Effect of simulated microgravity on vascular contractility

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Purdy, R. E., S. P. Duckles, D. N. Krause, K. M. Rubera, and D. Sara. Effect of simulated microgravity on vascular contractility. J. Appl. Physiol. 85(4): 1307–1315, 1998.—Microgravity was simulated in Sprague-Dawley (SD) and Wistar (W) rats by using a tail harness to elevate the hindquarters, producing hindlimb unweighting (HU). After 20 days of HU treatment, blood vessels from both HU and control rats were cut into 3-mm rings and mounted in tissue baths for the measurement of isometric contraction. HU treatment decreased the contractile response to 68 mM K⁺ in abdominal aorta from W rats. HU treatment also decreased the contraction to 68 mM K⁺ in carotid arteries from both rat strains and in femoral arteries from W but not SD rats. HU treatment reduced the maximal response of jugular vein from W rats to norepinephrine but had no effect on that response in femoral vein from either rat strain. HU treatment also had no significant effect on the maximal response to norepinephrine in veins. These results demonstrate that HU treatment caused a nearly universal reduction of contractility in arteries, but generally had no effect in veins.

As described by Watenpaugh and Hargens (31), there are several changes in cardiovascular function induced by microgravity. These include an initial increase in central venous pressure. However, this is variable, and, chronically, the central venous pressure is reduced. Hypovolemia also occurs as a result of reductions in both plasma and extracellular fluid volume and red blood cell mass. Whereas resting heart rate is increased in microgravity, stroke volume is reduced, probably reflecting the lower central venous and, therefore, cardiac, filling pressure. Several authors have suggested that the baroreflex response to gravitational challenge is impaired by exposure to microgravity (11, 27). However, this has been questioned, in part, because microgravity-adapted astronauts exhibit a marked postflight increase in heart rate in response to upright posture (3, 16). Thus the neural input and cardiac components of the baroreceptor reflex appear well able to respond to gravitational challenge. On the other hand, the vascular component of the baroreceptor reflex may be impaired (20); i.e., the normal vasoconstriction that occurs on standing does not occur or may be reduced postflight in the microgravity-adapted astronaut (31).

The purpose of the present study was to explore the effect of microgravity on vascular contractility at various sites in the arterial and venous systems. Microgravity was simulated by using a rat model in which the hindlimbs are unweighted (HU); i.e., by the use of a tail harness, the hindlimbs were elevated until they could not touch the floor of the cage. This produced an ~35° tilt of the body.

HU treatment in rats has been shown to mimic many of the cardiovascular changes seen in humans exposed to microgravity. For example, central venous pressure is elevated, at least during the first 24 h (25). Hypovolemia, due to decreases in both plasma volume and red blood cell mass, also occurs (8, 23). Heart rate is increased (19). However, Fagette and co-workers (10) found no evidence for impaired function of the baroreceptor reflexes. This may be in agreement with findings in humans (see above). Regarding the effect of HU treatment on vascular responses, Overton and Titpton (22) found that the mesenteric vascular resistance was reduced in HU rats, and visceral blood flow was found to remain elevated during exercise (19), in contrast to the reduction in flow seen in control animals.

Direct evidence of an effect of HU treatment on vascular function was provided by in vitro studies. Sayette and co-workers (24) found that both spaceflight and HU treatment decreased sensitivity of isolated rat vena cava to norepinephrine. Delp and co-workers (7) found that HU treatment reduced the contractility of rat aorta to several vasoconstrictor agents.
The study by Delp et al. (7) served as the basis for the hypothesis of the present study. Because the aorta is a centrally located, large, distributing artery without resistance or capacitance function, it was hypothesized that HU treatment would produce a generalized reduction in vascular contractility. To test this hypothesis, representative arteries and veins from the upper and lower parts of the body were isolated and their contractile responses to norepinephrine measured. It was found that, in general, HU treatment reduced the contractility of all arteries studied but had little or no effect on veins.

