Sympathetic nervous and hemodynamic responses to lower body negative pressure in hyperbaria in men

KATSUYA YAMAUUCHI, YUKA TSUTSUI, YUTAKA ENDO, SUEKO SAGAWA, FUMIO YAMAZAKI, AND KEIZO SHIRAKI

Department of Physiology, School of Medicine, University of Occupational and Environmental Health, Kitakyushu 807-8555, Japan

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Sympathetic nervous and hemodynamic responses to lower body negative pressure in hyperbaria in men. Am J Physiol Regulatory Integrative Comp Physiol 282: R38–R45, 2002.—The present study was designed to test the hypothesis that sympathetic nerve activity is attenuated in a hyperbaric environment. Response of muscle sympathetic nerve activity (MSNA) to central circulatory hypovolemic stress, lower body negative pressure (LBNP), was measured in nine men at normal and at 3 atm pressures. The stress consisted of 4 min each of control and LBNP at −20 and −40 mmHg. In addition to MSNA, heart rate, stroke volume (SV), forearm blood flow (FBF), and volume of the lower leg were recorded. A reduction of baseline HR occurred with increased forearm vascular resistance at 3 atm abs. The baseline MSNA decreased during hyperbaria. MSNA increased progressively with increasing LBNP in both atmospheric pressures, and the change from the baseline (∆MSNA) was similar in both conditions. Changes in SV, FBF, and volume of the lower legs in response to LBNP were not statistically different during exposure to 2 atm pressures. The present study suggests that hyperbaria attenuates sympathetic nerve activity; however, its responsiveness to hypovolemic stress was not affected by hyperbaric exposure.


Address for reprint requests and other correspondence: K. Shiraki, Dept. of Physiology, School of Medicine, Univ. of Occupational and Environmental Health, 1-1 Iseigaoka, Yahatanishi-ku, 807-8555 Kitakyushu, Japan (E-mail: shirak@med.uoeh-u.ac.jp).

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Cardiovascular and circulatory functions are regulated during acute orthostatic stress in humans by the sympathetic nervous system. However, it is not known whether hyperbaric exposure modifies the sympathetic control of these functions. Heart rate (HR) is reduced during both rest (5, 6, 16, 34) and exercise (7, 11, 30) under a variety of hyperbaric conditions. Hyperbaric bradycardia may be attributed to both oxygen-dependent and oxygen-independent factors (17). Hyperoxia causes bradycardia both at sea level and in hyperbaria. The bradycardia is attributable to either increased parasympathetic activity (36) and/or reduced sympathetic activity during exposure to hyperbaria. Plasma norepinephrine level (NE), as an indirect index of sympathetic nerve activity (SNA), was reported to decrease during exposure to hyperbaria (16), and a reduction in tolerance to orthostasis was observed during chronic exposure (7 days) to high pressure (1). The mechanism underlying these changes remains unclear.

Although reduced SNA has been suggested in the hyperbaric environment on the basis of plasma NE data (17), there has been no direct measurement of SNA in human.

The muscle sympathetic nerves regulate vascular resistance in the skeletal muscle of humans (31). An increase in muscle sympathetic nerve activity (MSNA) is associated with increases in vascular tone in the peripheral circulation, and decrease in MSNA is associated with decreases in vascular tone in the peripheral circulation (31). Lower body negative pressure (LBNP) is a means used for the study of the relationship between MSNA and hemodynamics, where increases in MSNA were observed during LBNP of various durations and pressures (15, 33). A tilt-table test has been also used as a means for the central hypovolemia, but in the present study we chose LBNP for the following technical reasons: 1) LBNP did not raise muscle tension in the lower extremities, which was crucially important when we monitored MSNA at the peroneal nerve, and 2) negative pressure of −20 or −40 mmHg gave the equal pressure effect on the lower extremities of the subject regardless of the ambient pressure because the negative pressure was produced by the pressure difference between ambient pressure and pressure inside the box, in which the lower extremities of the subject were placed (see METHODS).

