Altered central nervous system processing of baroreceptor input following hindlimb unloading in rats

Moffitt, J. A., J. C. Schadt, and E. M. Hasser. Altered central nervous system processing of baroreceptor input following hindlimb unloading in rats. Am. J. Physiol. 277 (Heart Circ. Physiol. 46): H2272–H2279, 1999.—The effect of cardiovascular deconditioning on central nervous system processing of baroreceptor afferent activity was evaluated following 14 days of hindlimb unloading (HU). Inactin-anesthetized rats were instrumented with catheters, renal sympathetic nerve electrodes, and aortic depressor nerve electrodes for measurement of mean arterial pressure, heart rate, renal sympathetic nerve activity (RSNA), and aortic depressor nerve activity (ADNA). Baroreceptor and baroreflex functions were assessed during infusion of phenylephrine and sodium nitroprusside. Central processing of baroreceptor afferent input was evaluated by linear regression relating RSNA to ADNA. The maximum baroreflex-elicited increase in RSNA was significantly reduced in HU rats (122 ± 3.8 vs. 144 ± 4.9% of baseline RSNA), whereas ADNA was not altered. The slope (−0.18 ± 0.04 vs. −0.40 ± 0.04) and y-intercept (121 ± 3.2 vs. 146 ± 4.3) of the linear regression relating increases in efferent RSNA to decreases in afferent ADNA during hypotension were significantly reduced in HU rats. There were no differences during increases in arterial pressure. Results demonstrate that the attenuation in baroreflex-mediated increases in RSNA following HU is due to changes in central processing of baroreceptor afferent information rather than aortic baroreceptor function.

Central processing of baroreceptor afferent activity due to hindlimb unloading.

METHODS

Hindlimb unloading. All procedures were in accordance with the National Institutes of Health Guide for the Care and Use of Laboratory Animals and were approved by the Institutional Animal Care and Use Committee of the University of Missouri-Columbia. Male Sprague-Dawley rats (n = 16) obtained from Sasco were randomly assigned to HU or control groups. HU rats (n = 9) were acclimated to the unloading procedure for 1–2 h a day for 3 consecutive days before the HU intervention. The hindlimbs of HU rats were then elevated with a harness attached to the proximal two-thirds of the tail by modification of a technique previously described (14). Briefly, two hooks were attached to the tail with mole-skin adhesive material. A curved rigid support made of lightweight plastic (X-lite splint, AO/AO/Kirschner Medical) was placed beneath the tail to allow adequate blood flow. The hooks were connected by a wire to a swivel apparatus at the top of the cage with the hindlimbs elevated so there was no contact with supportive surfaces. Rats were maintained at a suspension angle of ~30°–35°. A small cast made from plaster of Paris was applied to the thorax to reduce lordosis and to help prevent the rats from disturbing the tail apparatus. Control rats (n = 7) had the thoracic cast applied and were maintained in a normal cage environment. Animals remained in the HU or control condition for 14 days. This time period was chosen because 1) Spacelab Life Sciences missions...
Experimental procedures. The arterial catheter was connected to a pressure transducer for recording arterial pressure. Mean arterial pressure (MAP) was derived electronically using a low-pass filter. HR was determined with a cardiotachometer, which was triggered from the arterial pulse. Mean arterial pressure (MAP) was evaluated by expressing data as a percentage of baseline.

Surgical procedures. Rats were anesthetized with Inactin (100 mg/kg ip) and placed in a supine position for the experiment. The level of anesthesia was monitored carefully, and rats were given supplemental intravenous doses (5 mg) when necessary. Animals were tracheotomized through a midline cervical incision and ventilated with room air mixed with oxygen. Body temperature was maintained at 37°C with a circulating water heating pad. Polyethylene catheters (PE-50 fused to PE-10) were inserted into the abdominal aorta and vena cava via the femoral artery and vein for the measurement of arterial pressure and drug administration, respectively.

For recording renal sympathetic nerve activity (RSNA), the left kidney was exposed through a retroperitoneal approach and a sympathetic nerve branch dissected free (31). Two Teflon-insulated silver wire electrodes (Medwire; 0.005 in. diameter, 36 gauge) threaded through Silastic tubing (0.025 in. ID) were placed around the isolated nerve. Nerves and electrodes were covered with a polyvinylsiloxane gel (Coltene President) that was allowed to harden before closure. A ground wire was sewn to surrounding tissue, and incision sites were closed.

