Effects of lower body positive pressure on muscle sympathetic nerve activity response to head-up tilt

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Received 25 September 2000; accepted in final form 17 May 2001

THE BENEFITS OF LOWER BODY positive pressure (LBPP) are generally accepted for clinical treatment in medical emergencies caused by massive bleeding, especially from the lower body, to maintain the systemic blood pressure (7, 21, 29). They are also used by the National Aeronautics and Space Administration after spaceflights for preventing orthostatic hypotension in the astronauts (23). Application of LBPP during orthostasis is supposed to reduce the venous pooling in the lower body and to shift the blood centrally, producing an increment in the preload and then an increase in stroke volume (12, 33); in addition, LBPP raises the total peripheral resistance (TPR; 10, 11, 49), resulting in an elevation of the afterload and therefore an increase in mean arterial pressure (MAP). However, controversy still exists concerning the mechanisms underlying LBPP benefits.

Geelen et al. (14) investigated the hemodynamic and hormonal effects of LBPP during 70° head-up tilt (HUT) in healthy normovolemic humans and found that LBPP attenuated the forearm plasma norepinephrine response to HUT. They thereby concluded that application of LBPP could reduce the baroreflex-mediated enhancement in sympathetic activity. However, the plasma norepinephrine concentration provides a crude index of overall sympathetic nerve activity in normal humans under a wide variety of stressful conditions (6, 15, 20). In addition, sympathetic effects can sometimes be separated from those attributable to hormonal or other actions.

The purpose of this study was to test the hypothesis that the baroreflex-mediated enhancement in sympathetic activity would be attenuated by LBPP during an orthostatic challenge in humans. Specifically, we studied 1) the sympathetic activity responses by the microneurographic technique, using direct intraneural measurement of muscle sympathetic nerve activity (MSNA). This technique permits a close look at the timing of sympathetic activation or inactivation unimpeded by the much slower events at the effector sites of a target organ (46, 47). 2) We studied the contributions of preload and afterload to the changes in MSNA response during orthostasis on application of LBPP. To accomplish these issues, MSNA was recorded microneurographically from the tibial nerve, along with noninvasive measurement of the cardiovascular variables in all the subjects during exposure to a 70° HUT with 30 mmHg LBPP. Due to the limitations of our facilities, we could not apply LBPP over 30 mmHg. We hypothesized that MSNA would be enhanced at 70° HUT, while the enhancement could be attenuated by 30 mmHg LBPP.

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METHODS

Subjects. Eight healthy young men, 22.8 ± 1.4 (SE) years old, 63.1 ± 2.1 kg body wt (body fat <20%), and 171.0 ± 2.2 cm in height, were recruited from among the undergraduate students at Nagoya University. All had negative histories of cardiovascular disease, kidney disease, venous insufficiency, or other diseases, and were not on any medication at the time of the study. All had abstained from alcohol and caffeine consumption for 24 h before the procedure, and all reported no recent use of tobacco or other pharmacological agents. The subjects were informed of the purpose and the procedures used in the study and gave their consent to participate in the experiment. The present study was conducted under the guidelines proposed by the Japan Microneurography Society and was approved by the Human Research Committee of the Research Institute of Environmental Medicine, Nagoya University.