METHODS

Male Sprague-Dawley and Wistar rats weighing 200-250 g were obtained from Simonsen Laboratories (Gilroy, CA). These animals were separately caged in an air-conditioned room maintained at 22°C with a 12:12-h light-dark cycle. They received water and rat chow ad libitum. Animals were randomly placed in either control or HU treatment groups. HU was achieved by use of a tail harness to suspend the hindlimbs above the floor of the cage according to the method of Thompson et al. (28) as follows. The tail was cleaned, and a light coat of tincture of benzoin applied. The tail was air-dried until tacky. Then, adhesive strips (Fas-Trac Company of California, Van Nuys, CA) the width of the tail were looped through a swivel harness and applied to the four sides of the tail. The tail was wrapped with Elastoplast bandage (Bierlendorf, Norw, CT) followed by a thin layer of plaster cast material (Sammons Preston, Bolingbrook, IL). The rat was suspended by the swivel harness from a hook above the suspension cage, allowing free 360° rotation. The height of the hook was adjusted so that only the front limbs were in contact with the floor. The hindlimbs were elevated ~0.5 cm above the floor, tilting the body of the rat ~35°. HU treatment was applied for 20 days, after which animals were used in the in vitro experiments described below.

HU and control rats were euthanized by exposure to 100% CO2 for 90 s to produce deep anesthesia (13). The chest was then opened and the heart removed. Abdominal aorta, femoral, and carotid arteries, and femoral and jugular veins were collected, placed in Krebs bicarbonate solution at room temperature, and cleaned of extraneous fatty and connective tissue by using a dissecting microscope. All vessels were dissected into 3-mm rings, measured by using a stage-level millimeter grid, and mounted on two intraluminal stainless steel wires in tissue baths for the measurement of isometric force development (2). Thirty-gauge wires were used in aorta rings, 32-gauge wires in carotid arteries, and 34-gauge wires in femoral arteries and all veins to allow easy insertion through the lumen with little or no contact with the luminal surface. In preliminary experiments, removal of the endothelium had no effect on the response of two aorta rings from each of five control and five HU rats to either a depolarizing concentration (68 mM) of K+ or full concentration-response curves (CRCs) to norepinephrine. Thus no attempt was made to remove the endothelium in any of the tissues studied. Tissues were maintained in 30 ml of Krebs bicarbonate solution at 37°C. The Krebs bicarbonate solution was gassed continuously with 95% O2-5% CO2 and contained the following (in mM): 119.2 NaCl, 4.9 KCl, 1.3 CaCl2, 1.2 MgSO4, 25 NaHCO3, 11 glucose, 0.114 ascorbic acid, and 0.03 Na4EDTA. After a 30-min equilibration, experiments were conducted to determine the optimal resting force for each vessel type. Vessels were placed under 0.25 g of resting force and equilibrated for 20-30 min. They were then exposed to 68 mM KCl Krebs solution, made by equimolar replacement of Na+. The 68 mM K+ was chosen because this concentration of K+ causes a strong contraction in differing vessels from several species (29, 32), and there is no desensitization to repeated exposures. No attempt was made to determine whether 68 mM K+ was the maximally effective contractile concentration in the vessels assessed in the present study. After contraction to steady state, the vessels were washed twice with normal Krebs solution and were allowed to relax to baseline. Resting force was increased incrementally, and the rings were contracted with 68 mM KCl at each level until optimal resting force was identified, i.e., until the lowest resting force at which the maximum active force development was obtained. The respective optimal resting forces in each vessel were used in all subsequent experiments.

In typical experiments, vessel rings were mounted in tissue baths at optimal resting force and equilibrated for 30 min. They were then contracted to steady state by exposure to 68 mM K+. The baths were drained and refilled twice with normal Krebs solution, and the tissues were allowed to relax to baseline. Then, 20-30 min later, contraction with 68 mM K+ was repeated. In preliminary experiments, it was found that all tissues yielded uniform magnitudes of contraction to the second and all subsequent exposures to 68 mM K+. After tissue recovery from the second exposure to 68 mM K+, the following agents were added to the bathing medium: 30 µM cocaine and 30 µM deoxycorticosterone acetate to block neuronal (12) and extraneuronal (15, 17) catecholamine uptake, respectively, and 1 µM propranolol to block β-adrenoceptors (1). CRCs for the contractile effect of norepinephrine were obtained beginning 30 min later by cumulative addition to the bathing medium in 0.5-log increments.

At the end of the experiment, all tissues were blotted on moist filter paper, and wet weight was measured. Tissues were then dried for 2 h at 115°C and cooled to room temperature under desiccation for 24 h. Tissue dry weights were obtained at this point and after an additional 24 h of desiccation. No differences were found between the two dry-weight measurements.

Isometric contractions were recorded by using Grass FT03C strain gauges (Grass Instruments, Quincy, MA) connected to MacLab Electronic Data Acquisition Systems (Castle Hill, Australia). All agents were added to the bathing medium in volumes of 100 µl or less. Norepinephrine solutions were prepared fresh each day, and stock solutions of cocaine, deoxycorticosterone acetate, and propranolol were prepared weekly and maintained at 4°C. Deoxycorticosterone acetate was dissolved in 50% ethanol and all other drugs in double-distilled H2O.