For recording aortic depressor nerve activity (ADNA), the left carotid artery and vagus nerve were exposed through a midline ventral approach. The aortic depressor nerve (ADN) was carefully dissected free from the vagal sheath, with care taken to preserve both nerves. The ADN was placed on a silver wire bipolar recording electrode as described above for recording RSNA. The ADN was positively identified by the pulse phasic bursting pattern associated with the arterial pressure pulse. An example of resting arterial pressure, ADNA, and RSNA recorded simultaneously in a control animal is shown in Fig. 1.

Experimental protocol. After surgical preparation, baseline hemodynamic parameters were allowed to stabilize for ~20 min before any experimental manipulations. Arterial baroreflex curves were then generated by producing ramp changes in arterial pressure over ~2–3 min. Initially, MAP was increased to 180–185 mmHg by infusing phenylephrine at increasing rates (2–25 µg·kg

\textsuperscript{-1} · min

\textsuperscript{-1}). After MAP, HR, RSNA, and ADNA were returned to within 10% of control values (generally within 10 min), arterial pressure was decreased to 45–55 mmHg over 2–3 min by infusion of SNP at increasing rates (10–100 µg·kg

\textsuperscript{-1} · min

\textsuperscript{-1}). The rate of change of arterial pressure was controlled by observing the pressure change on the chart recorder and varying the rate of infusion to produce a smooth ramp increase or decrease in pressure. Care was taken to keep the rate of change of arterial pressure similar in all animals at ~1–2 mmHg/s. Volumes infused did not exceed 100 µl. Baroreceptors were always activated (phenylephrine infusion) before unloading (SNP infusion) to minimize any potential effects of reflexly released humoral agents (e.g., vasopressin or ANG II) on baroreflex function.

At the end of the experimental protocol, the soleus and plantaris muscles were dissected from the hindlimb and weighed. The adrenal glands were also removed and weighed. After tissue removal, rats were euthanized with an overdose of Inactin administered through a venous catheter.

Data analysis. Values for HR, RSNA, and ADNA were determined at different levels of MAP during phenylephrine and SNP infusion. The relationship of ADNA and RSNA to MAP was evaluated by expressing data as a percentage of baseline, before arterial pressure was changed. Baseline RSNA or ADNA was considered to be 100%. This analysis allows for direct evaluation of the animal’s ability to increase or decrease RSNA or ADNA relative to its basal level. Data
relating RSNA and ADNA to MAP were fit to a sigmoidal logistic function (15) using a standard software package (SigmaPlot, Jandel Scientific). The equation used for this mathematical model is

\[ RSNA \text{ or ADNA} = \frac{(P_1 - P_0)}{[1 + \exp(P_2(MAP - P_0))] + P_4} \]

Parameters \((P_1, P_0, P_2, P_3, P_4)\), which were used to describe basic baroreflex function, were generated from data fit to the logistic function. These parameters are 1) the maximum (RSNA) or minimum (ADNA) nerve activity achieved \((P_1)\), 2) the coefficient used to calculate the gain as a function of pressure \((P_2)\), 3) the inflection point (MAP at the midpoint of the curve, \(P_3)\), and 4) the minimum (RSNA) or maximum (ADNA) nerve activity \((P_4)\).

Because baroreflex-mediated changes in HR in response to arterial pressure manipulations are small in the anesthetized preparation, a sigmoidal curve could not be mathematically fit to the data with any reasonable degree of accuracy. Therefore, only the maximal and minimal HR in response to changes in MAP were reported. These data were compared between groups using independent Student’s t-tests. Figure 2, A and B, illustrates RSNA and ADNA in response to changes in arterial pressure in an HU rat. Recorded data points and the fit curves are shown. For each individual animal’s curve, the four parameters \((P_1, P_2, P_3, P_4)\) and maximum gain (gain at the midpoint of the curve) were derived. These parameters and the gain of the baroreflex curve were averaged within each group and statistically compared (control vs. HU) using independent Student’s t-tests. The mean parameters and gain were used to generate an average baroreflex curve for each group. To determine the arterial pressure ranges over which a given parameter differed between groups, specific values of pressure were applied to the curve fit equation for each animal to generate average RSNA or ADNA values at a given pressure. These curves then were compared using two-way ANOVA. When ANOVA indicated a significant interaction, differences between individual means were assessed by a least significant difference (LSD) test (28).