Experimental protocol and procedures. The experimental protocol was performed in the morning or at noon 1 h after a light meal and normal hydration. All experiments were carried out with the subject dressed in shorts without shirt and in a room with an ambient temperature of 25–26°C. MSNA was recorded microneurographically from the tibial nerve at the popliteal fossa in the right leg. The heart rate (HR; beats/min) was obtained from electrocardiogram (ECG). Indirect arterial blood pressure (BP; mmHg) was measured by two different methods: intermittently (every 2 min) from the right brachial artery with an autosphygmonanometer and continuously from the left radial artery at the wrist supported at the heart level by the tonometry method (model BP-508S, Nippon Colin, Komaki, Japan). Impedance plethysmography (models AI-601G and ED-601G, Nihon Kohden, Tokyo, Japan) was used to measure transthoracic impedance (Zo, Ω) and the differential of ΔZ/dZ/dt intermently for the estimation of stroke volume (SV, ml/beats). Two pairs of self-adhesive aluminum tape electrodes were attached around the neck and the trunk at the level of the xyphoid process. The dZ/dt was recorded intermittently at each period for 10 consecutive heartbeats with breath holding at the end of expiration to avoid respiration-related variations of thoracic Z0 and dZ/dt, and the respiration curves were derived from the impedance plethysmography. Electromyography (EMG) signals were picked up by surface electrodes placed on the skin overlying the belly of the left gastrocnemius-soleus muscles to observe the contraction of antigravity muscles of the leg during HUT. Forearm blood flow (FBF, ml·100 ml tissue⁻¹·min⁻¹) was measured intermittently at the interval of BP measurement from the right forearm supported slightly above the heart level using mercury strain gauge venous occlusion plethysmography (Hokanson EC5R plethysmograph, Hokanson, Bellevue, WA).

The protocol included two sessions: one was from the supine posture to 70° HUT without application of LBPP (control) and the other was from the supine to HUT with 30 mmHg LBPP. LBPP was induced while the subjects were supine for 6 min before HUT. These two sessions were performed randomly with a 10-min recovery interval. After an initial 30-min supine rest, the data of MSNA, HR, BP, respiration, Z0, dZ/dt, and FBF were recorded in the supine position (without or with LBPP) for 6 min and followed by passive 70° HUT (without or with LBPP) for another 6 min. During tilting, the subject was instructed to bear his body weight mainly on the left leg and was encouraged to lean backward against a support because this minimized muscle contraction in the legs. After 6-min HUT, the subject was tilted back to the supine position for recovery until all the parameters returned to the supine baseline levels (supine without LBPP condition). Then the second session began, and the data were recorded continuously. All variables were monitored throughout the procedures and stored on a digital audio tape recorder (model PC216Ax, Sony Precision Technology, Tokyo, Japan).

LBPP and HUT. The LBPP facility was affiliated with the Space Medical Research Center, Research Institute of Environmental Medicine, Nagoya University. LBPP was applied distally to the subject’s iliac crest by sealing the subject within a customized pressure box at the level of the iliac crest. Pressure was regulated within the LBPP chamber by controlling valves that adjusted airflow into the chamber with the help of a computer using a closed-loop servomechanism. The pressure applied was read via a pressure transducer connected to the inside of the chamber. The LBPP device could be tilted hydraulically, and a 70° HUT was used.

Recording of MSNA. MSNA was recorded from the tibial nerve at the popliteal fossa in the right leg by the microneurographic technique using a tungsten microelectrode with a tip diameter of ~1 μm and an electrode impedance of 2–5 MΩ (model 26–05–1, Frederic Haer, Bowdoinham, ME). Nerve signals were fed through a high-input impedance preamplifier with a 500- to 5,000-Hz band-pass filter. MSNA was then full-wave rectified and integrated with a time constant of 0.1 s. The identification of MSNA was based on the presence of the following discharge characteristics described elsewhere (46): 1) pulse-synchronous and rhythmic efferent burst discharges; 2) afferent activity evoked by tapping of the appropriate muscle but not in response to a gentle touch; 3) modulation by respiration; and 4) enhancement by maneuvers increasing intrathoracic pressure, such as the Valsalva maneuver.