The mesenteric vascular beds from five control and five HU rats were isolated and perfused as described by Li and Duckles (18). Briefly, the abdomen was opened, and the superior mesenteric artery was quickly cannulated at its origin at the aorta with PE-50 tubing and was perfused with oxygenated warm Krebs solution. Under perfusion, the intestine was separated from the mesentery by cutting close to the intestinal border of the mesentery, and the isolated mesenteric preparation was placed in a water jacket to maintain the temperature at 37°C. The isolated preparation was perfused continuously with warm oxygenated Krebs solution at 4.5 ml/min by using a peristaltic pump. This generated a resting perfusion pressure of 25-30 mmHg, adjusted to 0 mmHg on the digital read-out. The perfusion pressure was monitored and recorded by a pressure transducer, and the resulting signals were digitized by the MacLab analog and recorded by Macintosh computer. The isolated mesenteric vascular preparation was perfused for 60 min with Krebs solution before the
addition of any drugs. The preparation was perfused with Krebs solution containing 68 mM K⁺. When steady-state contraction was achieved, the perfusion medium was changed to normal Krebs solution and the preparation was allowed to relax, indicated by a decline of perfusion pressure to 0 mmHg. Norepinephrine was then added to the perfusion solution in cumulative concentrations, producing an increase in pressure.

The n values given in the legends of Figs. 1–7 indicate the number of animals used for each CRC. At least three vessel rings were used per animal, and the responses of these rings were averaged and used as a single observation for statistical purposes. CRCs were compared by repeated measures, two-way analysis of variance by using SuperANOVA software (Abacus Concepts, Berkeley, CA), and differences between individual points on different CRCs were analyzed by post hoc Scheffé’s test. Differences were considered significant when P < 0.05.

RESULTS

The goal of the present study was to determine whether HU treatment changes either the sensitivity or maximal contraction of rings of arteries and veins to norepinephrine. Preliminary experiments were carried out to determine the optimal resting forces in each vessel type studied. As shown in Table 1, the respective optimal resting forces were not different between rings from control and HU-treated rats in abdominal aorta, femoral artery, and femoral vein, but they were lower in carotid artery and jugular vein from HU-treated animals.

Delp and co-workers (7) found that HU treatment reduced the maximal vasoconstrictor response to various stimuli in isolated aorta from Sprague-Dawley rats. However, preliminary experiments in the present study revealed that HU treatment had no effect on femoral artery rings from this same strain of rat. Thus vessels from both Sprague-Dawley and Wistar strains were compared in the present study. The present study was not designed to test the effects of a range of depolarizing concentrations of K⁺. However, 68 mM K⁺ was used to contract tissues in every experiment during equilibration, before norepinephrine CRCs were obtained. Thus contractions to these stimuli could be compared. The response of abdominal aorta rings to K⁺ are shown in Fig. 1. HU treatment caused a small, nonsignificant (P < 0.15) reduction of contraction in aorta rings from Sprague-Dawley rats. However, power calculations on these data revealed that the number of experiments was insufficient to claim that the HU treatment had no effect. HU treatment caused a larger, significant reduction in aorta rings from Wistar rats. CRCs to norepinephrine are shown in Fig. 2. HU treatment caused a reduction in the maximal response to norepinephrine in aorta rings from both strains of rats. However, the magnitude of reduction in aorta rings from Wistar rats was nearly twice that in rings from Sprague-Dawley rats. The norepinephrine CRCs were normalized on the ordinate by expressing the grams contraction to norepinephrine in rings from control and HU rats as a percentage of the respective maximal contractions to norepinephrine. Thus potential differences in sensitivity could be detected as the magnitude of separation of the norepinephrine CRCs on the abscissa. However, this normalization caused the norepinephrine CRCs in control and HU rings to become completely superimposed for both rat strains (data not shown). This demonstrates that, whereas HU treatment reduced maximal contractile response to norepinephrine, it had no effect on tissue sensitivity to this agonist. In preliminary experiments, the endothelium was mechanically removed. In agreement with Delp and co-workers (7), this had no effect on the HU treatment-induced reduction in the maximal contractile response of aorta to either 68 mM K⁺ or norepinephrine. An analysis of the contribution of endothelium to the effect of HU treatment on other blood vessels will be presented in a separate report.