Results

Baseline hemodynamic parameters, muscle weights, and body weights before and after the experimental manipulation of control and HU rats are presented in Table 1. Baseline MAP and HR were similar in anesthetized control rats. Body weight did not differ significantly between groups in the preexperimental period. However, both body weight and the percent increase in body weight (12.5 ± 2.7% for control vs. 3.8 ± 2.2% for HU) in HU rats were significantly less compared with control rats. Soleus and plantaris muscle weights were significantly reduced (53.9% and 26.9%, respectively) in HU rats compared with control rats.

To further compare the characteristics of baroreceptor afferent activity between control and HU groups, the levels of MAP at threshold and at maximum ADNA firing rate were recorded. Threshold for ADN discharge was defined as the pressure at which ADNA resumed following complete inhibition in response to the SNP infusion \((P_{th})\). Pressure at maximum ADN discharge was defined as the pressure at which ADNA reached a plateau at its maximal level despite further increases in arterial pressure in response to phenylephrine infusion \((P_{max})\). These values were identified by visual inspection of the records at a fast paper speed. Thus they are the actual pressure values at which the ADN began to discharge and at which activity no longer increased despite a further increase in pressure, rather than values calculated from the fit curves. The \(P_{th}\) and \(P_{max}\) results between groups were compared using Student’s t-tests.

To evaluate CNS processing of baroreceptor information, ADNA (i.e., afferent input) was related to RSNA (i.e., efferent output). Because the relationships between arterial pressure and RSNA or ADNA are sigmoidal, the relationship between these variables is linear. In addition, the slope of the relationship was different for increasing baroreceptor afferent activity (phenylephrine infusion) vs. baroreceptor unloading (SNP infusion; Fig. 2C). Therefore, separate linear regression analyses were performed for baroreceptor activation and baroreceptor unloading (4). Linear regression analysis included calculations of the slope and y-intercept for each animal for data relating RSNA to ADNA. These values were averaged for each group, and the regression parameters were then compared statistically (control vs. HU) using independent Student’s t-tests.
When expressed relative to body weight, soleus muscle weight-to-body weight ratio was reduced by 49% and plantaris muscle weight-to-body weight ratio was reduced by 18% following hindlimb unloading. Significant atrophy in the soleus and plantaris muscles confirms the effectiveness of the hindlimb unloading intervention in producing a deconditioned state (29). Adrenal gland wet weight between groups was similar (24.8 ± 0.6 mg for control vs. 25.6 ± 0.8 mg for HU rats), indicating that HU rats did not experience excessive stress compared with control rats (26).

Baroreflex control of HR. HR changes in response to changes in MAP were minimal and were not statistically significant. There was no significant difference in the ability to increase HR to a maximal level in response to a decrease in MAP (319 ± 8.1 for control vs. 327 ± 7.1 for HU) or the ability to lower HR in response to changes in MAP (301 ± 11.7 for control vs. 306 ± 6.9 for HU).

Central processing of baroreceptor information. CNS processing of baroreceptor information was evaluated by relating changes in afferent input (ADNA) to reflex changes in efferent sympathetic output (RSNA). Average linear regression analyses comparing the percent change in ADNA to the percent change in RSNA in response to decreases and increases in MAP are depicted in Fig. 5. Average linear regression parameters for each group are included in Table 4. The increase in RSNA in response to a decrease in afferent input was less after hindlimb unloading. Slope and y-intercept of the afferent-efferent relationship during decreases in MAP were significantly reduced in HU rats compared with control rats (Fig. 5A, Table 4). However, there were no significant differences in slope and y-intercept during increases in pressure (Fig. 5B, Table 4).

Fig. 3. Mean baroreflex curves describing reflex control of RSNA expressed as a percentage of baseline activity. Symbols represent %baseline RSNA and baseline MAP for control (○) and HU (●) animals. Dotted lines represent control values ± 1 LSD (least significant difference). Therefore, points for HU animals that are outside the dotted lines represent a significant difference from control. HU rats (n = 9) exhibited a significant attenuation in the ability to increase RSNA in response to a decrease in MAP compared with control rats (n = 7).
DISCUSSION