FBF measurement. FBF was measured by venous occlusion plethysmography with a mercury-in-Silastic double-strain gauge (48). The subject’s right arm was supported on a platform, with the forearm positioned slightly above the heart level to facilitate venous emptying. A strain gauge was arranged around the right forearm 5 cm below the elbow fossa. The right hand was occluded from the circulation by inflation of a wrist cuff to a pressure ~250 mmHg about 45 s before starting the measurement of the first FBF curve. The venous congesting cuff was placed just proximal to the right elbow. For measurement of FBF, the occlusion cuff was inflated quickly to 50 mmHg to stop blood flow from leaving the measurement site, but not to hinder the arterial inflow. After 5 s inflation, the cuff was then deflated for a 15-s interval. The forearm swelling due to the arterial inflow and the rate of blood flow were determined by measuring the rate of increase in volume. The inflow rate was determined by drawing a line on the recorded output tangent to the first few pulses after cuff inflation. The slope of this line was defined as the rate of volume change that was caused by arterial inflow (25). Flow rate was expressed as volume change per unit time [(ml of blood flow)/(100 ml tissue)·1·min⁻¹]. The measurement was repeated eight times at each stage, and the mean value was obtained.

Data collection and analysis. Data from the last 5 min of each period were selected for analysis. The integrated MSNA trace was displayed along with the ECG and BP on a pen recorder (Recti-Horiz, NEC Medical Systems, Tokyo, Japan) for quantifying MSNA. Muscle sympathetic bursts were identified by visual inspection of the integrated trace of MSNA on a paper recording with the guidance of simultaneous sound monitoring. The number of bursts per minute (burst rate), the number of bursts per 100 heart beats (burst incidence), and the sum of the integrated burst amplitudes per minute

AJP-Regulatory Integrative Comp Physiol • VOL 281 • SEPTEMBER 2001 • www.ajpregu.org
Effects of LBPP on cardiovascular responses to 70° HUT with LBPP

Table 1. Effects of LBPP on cardiovascular responses to 70° HUT

<table>
<thead>
<tr>
<th>Variables</th>
<th>Control</th>
<th>70° HUT</th>
<th>30 mmHg LBPP</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Supine</td>
<td>70° HUT</td>
<td>Supine</td>
</tr>
<tr>
<td>SBP, mmHg</td>
<td>121.1 ± 3.2</td>
<td>129.3 ± 7.9</td>
<td>137.0 ± 4.6†</td>
</tr>
<tr>
<td>DBP, mmHg</td>
<td>61.0 ± 2.8</td>
<td>76.4 ± 3.6*</td>
<td>75.6 ± 3.7†</td>
</tr>
<tr>
<td>PP, mmHg</td>
<td>60.1 ± 2.9</td>
<td>52.9 ± 2.4*</td>
<td>61.4 ± 4.4</td>
</tr>
<tr>
<td>CO, l/min</td>
<td>5.2 ± 0.6</td>
<td>4.9 ± 0.4</td>
<td>5.1 ± 0.4</td>
</tr>
<tr>
<td>FBF, ml-100 ml-1·min-1</td>
<td>5.6 ± 1.3</td>
<td>3.9 ± 0.8*</td>
<td>4.8 ± 1.1</td>
</tr>
<tr>
<td>FVR, unit</td>
<td>21.7 ± 4.5</td>
<td>34.7 ± 6.1*</td>
<td>31.1 ± 4.7†</td>
</tr>
</tbody>
</table>

Values are means ± SE; n = 8 subjects. LBPP, lower body positive pressure; HUT, head-up tilt; Control, without LBPP; SBP, systolic blood pressure; DBP, diastolic blood pressure; PP, pulse pressure; CO, cardiac output; FBF, forearm blood flow; FVR, forearm vascular resistance. *P < 0.05 vs. supine; †P < 0.05 vs. control; ‡P < 0.01 vs. control.