The effect of HU treatment on the response to 68 mM K⁺ of carotid and femoral artery rings in the two strains of rat are shown in Fig. 3. HU treatment significantly reduced the K⁺-induced contraction in both vessels from the Wistar rat and in the carotid artery from the Sprague-Dawley rat, but it had no effect in the femoral artery from the latter strain. A similar pattern was observed in the response of these vessels to norepinephrine. Namely, HU treatment reduced the maximal response to norepinephrine in carotid (Fig. 4A) and femoral (Fig. 4B) artery rings.
from Wistar rats and in carotid arteries (Fig. 4A) from Sprague-Dawley rats, but it had no effect on the response to norepinephrine in femoral arteries (Fig. 4B) from Sprague-Dawley rats. Normalization of the ordinate (see above) caused the norepinephrine CRCs from control and HU arterial rings to become completely superimposed (data not shown). As with the aorta, HU treatment had no effect on the sensitivity to norepinephrine of the femoral or carotid arteries from either rat strain.

The effect of HU treatment on K^+ -induced contractions of jugular and femoral veins is shown in Fig. 5. HU treatment either had no effect (femoral vein) or a trend toward increased contraction was exhibited. Power calculations confirmed the lack of HU effect in femoral vein from both Sprague-Dawley and Wistar rats but revealed that the number of experiments in the Sprague-Dawley jugular vein was insufficient to claim that HU had no effect. The HU effect was significant in the jugular vein of Wistar rat, in which the contraction to 68 mM K^+ was nearly three times greater in rings from the HU-treated rats compared with controls. The responses of the vein rings to norepinephrine were highly variable, and HU treatment had no significant effect (see Fig. 6). Power calculations demonstrated that the number of experiments was sufficient to support the conclusion of a lack of HU effect.

The results of studies in the isolated perfused mesenteric vasculature are shown in Fig. 7. Perfusion with 68 mM K^+ elevated the perfusion pressure, but HU treatment had no effect in preparations from either strain.
Similarly, norepinephrine caused a concentration-dependent increase in perfusion pressure that was not different in preparations from HU-treated compared with control rats of either strain.

Body weights of 11 Sprague-Dawley rats per treatment, before and after 20 days of treatment, were measured. The respective values in control rats were 307 ± 13 and 377 ± 9 g, representing a significant weight gain (P < 0.01; paired t-test). In contrast, the respective values at 0 and 20 days of treatment in HU rats were 319 ± 20 and 318 ± 11 g, representing no significant change (P > 0.05). Body weights before and after 20 days treatment in 21 Wistar rats per treatment were 316.18 ± 9 and 376 ± 7 g, respectively, in control animals, representing a significant weight gain (P < 0.01). Respective values in HU animals were 311 ± 7 and 322 ± 6 g, a nonsignificant increase (P > 0.05).

Both wet and dry weights of vessel rings from Wistar rats were measured, and the results are presented in Table 2. No significant differences were found between either wet or dry weights in tissues from control compared with HU-treated rats.

**DISCUSSION**

The hypothesis of the present study was based on the findings of Delp and co-workers (7) in rat aorta. These investigators found that HU treatment depressed the maximal responses of this vessel to a variety of vasoconstrictor stimuli. The aorta is a distributing artery and lacks both resistance and capacitance functions. This suggested to us that HU treatment effect is not associated with a specific vascular function or with blood vessels located in a particular vascular bed. Therefore, it was hypothesized that HU treatment causes a generalized depression of vascular maximal contraction. This was tested in the present study by measuring the effect of HU treatment on both artery and vein rings from both the upper and lower parts of the body as well as the isolated mesenteric vasculature.

The present hypothesis was tested by measuring the vasoconstrictor response to norepinephrine. However, 68 mM K⁺ was used during tissue equilibration as a standard contractile stimulus. The study by Delp and co-workers (7) showed that this concentration of K⁺ caused the rat aorta to contract ~80% or more of the contractile response caused by the maximally effective concentration of K⁺. Thus it was considered useful to analyze the contractions to 68 mM K⁺, in addition to those to norepinephrine.