In the present study, we hypothesize that hyperbaria attenuates SNA in humans, which in turn modulates the hemodynamic variables with the result of decreased orthostatic tolerance. Therefore, we measured MSNA, HR, blood pressure (BP), stroke volume (SV), forearm blood flow (FBF), and leg volume during LBNP in a hyperbaric environment at 3 atm abs compared with those at normal atmosphere.
METHODS

Subjects. Nine healthy male volunteers, ranging in age from 19 to 23 yr (21.0 ± 1.4 yr, means ± SE) and having a mean body weight of 65.1 ± 3.5 kg and mean height of 173.4 ± 5.8 cm, participated in this study. Written informed consent was obtained from all subjects after they were fully acquainted with the procedures and purpose of the study. All subjects were healthy and had no history of cardiovascular or kidney disease, as indicated by normal hematological data and electrocardiogram (ECG). The experimental protocol was approved by the Research and Ethics Committee of the University of Occupational and Environmental Health. We chose to use only male subjects, because we wanted to avoid large individual variations of MSNA. MSNA has been reported to be lower in young women than in men (14, 19). Also, less tolerance to LBNP has been observed in women (4, 8, 10, 35).

The thermoneutral temperature at 3 atm abs was 31°C and the temperature and RH of the chamber at 3 atm abs was 30°C, 60%. Subjects were sealed at the level of the iliac crests in a box designed for administering LBNP at 1 atm abs in the pressure control chamber. The chamber was compressed with air at a rate of 0.25 atm/min, and the temperature and RH of the chamber at 3 atm abs was maintained at thermoneutrality (31°C) and 60%, respectively. The thermoneutral temperature at 3 atm abs was reported elsewhere (11). Each subject was maintained in the supine position throughout the experimental period. Control values of all measured variables were obtained for at least 20 min before the initiation of LBNP. Temperature and humidity of the chamber were stabilized 20 min after reaching the designated pressure; thus the subject rested at 3 atm abs for 30 min before the measurements were started. LBNP was given for a 4-min period each at −20 and −40 mmHg, followed by a 5-min recovery period.

Microneurography. MSNA was recorded from the right peroneal nerve by microneurography. A tungsten microelectrode, with a shaft diameter 200 μm, a tip diameter of 1−5 μm, and an impedance of 2−4 MΩ (Frederick Haer, Bowdo-inham, ME), was inserted percutaneously without anesthesia in the muscle nerve fascicle of the peroneal nerve behind the tubular head. A subcutaneous reference electrode was placed 2−3 cm from the recording electrode. The nerve signal was amplified by a differential amplifier, and the signal was routed through a band-pass filter (E3201A, NF Electronic Instruments, Yokohama, Japan) with a bandwidth of 500−1,500 Hz. The filtered neurogram, which was made audible through a loudspeaker, was routed through a resistance-capacitance integrator unit with time constant 0.1 s (1322 Integrate unit, NEC San-Ei, Tokyo, Japan) from which an average voltage display of the nerve signal was obtained. Both filtered and integrated neurograms were stored in an eight-channel analog tape recorder (RD111T PCM Data Recorder, TEAC, Tokyo, Japan) and recorded on an eight-channel recorder with a maximum frequency response of 2.5 kHz (8M24, NEC San-Ei).

The identification of MSNA was made by applying the following criteria: 1) weak electrical stimulation through the electrode elicited involuntary muscle contractions of the appropriate muscles but not paresthesia, 2) tapping of muscles or tendons innervated by the impaled nerve fascicle evoked afferent mechanoreceptor discharges, but stroking the skin did not elicit afferent activity, 3) sympathetic impulses occurred as spontaneous bursts synchronized within the cardiac rhythm, 4) sustained expiration (apnea) resulted in increased SNA, and 5) a sudden arousal stimulus (shout) did not elicit an increase in SNA. These criteria were derived from previous reports (20). MSNA was expressed in terms of both burst rate (bursts/min) and total activity, calculated by bursts per minute times mean burst amplitude (arbitrary unit) and expressed in units per minute.

A preliminary time-control experiment was carried out at 1 and 3 atm abs in six of nine subjects to evaluate whether the MSNA fluctuated during the identical time course. MSNA was continuously recorded over 40 min at both atmospheres on separate days.