[total activity (tMSNA), arbitrary units (AU), and expressed in AU/min] were used as quantitative indexes. MAP (mmHg) was calculated as MAP = DBP ± 1/3 (SBP − DBP), and arterial pulse pressure (PP, mmHg) = SBP − DBP, where SBP and DBP represent systolic and diastolic BP, respectively. SV was calculated from the following equation (24): \[ SV = \frac{r}{T} \left( L \cdot Z_0 \right)^2 \frac{dZ}{dt}_{\text{min}} \cdot T \], where \( r \) is a constant with a value of 135 \( \Omega \)-cm, \( L \) is the distance between the two inner circular electrodes, \( Z_0 \) is the total impedance of the thorax, \( \frac{dZ}{dt}_{\text{min}} \) is the differential of \( Z \) per minute, and \( T \) is the left ventricular ejection time. Cardiac output (CO, l/min) was obtained as the product of SV and HR. TPR (mmHg·s·ml⁻¹) was the ratio of MAP to CO. Forearm vascular resistance (FVR, unit) was derived from the ratio of MAP to FBF.

Statistical analysis. The data were expressed as means ± SE. An analysis of two-way repeated-measures ANOVA using Fisher’s post hoc procedure was employed to determine the effects of LBPP on the MSNA and cardiovascular responses to 70° HUT. P < 0.05 was considered statistically significant. All analyses were conducted using a computerized statistical analysis system (StatView J-4.5, Power PC Version, 1992–98, Abacus Concepts) on a Power Macintosh computer (6300/120).

RESULTS

Complete data were obtained in all studies. There was no presyncope during 6 min 70° HUT and no untoward effects from 30 mmHg LBPP. Results are shown in Table 1 and Figs. 1–3.

Effect of 70° HUT on MSNA and cardiovascular responses. MSNA burst rate, burst incidence, and tMSNA were significantly enhanced during HUT (all \( P < 0.01 \), Fig. 2). MAP was elevated and PP decreased (both \( P < 0.05 \), Fig. 3, A and B), and HR was markedly increased (\( P < 0.01 \), Fig. 3C) in HUT. \( Z_0 \) was significantly higher (\( P < 0.05 \), Fig. 3D), indicating a fluid shift toward the lower body during HUT. SV was markedly reduced (\( P < 0.01 \), Fig. 3E), but CO remained unchanged (Table 1). TPR was markedly increased in HUT (\( P < 0.01 \), Fig. 3F). FBF decreased and FVR increased at 70° HUT (both \( P < 0.05 \), Table 1).

Supine rest and LBPP. Application of 30 mmHg LBPP in the supine position did not change the MSNA burst rate, burst incidence, and tMSNA responses. MAP was elevated by 15.1 ± 3.1 mmHg (\( P < 0.01 \)), PR did not alter, HR remained unchanged, and \( Z_0 \) tended to be reduced by LBPP. Both SV and CO were not changed, and TPR was increased (\( P < 0.05 \)). FBF did not alter significantly, but FVR was increased by LBPP (\( P < 0.05 \)).

70° HUT and LBPP. Application of 30 mmHg LBPP at 70° HUT significantly reduced the increments of MSNA burst rate, burst incidence, and tMSNA (all \( P < 0.05 \), Fig. 2, A–C). MAP was higher (\( P < 0.05 \), Fig. 3A), and the decreased PP was nearly abolished (Fig. 3B) in HUT with LBPP. The increment in HR was markedly reduced by LBPP (\( P < 0.01 \), Fig. 3C). The increase in \( Z_0 \) during HUT was attenuated by LBPP (\( P < 0.05 \), Fig. 3D). SV decreased less (\( P < 0.05 \), Fig. 3E), and CO did not change significantly in HUT with LBPP. TPR was increased (\( P < 0.05 \)), but the value was not different.
from that of HUT without LBPP (Fig. 3F). FBF decreased in HUT with LBPP, but it was not different from that of HUT without LBPP; FVR was higher in HUT with LBPP ($P < 0.05$, Table 1). Additionally, the EMG activity of the antigravity muscles increased during HUT; however, it increased less in HUT with LBPP (Fig. 1).