Previous studies indicate that arterial baroreflex control of sympathetic nervous system activity is attenuated following cardiovascular deconditioning due to hindlimb unloading in rats (19). The present study was designed to test the hypothesis that baroreflex dysfunction associated with cardiovascular deconditioning is due to a change in CNS processing of baroreceptor afferent information. To test this hypothesis, we simultaneously recorded baroreceptor afferent activity and efferent sympathetic outflow in response to changes in arterial pressure following hindlimb unloading in rats. The major finding of this study was that the attenuated baroreflex control of RSNA following HU is due to changes in the CNS component of the arterial baroreceptor reflex. The slope and y-intercept of the line relating increases in RSNA to decreases in ADNA were significantly reduced in HU rats. There was no change in the afferent limb of the baroreflex, as indicated by the discharge characteristic of the whole ADN in response to changes in pressure. The parameters of the baroreceptor afferent activity curve, $P_{th}$, and $P_{max}$ for ADNA were similar between groups. Thus baroreceptor afferent function appeared to be unaltered.

In the present study, baroreflex control of efferent sympathetic nervous system activity in response to decreases in MAP was attenuated following hindlimb unloading. This observation is in agreement with data reported in a previous study using conscious animals (19). In the current study, anesthetized animals were used to allow simultaneous recording of ADNA and RSNA. The typical tachycardia after cardiovascular deconditioning was not observed in Inactin-anesthetized HU rats. In addition, the degree of sympathoexcitation attained during hypotension was blunted during anesthesia. The blunted sympathoexcitation appeared to be similar in both groups so that the percent attenuation of maximum RSNA in HU rats compared with control rats was similar to our previous results in conscious animals (55% for conscious vs. 49% for anesthetized animals). Thus, although anesthesia blunted the absolute maximum levels of sympathoexcitation in both groups, it did not appear to alter the effect of HU to attenuate baroreflex activation of the sympathetic nervous system.

It is possible that the effects of anesthesia may have masked any differences between groups with respect to the afferent limb of the arterial baroreflex. Several observations have led us to conclude that this is not likely and alone could not account for the change in reflex function. First, the pulse phasic synchronicity between ADNA and the arterial pressure pulse was maintained in HU animals. Second, both groups of animals exhibited robust increases and decreases in ADNA in response to increases and decreases in arterial pressure, respectively. The levels of MAP at $P_{th}$ and $P_{max}$ for ADNA were not different between control and HU animals. In addition, the maximum ADNA was not different between groups. Most importantly, in both groups ADNA was completely eliminated in response to decreases in arterial pressure, and this occurred at similar levels of pressure. Despite this similar degree of inhibition of baroreceptor afferent input, reflex sympa-

Table 2. Curve parameters describing reflex changes in RSNA and ADNA

<table>
<thead>
<tr>
<th></th>
<th>n</th>
<th>Maximum, %NA</th>
<th>Midpoint, mmHg</th>
<th>Minimum, %NA</th>
<th>Peak Gain, %NA/mmHg</th>
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<td>RSNA</td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td>Control</td>
<td>7</td>
<td>144 ± 4.9</td>
<td>128 ± 3.4</td>
<td>−4 ± 1.7</td>
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<td>HU</td>
<td>9</td>
<td>122 ± 3.8*</td>
<td>135 ± 5.3</td>
<td>−9 ± 4.1</td>
<td>−2.5 ± 1.1</td>
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<tr>
<td>ADNA</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>7</td>
<td>396 ± 41.7</td>
<td>139 ± 3.3</td>
<td>9 ± 4.6</td>
<td>5.2 ± 2.2</td>
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<tr>
<td>HU</td>
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<td>445 ± 35.3</td>
<td>135 ± 3.6</td>
<td>0.7 ± 7.3</td>
<td>4.9 ± 1.7</td>
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Values are means ± SE; n = no. of rats. RSNA, renal sympathetic nerve activity; ADNA, aortic depressor nerve activity; %NA, %baseline nerve activity. *P < 0.01 vs. control.

Table 3. MAP at threshold and maximum ADNA

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>$P_{th}$, mmHg</th>
<th>$P_{max}$, mmHg</th>
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<tbody>
<tr>
<td>Control</td>
<td>7</td>
<td>66 ± 4.1</td>
<td>172 ± 2.4</td>
</tr>
<tr>
<td>HU</td>
<td>9</td>
<td>64 ± 2.4</td>
<td>174 ± 2.4</td>
</tr>
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Values are means ± SE; n = no. of rats. $P_{th}$, MAP at threshold ADNA; $P_{max}$, MAP at maximum ADNA.
the overall ability of aortic baroreceptors to sense deconditioning. System activity is blunted following cardiovascular appropriate reflex increase in sympathetic nervous system activity. To respond to decreases in afferent activity and elicit an

\[ B \]

was not significantly different between groups (Fig. 5). These data suggest that the ability of the CNS to respond to increases in baroreceptor afferents at a given %ADNA; lines represent average linear regression using the mean slope and y-intercept calculated from the values generated from individual animals. Central integration of baroreceptor afferent activity was significantly attenuated following hypotension in HU rats.