Hemodynamics. HR was measured from the three leads of an ECG. BP was measured noninvasively on the left wrist beat to beat by using the arterial tonometric method (JEN-TOW-7700, Colin, Tokyo, Japan). In short, the principle of arterial tonometry is that BP at the radial artery can be obtained by measuring the reaction forces produced by flattening the radial artery. Recently, this method has become preferred over the conventional finger photoplethysmographic method (Finapres), and the accuracy and reliability of BP measured by tonometry can be confirmed when compared with the intra-arterial method (25). Mean arterial pressure (MAP) was calculated as one-third pulse pressure plus diastolic pressure. SV was measured with a Minnesota impedance cardiograph (model 304B, Minneapolis, MN) with the standard four-band electrode arrangement. FBF was determined by venous occlusion plethysmography, with a gallium-indium strain gauge plethysmograph (Vasculab, model SPG 16 Medsonics, Mountain View, CA). A strain gauge was placed on the right midforearm, and cuffs were secured on the upper arm and the wrist. The venous occlusion cuff was placed just above the elbow inflated to a pressure of 50 mmHg, and the hand circulation was occluded by inflation of a wrist cuff with a pressure of 250 mmHg. Care was taken to support the forearm above heart level (not standardized level) to ensure adequate venous drainage during recording. Forearm vascular resistance (FVR) was calculated as MAP/FBF. Lower limb volume was determined by using four gallium-indium strain gauges (3). Two gauges were placed on the thigh: one at the junction between the upper third and the lower two-third of the thigh and the other one at the minimum circumference above the knee. On the calf, the two gauges were placed at the maximum calf girth and 5 cm above the lateral malleolus, respectively. All strain gauges were calibrated individually at 1 and 3 atm abs.

Blood sampling and plasma NE. Blood samples were taken through a 21-gauge Teflon catheter inserted in a left antecubital vein twice at control and at the end of −20 and −40 mmHg LBNP each and again at the end of recovery (5th min). Three milliliters of blood was placed into a chilled tube containing heparin for measurement of NE. The plasma was separated by centrifugation (3,000 rpm, 15 min) at 3°C and stored frozen at −70°C until assayed. Plasma NE was partially purified with absorption on activated alumina, eluted with 2% acetic acid, separated with high-performance liquid chromatography (Nanospace SI-1, Shiseido, Tokyo, Japan), and quantified with an electrochemical detector (Nanospace SI-1/2005, Shiseido). The detection limit of the assay was 0.05 nmol/l.

Statistical analysis. Because the two control measures of NE were similar, the average value was taken as the control value. Two-way ANOVA for repeated measures (LBNP treatments and atmospheric pressure as factors) was used to evaluate the various responses to LBNP. When significance
was found, Fisher’s least-significant difference test was used to identify differences between specific means. Values were expressed as means ± SE. Differences with $P < 0.05$ were considered significant.

**RESULTS**

**MSNA.** Figure 1 depicts a typical recording of MSNA and ECG from one subject at 1 and 3 atm abs. MSNA during the time-control experiment was constant at $11 = 3$ and $7 = 2$ bursts/min at 1 and 3 atm abs, respectively, being significantly ($P < 0.05$) lower at 3 atm abs compared with 1 atm abs.

The control MSNA burst rate at 1 atm abs (9 ± 1 bursts/min) increased ($P < 0.05$) during exposure to −20 mmHg LBNP (17 ± 1 bursts/min) and increased further ($P < 0.05$, vs. −20 mmHg) during −40 mmHg LBNP (29 ± 2 bursts/min) as shown in Table 1. During recovery, the value was less ($P < 0.05$) than that of the control level. A similar change was observed in total MSNA.

The control MSNA burst rate at 3 atm abs (4 ± 1 bursts/min) increased ($P < 0.05$, vs. control) during exposure to −20 mmHg (11 ± 1 bursts/min) and increased further ($P < 0.05$, vs. −20 mmHg) during

![Fig. 1. Muscle sympathetic nerve activity (MSNA) from 1 subject at 1 and 3 atm abs. Top to bottom: electrocardiogram (ECG), blood pressure, filtered neurogram of MSNA, and integrated neurogram of MSNA. MSNA shows intermittent and pulse-synchronous bursts.](http://ajpregu.physiology.org/)

Table 1. Changes in FBF, FVR, MSNA, and plasma NE content during LBNP at 1 and 3 atm abs