The present hypothesis was partially supported by the results in the arteries studied. Namely, the contractile responses to both 68 mM K⁺ and norepinephrine were depressed by HU treatment in aorta, carotid, and femoral arteries from Wistar rats and in aorta and...
carotid arteries from Sprague-Dawley rats. In aortas from Sprague-Dawley rats, the HU-mediated depression of contraction to 68 mM K\(^+\) was nonsignificant, but power calculations indicated the possibility that the contraction to K\(^+\) might still be reduced by HU. The contractile responses to both 68 mM K\(^+\) and norepinephrine point to a strain difference. The responses of aortas from Sprague-Dawley rats to both 68 mM K\(^+\) and norepinephrine were reduced less by HU treatment than were those of aortas from Wistar rats. Moreover, HU treatment had no effect on the maximal contraction of femoral arteries from Sprague-Dawley rats, in contrast to the effect on femoral arteries from Wistar rats. Presently, there is no explanation for these strain differences. However, the present findings in arteries from Sprague-Dawley rats suggest that the depression of maximal contraction caused by HU treatment is not generalized to all vascular smooth muscle as originally hypothesized.

The veins that were studied generally gave weaker contractile responses to norepinephrine than did the arteries. This was particularly true of the jugular vein. However, the contractions of this vein to 68 mM K\(^+\) were stronger than those to norepinephrine. The jugular vein is known to have little α-adrenoceptor-mediated vasoconstrictor response (5). This property of the jugular vein probably accounted for the weak vasoconstrictor response in the present experiments. The femoral veins gave stronger contractile responses to norepinephrine that closely approximated those to 68 mM K\(^+\), probably reflecting a greater density of α-adrenoceptors in this vessel compared with the jugular vein.

HU treatment had no effect on the contractile responses of veins, with one exception. HU treatment actually increased the response of jugular veins from Wistar rats to 68 mM K\(^+\) (power calculations revealed that insufficient numbers of animals were used to draw conclusions regarding possible HU effects on the Sprague-Dawley jugular vein response to 68 mM K\(^+\)). These findings also argue against the hypothesis that HU treatment causes generalized depression of vascular smooth muscle contractility.

Previous in vivo studies have shown that HU treatment results in a reduced resistance to blood flow in the mesenteric vascular bed (22). Moreover, this bed maintained elevated blood flow in HU rats during exercise (19), in contrast to the reduction in flow seen in control rats. These results suggest that HU treatment reduces the capacity of the mesenteric vascular bed to vasoconstrict. When the isolated mesenteric bed was assessed in the present study (Fig. 7), HU treatment had no effect on vascular contraction to either 68 mM K\(^+\) or norepinephrine. Because of the experimental design used, these results may not necessarily contradict the in vivo findings cited above. The isolated mesenteric vasculature was perfused at constant flow, and an increase in pressure was used as a measure of vasoconstriction. Under these conditions, the maximal contractile response could not be determined. This is because the preparations rupture at pressures higher than those reported in Fig. 7. However, the responses to all submaximal concentrations of norepinephrine used were not different between control and HU. This suggests that HU treatment had no effect on the sensitivity of the mesenteric vasculature to norepinephrine. The present results in the isolated mesenteric bed are in agreement with those in the aorta and the carotid and femoral artery rings. Namely, HU treatment had no effect on the sensitivity to norepinephrine in those tissues. Future experiments that use a different experimental design are required to assess the effect of HU treatment on the maximal contractile response of the mesenteric bed to norepinephrine.

The mechanism underlying the effect of HU treatment is unknown. The presently observed differences of effect of HU treatment on the arteries studied, between
the two strains of rats, and between arteries and veins, demonstrate that HU treatment has a differential effect on the vasculature.

It is possible that weightlessness may cause vascular smooth muscle atrophy, accounting for reduced contractility in vitro. As a first approach, this possibility was assessed in the present study by measuring tissue weights. In arterial rings from control and HU-treated rats, the respective wet and dry weight values were nearly identical, arguing against vascular atrophy. Both wet and dry weights of venous rings from HU-treated rats tended to be lower than those from control rats, but this trend did not achieve significance.

In the present study, HU treatment reduced the maximal responses of arteries to norepinephrine but had no effect on vascular sensitivity to norepinephrine. This is in agreement with Delp and co-workers (7) and argues against an effect of HU treatment on \( \alpha \)-adrenoceptor function. Delp and co-workers (7) suggested that HU treatment is likely to have produced a specific change in one or more proteins associated with contraction, such as actin, myosin, myosin light chain kinase, or calmodulin. The present results are consistent with this possibility.