DISCUSSION

The major findings from the present investigation were that application of 30 mmHg LBPP in the supine position did not change the MSNA response, whereas the enhancement of MSNA at 70° HUT was reduced by 30 mmHg LBPP. The former result was consistent with our previous report (11).

Effects of 30 mmHg LBPP on MSNA response in the supine position. On application of 30 mmHg LBPP in the supine position, MSNA remained unchanged despite a fluid shift from the lower body toward the thorax by LBPP (12, 33), probably due to the counteraction of the intramuscular mechanoreflexes.

In the present study, although the amount of blood shifting to the central part of the body was not very large by 30 mmHg LBPP in the supine posture (evidenced by the decreased tendency of transthoracic impedance), loading of the cardiopulmonary baroreceptors was elicited (4, 42). This notion was supported by our previous finding in which the left atrial dimension was enlarged by 30 mmHg LBPP (11). The cardiopulmonary baroreceptors convey tonic afferent nerve traffic to the cardiovascular center and inhibit efferent sympathetic nerve activity to the muscle (9, 26, 45), which should result in a suppression of MSNA.

In addition, MAP was significantly elevated by 30 mmHg LBPP, and the arterial baroreceptors may have also been loaded (40). Because MAP is a product of TPR and CO, our results demonstrated that 30 mmHg LBPP failed to produce any increase in CO, and therefore the significant increase in MAP was considered to be the result of a marked increase in TPR, referring to an increase in afterload. Furthermore, neither HR nor arterial PP was changed by LBPP in the supine position. We would suppose that the arterial baroreceptors were “statically” loaded. It is likely that such a static stimulation of arterial baroreceptors would lack effects on MSNA response.

Prior work has shown that activation of the intramuscular mechanoreflexes can augment MSNA responses (18, 28). It was reported that 30 mmHg LBPP may activate the intramuscular pressure-sensitive receptors (42). The presence of these receptors, which are linked to the group III and/or IV afferent nerve fibers, could increase afferent nerve traffic via the dorsal spinal root pathways (4, 17), integrate with the cardiovascular center (1, 43), and cause an increase in vasomotor sympathetic activity, without activation of central command mechanisms (49), which is likely to enhance MSNA. Therefore, the sympathoexcitatory effect of the intramuscular mechanoreflexes could counteract the sympathoinhibitory effect of baroreflexes, which kept MSNA at nearly the control baseline value.

Effects of 30 mmHg LBPP on MSNA response at 70° HUT. We observed that MSNA was significantly enhanced at 70° HUT, but the enhancement was markedly attenuated by 30 mmHg LBPP.

During HUT, the higher hydrostatic pressure in the lower body causes a pooling of blood in that part of the body (13). This leads to several compensating reactions, mainly via arterial and cardiopulmonary baroreflexes that tend to restore the BP and the total blood volume in the central part of the body (38). In healthy normovolemic subjects in the supine position, even 100 mmHg LBPP appeared to displace <5% of the total blood volume from the lower body to the thorax (4, 17), but during passive HUT, when there was much blood pooling in the lower body, the cephalad fluid shift volume would be markedly increased by LBPP. Thus the fall in central blood volume could have been at least partially reversed. This notion was supported by the
smaller increase in transthoracic impedance at 70° HUT with LBPP in our study. The partial restoration of the central blood volume decreased the unloading of the cardiopulmonary baroreceptors during HUT and thereby reduced the enhancement of MSNA response. It was found that arterial PP decreased in HUT, but it decreased much less with LBPP. This lesser decrease in PP may also attenuate the enhancement of MSNA. It is known that although levels of muscle sympathetic outflow are related inversely to diastolic BP, they are related directly to PP (44). MAP was higher in HUT than in the supine position, and we would expect that the arterial baroreceptors were loaded. However, it was unclear what role arterial baroreceptor loading had on the MSNA response in this study, because the loading occurred in both HUT and HUT with LBPP. The EMG activity of the antigravity muscles increased at 70° HUT, and it increased less on application of LBPP. The mechanism of this lower increase in EMG activity is not clear. We suppose that the subject could be slightly suspended by the positive pressure during HUT with LBPP, and this might produce a smaller increase in antigravity muscle activity. Indeed, all subjects reported that their bodies felt shifted cephaladly by LBPP. It was suggested thatafferent input from mechanoreceptors in the antigravity muscles can increase orthostatic enhancement of MSNA in humans (41); therefore, the lower increase in antigravity muscle activity by LBPP in HUT might attenuate the MSNA response.