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>−20 mmHg</th>
<th>−40 mmHg</th>
<th>Recovery</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Δ FBF, ml·100 ml⁻¹·min⁻¹</strong></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>1 atm abs</td>
<td>0</td>
<td>−1.0 ± 0.2†</td>
<td>−1.2 ± 0.5†</td>
<td>−0.2 ± 0.5</td>
</tr>
<tr>
<td>3 atm abs</td>
<td>0</td>
<td>−1.1 ± 0.3†</td>
<td>−1.1 ± 0.2†</td>
<td>0.2 ± 0.3</td>
</tr>
<tr>
<td>Δ FVR, mmHg·ml⁻¹·100 ml·min⁻¹</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 atm abs</td>
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<td>5.7 ± 1.0†</td>
<td>7.4 ± 1.8†</td>
<td>3.3 ± 2.0</td>
</tr>
<tr>
<td>3 atm abs</td>
<td>0</td>
<td>9.2 ± 1.9†</td>
<td>6.5 ± 2.5†</td>
<td>1.0 ± 1.9</td>
</tr>
<tr>
<td><strong>Δ MSNA, burst rate/min</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 atm abs</td>
<td>9 ± 1</td>
<td>17 ± 1†</td>
<td>29 ± 2†</td>
<td>5 ± 1†</td>
</tr>
<tr>
<td>3 atm abs</td>
<td>4 ± 1†</td>
<td>11 ± 1†</td>
<td>22 ± 2†</td>
<td>4 ± 1†</td>
</tr>
<tr>
<td>Δ burst rate/min</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 atm abs</td>
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<td>8 ± 1†</td>
<td>20 ± 2†</td>
<td>−4 ± 1†</td>
</tr>
<tr>
<td>3 atm abs</td>
<td>0</td>
<td>7 ± 1†</td>
<td>18 ± 2†</td>
<td>−1 ± 1†</td>
</tr>
<tr>
<td>Δ total, U/min</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 atm abs</td>
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<td>1,090 ± 280†</td>
<td>3,111 ± 621†</td>
<td>−420 ± 104</td>
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<tr>
<td>3 atm abs</td>
<td>0</td>
<td>698 ± 92†</td>
<td>2,112 ± 288†</td>
<td>−98 ± 55</td>
</tr>
<tr>
<td><strong>Δ Plasma NE, nmol/l</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 atm abs</td>
<td>0</td>
<td>0.63 ± 0.15†</td>
<td>1.85 ± 0.40†</td>
<td>0.10 ± 0.12</td>
</tr>
<tr>
<td>3 atm abs</td>
<td>0</td>
<td>0.43 ± 0.08</td>
<td>1.57 ± 0.21†</td>
<td>0.12 ± 0.08</td>
</tr>
</tbody>
</table>

Values are means ± SE. FBF, forearm blood flow; FVR, forearm vascular resistance; MSNA, muscle sympathetic nerve activity; NE, norepinephrine. Δ burst rate/min, change in burst rate/min from control value. Δ total MSNA U/min, change in total MSNA arbitrary unit (U)/min from control value. †$P < 0.05$ vs. 1 atm abs. ‡$P < 0.05$ vs. control value.

_AJP-Regulatory Integrative Comp Physiol • VOL 282 • JANUARY 2002 • www.ajpregu.org_
–40 mmHg LBNP (22 ± 2 bursts/min). These values returned to control level during recovery (4 ± 1 burst/min), and similar change was observed in total MSNA (Fig. 2). MSNA was consistently lower at 3 atm abs compared with that of 1 atm abs. The response of MSNA (ΔMSNA) to LBNP was compared as a change from the respective control level (Table 1). The ΔMSNA during exposure to −20 and −40 mmHg LBNP was independent of ambient pressure in both burst rate and total MSNA. Because interaction between LBNP treatment and atmospheric pressure was not significant by two-way ANOVA analysis, the atmospheric pressure per se was probably not a significant factor for the different response of MSNA to LBNP.

Hemodynamics. Data on HR at 1 and 3 atm abs and during LBNP are shown in Table 2. Throughout the experiment, HR was significantly less (P < 0.05) at 3 atm abs compared with the value at 1 atm abs. HR increased significantly from control levels with graded LBNP load at both 1 and 3 atm abs. However, ΔFBF during exposure to −20 and −40 mmHg LBNP was independent of ambient pressure (Table 1).