Figure 5. Central integration of baroreceptor afferent activity analyzed on aortic baroreflex control of sympathetic nerve activity using the mean slope and y-intercept calculated from the values generated from individual animals. Central integration of baroreceptor afferent activity was significantly attenuated following hypotension in HU rats.

Figure 5. Central integration of baroreceptor afferent activity analyzed by comparing mean linear regression lines fit to data expressing the %change in RSNA to decreases (A) and increases (B) in arterial pressure in HU (●, dashed lines) and control (○, solid lines) groups. Symbols represent mean values of %RSNA at a given %ADNA; lines represent average linear regression using the mean slope and y-intercept calculated from the values generated from individual animals. Central integration of baroreceptor afferent activity was significantly attenuated following hypotension in HU rats.

Data indicating normal baroreceptor afferent function following hindlimb unloading, when considered in conjunction with current and previous (19) data indicating impaired baroreflex control of efferent RSNA, suggest a change in the central component of the arterial baroreflex following cardiovascular deconditioning. This point is emphasized further because measurements of afferent (ADNA) and efferent (RSNA) activity were made simultaneously in each animal. The relationship between the afferent and efferent components of the arterial baroreflex provides an indication of the CNS processing of the arterial baroreflex. Linear regression analysis performed on this relationship revealed that HU rats exhibited a significant attenuation in CNS processing of decreases in baroreceptor afferent activity due to a reduction in MAP (Fig. 5A). Thus, for any given decrease in ADNA, the increase in RSNA was less. The ability of the CNS to respond to increases in baroreceptor afferent activity during a hypertensive stimulus was not significantly different between groups (Fig. 5B). These data suggest that the ability of the CNS to respond to decreases in afferent activity and elicit an appropriate reflex increase in sympathetic nervous system activity is blunted following cardiovascular deconditioning.

The present data indicate that there is no change in the overall ability of aortic baroreceptors to sense changes in arterial pressure following cardiovascular deconditioning. However, the possibility remains that there may be alterations in the response of subpopulations of aortic afferents (myelinated vs. unmyelinated afferents, for example). In the current study, we recorded ADNA because the ADN is almost entirely composed of baroreceptor fibers, whereas carotid sinus afferent nerves contain both chemoreceptor and baroreceptor afferent fibers. It is possible that changes in baroreceptor afferent function could account in part for the attenuated ability to increase RSNA during decreases in MAP following hindlimb unloading. Nevertheless, by simultaneously recording RSNA and ADNA in response to changes in pressure, the CNS component of aortic baroreflex control of sympathetic nerve activity may be evaluated. The relationship of ADNA to RSNA was attenuated in HU animals, and ADN discharge (both myelinated and unmyelinated fibers) was completely inhibited at similar pressures. Thus, although it is possible that there may also be changes in subpopulations of aortic baroreceptor afferents or carotid baroreceptor afferent reactivity after HU, the central component of the aortic baroreflex arc appears to be blunted.

There are several possibilities as to the sites within the CNS, which may be involved in altered processing of baroreceptor afferent activity. These could include an alteration within the baroreflex arc itself or changes in inputs from regions impinging on the baroreflex arc. The arterial baroreflex pathway is multisynaptic, primarily utilizing three brain stem regions to elicit reflex responses. These regions are the nucleus of the solitary tract (NTS), the caudal ventrolateral medulla, and rostral ventrolateral medulla (RVLM). In addition, neurons within the RVLM terminate on sympathetic preganglionic neurons in the intermediolateral cell column of the spinal cord. The baroreflex arc can also be modulated by other nuclei located within the brain stem or through the influence of forebrain sites. It is possible that a change in input to one of these regions, or a change in neurotransmitter mechanisms at any of these sites, could be responsible for the attenuation in CNS arterial baroreflex processing. For example, the RVLM has been shown to be the final common pathway for eliciting increases in sympathetic nervous system activity in response to baroreceptor unloading (9).