The intramuscular mechanoreflexes should have also been elicited during HUT with 30 mmHg LBPP, and its sympathoexcitatory effect could also have counteracted the sympathoinhibitory effect of baroreflexes. Although many studies have shown that activation of the intramuscular mechanoreflex alters baroreceptor control of BP and HR (30, 42, 43, 49), it is unclear whether activation of the intramuscular mechanoreflex alters baroreceptor control of MSNA. Further investigations are necessary.

In addition to the baroreflex and somatosensory reflex systems mentioned above, it may also be necessary to consider how the vestibular system affects the vaso-motor sympathetic responses to gravitational stress. Recent studies have found that stimulation of the vestibular system modifies MSNA responses (8, 27, 35). We observed that MSNA was suppressed during HUT with lower body negative pressure (LBNP) around 10 mmHg (22). The cephalad fluid shift produced by HUT was completely blocked by LBNP, indicating no loading of the cardiopulmonary baroreceptors. Therefore, the suppressed MSNA response was thought to be mainly due to the vestibular reflexes, but we do not know whether the
result should be the opposite in HUT with LBPP. If the fluid shift during HUT could have been completely equilibrated by LBPP, we would have been able to determine how the vestibular system exerted an influence on the MSNA response. Due to the limitations of our facilities, it is very difficult to raise the chamber pressure beyond 30 mmHg. We are planning to adjust the degree of HUT to block the fluid shift in the next study.

Effects of 30 mmHg LBPP on HR and TPR. Despite the marked increase in MAP, the HR remained unchanged in the supine position with 30 mmHg LBPP. Activation of the arterial baroreceptors reduces the HR (38); however, it may be difficult to further suppress the HR in the supine position, because the HR is near to a minimum already. We suppose that the arterial baroreceptors might be “statically” activated and probably lack effects on HR. Previous studies have suggested that activation of the muscle afferent nerve traffic to the cardiovascular center (31, 32, 34), when integrated with afferent information from the arterial baroreceptors, results in suppression of the expected reflex bradycardia (3, 12). It has also been reported that the activated intramuscular mechanoreflexes produced by LBPP can reduce the carotid baroreflex responsiveness (43) and override the baroreflex bradycardia (5, 42). Unfortunately, we do not have enough evidence to confirm these notions.

HR was markedly increased at 70° HUT, but it increased less on application of 30 mmHg LBPP. It was observed that both arterial PP and SV decreased significantly during HUT; however, the decrease in PP was nearly abolished while the decrease in SV was less when LBPP was applied. These results suggested that the pulsation was attenuated by LBPP, and this could reduce the HR response to HUT (38). In the present study, HR increased as MAP increased during HUT without LBPP, so this would not be considered a classic baroreflex response. Because the HR is believed to be influenced by arterial baroreceptors (38), we would have expected a decrease in this parameter when MAP was increased in HUT. However, this was obviously not the case. An increase in peripheral vascular resistance due to gravitational stress might have accounted for the increase in MAP. As the SV markedly declined with HUT due to a reduction in venous return, HR was thereby increased to maintain the CO. During HUT with LBPP, the attenuated increase in HR was not due to the higher MAP, but due to the smaller decreases in SV and arterial PP by LBPP.