Delp and co-workers (7) also explored the possible contribution of vascular vasodilator mechanisms to the vascular effect of HU treatment. With use of a similar level of tension to submaximal norepinephrine, they found that endothelium removal had no effect. In addition, by using control and HU aorta rings precontracted to the same level of tension, they found no differences in the relaxation responses to either sodium nitroprusside or acetylcholine. In agreement with Delp and co-workers, we also found no effect of endothelium removal in both aorta and femoral artery (unpublished observations). However, other preliminary results (unpublished observations) may point to a role for the endothelium in the HU effect. Endothelium removal did cause a modest reversal of the HU treatment effect in carotid artery. Moreover, nitric oxide synthase protein mass was found to be modestly higher in femoral and carotid arteries from HU-treated compared with control rats. Detailed experiments are currently under way to elucidate the possible role of endothelium in the vascular effect of HU treatment. It should be noted that, whereas our preliminary results and those of Delp et al. showed no HU-mediated effect on vasodilator mechanisms in Sprague-Dawley or Wistar rats, Delp and co-workers in a separate study (6) found an HU effect on vasodilation in Fischer 344/Brown Norway rats.

The present results and those of Delp and co-workers (7) differ from those of Sayette et al. (24), who studied the rat vena cava. Sayette and co-workers assessed the effect of HU treatment on the response of rat vena cava to norepinephrine and found a reduced sensitivity to
this agonist but no HU treatment effect on maximal contractile response. The change in norepinephrine sensitivity was accompanied by a reduced affinity of prazosin for vena cava \( \alpha \)-adrenoceptors, as measured by radioligand binding. Taking the studies by Delp et al. (6) and Sayette et al. (24), and the present findings together, it is clear that simulated weightlessness produces a complex change in vascular responsiveness to vasoconstrictor stimulation.

Fig. 7. Contractile responses of perfused mesenteric vasculature from control and 20-day HU Sprague-Dawley and Wistar rats. Contraction is reflected by treatment-induced changes in perfusion pressure. A: effects of perfusion with 68 mM K\(^+\); B: effects of perfusion with norepinephrine. Values are means \( \pm \) SE; \( n = 5-9 \).

Table 2. Wet and dry weights of vessel rings from Wistar rats

<table>
<thead>
<tr>
<th>Vessel Ring</th>
<th>Control Rats</th>
<th>HU Rats</th>
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<tbody>
<tr>
<td></td>
<td>Wet weight</td>
<td>Dry weight</td>
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<tr>
<td>Abdominal aorta</td>
<td>3.99 ( \pm ) 0.35 0.43 ( \pm ) 0.03 (3)</td>
<td>3.96 ( \pm ) 0.38 0.48 ( \pm ) 0.02 (3)</td>
</tr>
<tr>
<td>Carotid artery</td>
<td>1.62 ( \pm ) 0.28 0.31 ( \pm ) 0.03 (4)</td>
<td>1.66 ( \pm ) 0.32 0.32 ( \pm ) 0.02 (4)</td>
</tr>
<tr>
<td>Femoral artery</td>
<td>1.45 ( \pm ) 0.08 0.29 ( \pm ) 0.03 (5)</td>
<td>1.56 ( \pm ) 0.41 0.27 ( \pm ) 0.04 (5)</td>
</tr>
<tr>
<td>Jugular vein</td>
<td>1.92 ( \pm ) 0.22 0.49 ( \pm ) 0.08 (4)</td>
<td>1.89 ( \pm ) 0.20 0.39 ( \pm ) 0.00 (4)</td>
</tr>
<tr>
<td>Femoral vein</td>
<td>1.88 ( \pm ) 0.47 0.32 ( \pm ) 0.07 (5)</td>
<td>2.01 ( \pm ) 0.45 0.22 ( \pm ) 0.04 (5)</td>
</tr>
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Values are means \( \pm \) SE in mg. Nos. in parentheses are no. of experiments.

It is clear that HU treatment of rats produces a substantial reduction in the arterial contractile responses to norepinephrine. If the effects seen in this simulation model of weightlessness occur in humans exposed to microgravity, these arterial changes are likely to contribute to the postural intolerance experienced by humans. Exposure to gravity in the standing position in a spaceflight-adapted human triggers a powerful sympathetic stimulation, as revealed by marked elevations in heart rate (3, 16). Nevertheless, postural intolerance occurs. It is possible that the reduced capacity for arterial constriction in response to sympathetic stimulation yields reduced peripheral resistance and lowered blood pressure, contributing to postural intolerance. Future experiments may reveal the specific mechanisms underlying the weightlessness-induced reduction of arterial vasoconstriction. In turn, this may lead to the development of specific therapeutic interventions to restore vasoconstrictor responsiveness. Such treatments could then be used to ameliorate postural intolerance.

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