Table 4. Linear regression parameters in response to decreasing and increasing MAP

<table>
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<th>Group</th>
<th>n</th>
<th>Decreasing MAP</th>
<th>Increasing MAP</th>
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<tbody>
<tr>
<td></td>
<td></td>
<td>Slope y-intercept</td>
<td>Slope y-intercept</td>
</tr>
<tr>
<td>Control</td>
<td>7</td>
<td>-0.40 ± 0.04</td>
<td>145 ± 4.3</td>
</tr>
<tr>
<td>HU</td>
<td>9</td>
<td>-0.18 ± 0.04*</td>
<td>121 ± 3.2*</td>
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Values are means ± SE; n = no. of rats. *P < 0.01 vs. control.
Neurons in the RVLM are active under baseline conditions and receive both tonic excitatory and inhibitory inputs. It is possible that the attenuated reflex sympathoexcitation in response to hypotension following HU is due to enhanced inhibition or decreased excitatory influence on RVLM neurons.

Several changes that occur as a result of hindlimb unloading could contribute to altered CNS processing of the arterial baroreflex. During the initial phase of hindlimb unloading, a central shift in body fluids occurs (27). Thus cardiopulmonary receptors may be activated. The cardiopulmonary baroreflex exerts an inhibitory interaction with arterial baroreflex function similar to that produced by hindlimb unloading (1, 22), and adaptations within the cardiopulmonary reflex could contribute to the effects of hindlimb unloading on the baroreflex. These effects would most likely be mediated through interactions at the NTS where both arterial and cardiopulmonary baroreflex afferents are known to terminate (22).

It also is plausible that hormonal changes as a result of the hindlimb unloading intervention could mediate effects on the CNS through circumventricular organs (e.g., area postrema) known to exert interactions on the arterial baroreflex (13, 23). In addition, chronic changes in body position due to hindlimb unloading may elicit alterations in afferent inputs to the CNS originating from the vestibular system. Recent evidence (7) indicates that acute vestibular stimulation in humans inhibits vagally mediated baroreflex control of HR. Because the vestibular system is also known to exert influences on the sympathetic nervous system and have projections to the RVLM (32, 33), this may be a mechanism whereby chronic changes in body position may alter sympathetic outflow and possibly reflex changes in sympathetic nerve activity.

Orthostatic intolerance is a common problem associated with prolonged bed rest or exposure to microgravity in humans (3, 6). Baroreflex activation of the sympathetic nervous system increases peripheral vascular resistance and is of primary importance for maintaining arterial pressure during an orthostatic challenge (24, 30). Thus arterial baroreflex dysfunction may be a mechanism responsible for the orthostatic intolerance following cardiovascular deconditioning. Data from the current study indicate that the attenuation in arterial baroreflex function following cardiovascular deconditioning involves changes within the CNS. Thus, although the arterial baroreceptors may appropriately sense perturbations in arterial pressure when an orthostatic challenge is encountered, the CNS may not respond adequately to the afferent information, resulting in attenuated increases in sympathetic outflow. Previous data (19) suggest that the ability to increase sympathetic nervous system activity to both the kidney and skeletal muscle is attenuated, which would reduce the ability to increase total peripheral resistance. Hypotension and the typical clinical presentation of syncope would result. It seems likely that the factor(s) responsible for orthostatic intolerance is related to the physiological responses that occur during the adaptation to deconditioning and that these factors would also influence arterial baroreflex function via the CNS. In addition, these results provide further insight into potential mechanisms responsible for orthostatic intolerance following cardiovascular deconditioning. It remains to be determined whether the response is specific to CNS processing of baroreceptor afferent information or a more generalized suppression of CNS sympathoexcitation.

In conclusion, previous work (19) indicates that baroreflex control of sympathetic nervous system activity is attenuated following cardiovascular deconditioning due to hindlimb unloading in rats. In this study, there was a significant attenuation in the ability of HU rats to increase efferent sympathetic outflow for a given decrease in afferent baroreceptor input. There appeared to be no change in the afferent limb of the arterial baroreflex (ADNA). These data indicate that the attenuation in baroreflex control of sympathetic nerve activity following cardiovascular deconditioning is due to changes in the CNS processing of baroreceptor input and not due to changes in baroreceptor afferent discharge characteristics.

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REFERENCES