The possible mechanisms for the increased TPR in the supine position were discussed in our previous study (11). Briefly, one possibility is a neurally mediated increase in TPR via an enhancement of vasomotor sympathetic nerve activity due to the intramuscular mechanoreflexes. The second mechanism is a mechanical increase in TPR by LBPP itself. The third possibility may be a hormone-related increment in TPR under 30 mmHg LBPP. Nishiyasu et al. (33) found that a given value of LBPP would cause a greater increase in resistance to flow in the lower body when applied in the supine posture than in the upright position. Our result of TPR at 70° HUT was consistent with their findings. A possible explanation is that in the supine posture the transmural pressure of the vessels is markedly lower than that in the upright posture (37), and it is possible that 30 mmHg LBPP could reduce the cross-sectional area of the tube, significantly increasing the viscous resistance to flow (19). However, this effect on TPR could be diminished by the high transmural pressure of the vessels at 70° HUT, which is why the increased TPR during HUT was not significantly different between without and with LBPP.

The increased FVR during HUT with LBPP was contrary to our expectation. The mechanism is unclear, but is probably due to the intramuscular mechanoreflexes. We speculate that activation of the intramuscular pressure-sensitive receptors may have overridden the cardiopulmonary baroreceptor withdrawal of inhibition of the forearm vasoconstriction. On the basis of the increased FVR, one would expect the forearm efferent sympathetic nerve activity to be increased by LBPP. Although a dissociation between arm and leg MSNA has been reported in the stressful condition produced by a mental task (2), arm MSNA is identical with leg MSNA during rest and orthostatic challenge (36). We cannot be sure that the direct measurement of sympathetic activity is quantitatively related to the effector response, namely, to increased vascular resistance in the target organ. Rowell and Seals (39) found close correlations between changes in FVR and MSNA in individual subjects undergoing lower body suction, but the slopes relating the two variables varied by orders of magnitude among different subjects, making correlation coefficients for pooled data statistically insignificant. Thus it is not possible to predict from a given change in MSNA what will happen at the effector site.

Limitations. Due to the limitations of our LBPP facilities, we could not apply LBPP over 30 mmHg or HUT of more than 70°. Our results showed that 30 mmHg LBPP only reduced but did not completely block the fluid shift toward the lower body during HUT. Therefore, the underlying mechanisms for the changes of MSNA response in this study became complicated. Moreover, our experimental design did not allow us to determine directly how the intramuscular mechanoreflexes and vestibular reflexes affected the MSNA responsiveness. Further investigations are needed to clarify these mechanisms.

Noninvasive impedance plethysmography was used to evaluate the SV in the present study. This method has been shown to be a reliable measure of SV as well as the change in SV during LBNP (16). However, leg fluid shifts out of the vascular compartment during HUT would change the hematocrit, which might influence the measurement of SV by this method. Hematocrit was not measured in the present study, but we suppose that the leg filtration volume during 6-min HUT would not have been very large, and the change in hematocrit might not have been very significant.
Nevertheless, using impedance plethysmography to detect the SV should be considered one of the limitations of our study.

Perspectives

This study represents the first description of how LBPP affects the vasomotor sympathetic responses to gravitational stress in humans. We found that application of 30 mmHg LBPP at 70° HUT reduced the enhancement of MSNA response. This observation can be viewed as an attempt by the cardiovascular system to oppose the sustained increase in MAP caused by LBPP through a reduction in vascular resistance, because MSNA response at least partially contributes to the increase in TPR. Moreover, our finding that LBPP restored the decrease in arterial PP during HUT may be important for the further understanding of LBPP benefits. These results provide a new insight into the mechanisms for neural control of vasomotor and cardiovascular responses to LBPP during orthostatic challenge in humans.

In conclusion, we found in the present study that application of 30 mmHg LBPP at 70° HUT reduced the increases in MSNA and HR, elevated MAP, main-
diovascular responses to LBPP during orthostatic challenge in humans. Nevertheless, using impedance plethysmography to detect the SV should be considered one of the limitations of our study.

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