. (27) suggest that most or all of the cutaneous vasodilator responses to prolonged local heating are blocked by inhibition of nitric oxide synthase. It is interesting to note that endothelial-dependent and -independent nitric oxide-mediated vasodilation of iso-

lated vessels perfusing gastrocnemius and soleus muscles is reduced in hindlimb-suspended rats (8, 16, 26, 37), which is an analog of microgravity exposure. However, in two of the cited studies, hindlimb suspension did not impair endothelial-independent vasodilation (via sodium nitroprusside administration), whereas endothelial-dependent vasodilation (via acetylcholine administration) was reduced (16, 37). Consistent with these observations, endothelial nitric oxide synthase mRNA and protein content were lower in soleus blood vessels from the hindlimb-suspended rats (16, 37). As for human studies, Shoemaker et al. (39) showed that HDT bed rest attenuated the increase in forearm vascular conductance after an ischemic challenge, which has a significant nitric oxide component (9, 17, 40). Taken together, it seems plausible that reduced maximal cutaneous vasodilation due to HDT bed rest may be due to a reduction in local heat-induced nitric oxide production and/or responsiveness to nitric oxide. In the present experiment, aerobic exercise during HDT bed rest preserved cutaneous vasodilatory responses to local heating. Aerobic exercise training has been shown to enhance endothelial-dependent vasodilation (via brachial artery infusion of acetylcholine) without altering endothelial-independent vasodilation in humans (14). Thus a viable hypothesis leading to the observed response after HDT bed rest could be that exercise during HDT enhanced endothelial nitric oxide release during local heating, which may counter a hypothesized effect of HDT bed rest on attenuating vessel nitric oxide responsiveness.

Elevated vasoconstrictor tone during local heating and/or structural alterations of the cutaneous vasculature as a result of HDT bed rest could also contribute to

Table 2. Effect of 14 days of 6° HDT bed rest, with and without an exercise countermeasure, on modeled responses during exogenous ACh administration and on the number of activated sweat gland at the highest dose of ACh

	EC <sub>50</sub> , log M dose of ACh	Maximal Sweating Response, mg · cm <sup>-2</sup> · min <sup>-1</sup>	No. of Activated Sweat Glands per 0.5 mm <sup>2</sup>
<i>Nonexercise group (n = 8)</i>			
Pre-bed rest	-1.2 ± 0.2	0.63 ± 0.06	39 ± 3
Post-bed rest	-1.1 ± 0.2	0.42 ± 0.03*	39 ± 4
<i>Exercise group (n = 12)</i>			
Pre-bed rest	-1.4 ± 0.2	0.81 ± 0.15	38 ± 3
Post-bed rest	-1.4 ± 0.1	0.77 ± 0.10	37 ± 2

Values are means ± SE; n, no. of subjects. In both groups, the dose of ACh resulting in 50% of the maximal sweating response (EC<sub>50</sub>) was not affected by 14 days of HDT bed rest. In contrast, bed rest significantly reduced maximal stimulated sweat rate in the nonexercise group, whereas this response was preserved in the exercise group. Skin temperature was held constant (40°C) throughout the ACh challenge. The EC<sub>50</sub> and maximal sweating response values were derived from the mathematical model (see text). \*P < 0.05 vs. pre-bed rest values.

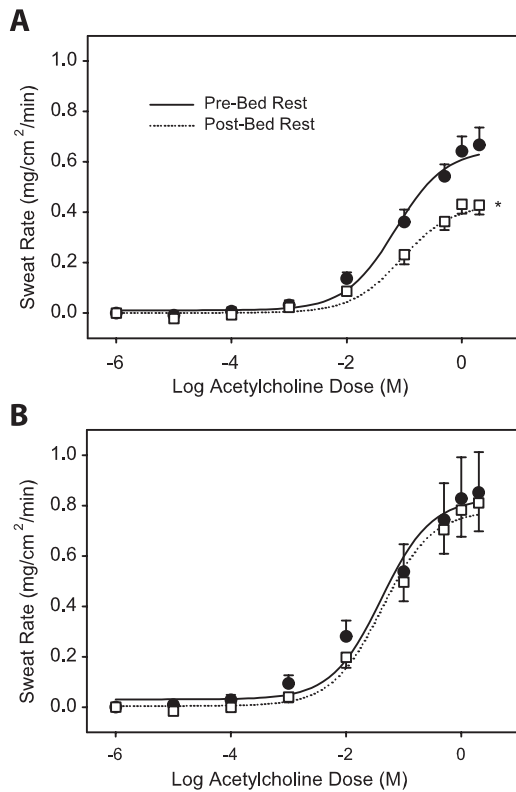


Fig. 2. Sweating responses to exogenous administration of acetylcholine from the nonexercise group (A) and the exercise group (B) before (● and solid line) and after (□ and dashed line) HDT bed rest. The symbols represent actual data (means  $\pm$  SE) obtained during administration of varying doses of acetylcholine, and the lines represent the averaged values from the nonlinear regression model. HDT bed rest significantly reduced maximal stimulated sweat rate in the nonexercise group, whereas this response was preserved in the exercise group. The calculated dose of acetylcholine resulting in 50% of maximal stimulated sweating (i.e.,  $EC_{50}$ ) was not significantly altered by bed rest in either group. \* $P < 0.05$  vs. pre-HDT bed rest.

reduced vasodilator responsiveness to local heating. Regarding the first point, we recently identified that cutaneous vasoconstrictor responsiveness, via intradermal microdialysis administration of norepinephrine, was unaffected by HDT bed rest (42). However, these data do not address the unlikely possibility that HDT bed rest elevates cutaneous vasoconstrictor tone during local heating. Moreover, we are unaware of reports suggesting that HDT bed rest increases skin sympathetic nerve activity. Regarding structural alteration, a number of studies have shown that rat hindlimb suspension can cause structural changes of arterioles as evidenced by reduced baseline and maximal vessel diameters (via placing the vessel in a calcium-free medium) of isolated vessels (26, 37), as well as morphological adaptations (8). Delp et al. (8) suggested that vascular remodeling during hindlimb suspension may be related to decreases in blood flow and shear stress during suspension. Given this possibility, it may be that increases in cutaneous blood flow, and presumably shear stress, as a result of exercise throughout HDT bed rest (with the accompanied heat stress) may prevent this remodeling from occurring.

**Sweating responses.** Despite the observation by Fortney et al. (11) that sweating responses are attenuated after spaceflight, conclusions from ground-based studies investigating the effects of prolonged bed rest on sweating responses are less clear (10, 13, 23). In the present study, HDT bed rest did not alter the  $EC_{50}$  of acetylcholine, did not alter the number of stimulated sweat glands at the highest dose of acetylcholine, but significantly attenuated maximal sweat rate. However, exercise training during HDT preserved maximal sweat rate without altering the number of activated sweat glands. These data imply that HDT bed rest does not affect the sensitivity of the sweat gland in secreting sweat to an exogenous acetylcholine stimulus or the number of sweat glands activated but rather that it reduces the maximal sweat capacity per gland. Moreover, these data suggest that the maintenance of aerobic capacity via exercise training during HDT preserves maximal sweat gland capacity. To our knowledge, this is the first study to demonstrate an impairment of sweat gland function due to detraining associated with HDT bed rest. Although speculative, a possible mechanism for reduced maximal sweat rates after HDT bed rest may be sweat gland atrophy, because maximal stimulated sweat rate correlates with sweat gland size (36).

Others have shown that sweat production, due to exogenous administration of cholinergic agents (i.e., pilocarpine and methacholine), increases with aerobic exercise training (3, 15). These results suggest that sweat gland function can be improved by aerobic exercise training independent of neural control governing the sweating response, which is consistent with the present findings. In the present study, the number of activated sweat glands was not affected by HDT bed rest or exercise during HDT bed rest. This observation is in agreement with the findings of Inoue et al. (15), who showed that heat acclimation and aerobic exercise training did not change the number of activated sweating glands. In contrast, Buono and Sjöholm (3) showed that chronic aerobic exercise training (cross-sectional study of individuals who ran  $\sim 38$  miles/wk) significantly increased the number of activated sweat glands. Thus it may be that the duration of aerobic exercise training during HDT bed rest (i.e., 14 days) was insufficient to increase the number of activated sweat gland, relative to changes in this variable associated with years of aerobic exercise training, but is sufficient to prevent the effects of detraining on maximal sweating responses.

**Conclusion.** Prior studies have identified that after actual and simulated spaceflight thermoregulatory responses are impaired as evidenced by elevated internal temperatures during exercise as well as reduced cutaneous vasodilator and sweating responses after actual and/or simulated microgravity exposure (7, 11, 13, 23). Attenuation of cutaneous vasodilator capacity and sweat gland function after HDT bed rest observed in the present study provides some mechanistic possibilities as to why thermoregulatory responses are impaired after this exposure. However, these findings do

not exclude the possibility that factors associated with HDT bed rest deconditioning alter central control of sweating and cutaneous vasodilation during a heat stress. Finally, data from the present study raise the possibility that thermoregulatory responses to an internal (i.e., exercise) or external (i.e., elevated environmental temperature) heat stress may be preserved in subjects who exercise throughout simulated or actual microgravity exposure.

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