Control FBF decreased from 5.5 ± 0.9 ml·100 ml−1·min−1 at 1 atm abs to 4.2 ± 0.7 ml·100 ml−1·min−1 (P < 0.05) at 3 atm abs (Fig. 3). FBF decreased with increasing LBNP load at both 1 and 3 atm abs. FBF was consistently lower (P < 0.05) at 3 atm abs than at 1 atm abs. However, ΔFBF during exposure to −20 and −40 mmHg LBNP was independent of ambient pressure at both 1 and 3 atm abs (Table 1).

Control FVR increased from 16.8 ± 2.1 mmHg·ml−1·100 ml·min at 1 atm abs to 23.2 ± 2.6 mmHg·ml−1·100 ml·min (P < 0.05) at 3 atm abs (Fig. 3). FVR increased with increasing LBNP load at both 1 atm abs and 3 atm abs (Fig. 3).

MAP was constant throughout the experiment (Table 2). SV at control was the same in both atmospheric pressures, decreased with increasing LBNP load, and rose significantly (P < 0.05) during the recovery period in both environments. The changes of SV with LBNP were independent of ambient pressure.

Fig. 2. Changes in plasma norepinephrine content (A) and MSNA during lower body negative pressure (LBNP) at 1 and 3 atm abs. MSNA was expressed in terms of total activity (B) [calculated by bursts/min mean burst amplitude (arbitrary unit) and expressed in U/min]. Values are means ± SE. *P < 0.05 vs. 1 atm abs. #P < 0.05 vs. control value.
and 3 atm abs. FVR was consistently higher ($P < 0.05$) at 3 atm abs than at 1 atm abs; however, AFVR during exposure to $-20$ and $-40$ mmHg LBNP was independent of ambient pressure at 1 and 3 atm abs (Table 1).

Thigh and calf volumes increased with increasing LBNP load and returned to control level during recovery at both 1 and 3 atm abs. These changes were independent of ambient pressure (Table 2).

**Plasma NE.** The control plasma NE decreased from $1.54 \pm 0.08$ nmol/l at 1 atm abs to $1.21 \pm 0.07$ nmol/l at 3 atm abs. Plasma NE increased with increasing LBNP load at 1 and 3 atm. Plasma NE during exposure to $-20$ and $-40$ mmHg LBNP were not significantly different between 1 and 3 atm abs (Fig. 2).

**DISCUSSION**

In previous reports (1, 16), we postulated a reduction of SNA in hyperbaric environments based on reduced orthostatic tolerance, cardiovascular deconditioning, and low plasma NE level. To our knowledge, this is the first study to directly measure SNA in a hyperbaric environment in humans. The major results we obtained in the present study were 1) MSNA was reduced at 3 atm abs and 2) responsiveness of MSNA to central circulatory hypovolemic stress was not significantly different at both 1 and 3 atm abs. The present study revealed that hyperbaria attenuated SNA, but the detailed mechanisms involved are not clear. What are the mechanisms underlying a reduced SNA in hyperbaric environments?

In a hyperbaric environment, both pressure and gas density are elevated. Torii et al. (32) reported that a threefold increase in normal gas density at 3 atm abs (from 1.2 kg/m$^3$ at 1 atm abs to 3.5 kg/m$^3$ at 3 atm abs) caused increased resistance in the respiratory tract, resulting in increasing negativity of the inspiratory intrathoracic pressure (Pes). This increased negative Pes could lead to an increased venous return and hence to an increased central venous pressure (CVP). The increased CVP may result in a reduced SNA. The lack of significantly greater SV in hyperbaric conditions of the present study argue against increased CVP as a mechanism for hyperbaric sympathoinhibition. However, a trend for increase in SV was observed at three of four measurements (Table 2). Therefore, this afferent input warrants further study. Other mechanisms, such as the carotid baroreflex and the chemoreceptors, are possibly involved. Because we did not observe differences in MAP, the afferent input from the carotid baroreflex had little effect on the reduced SNA. It has been suggested that the O$_2$ partial pressure inversely enhances SNA in humans. Seals et al. (26) reported that hyperoxia lowered MSNA. The reduction of MSNA in the hyperbaric environment was coincident with a decrease in plasma NE levels. It is well known that there is a close relationship between MSNA and plasma NE concentration. For example, dynamic exercise (27), a cold pressor test (33), and negative pressure breathing (29) have been reported to correlate between the level of MSNA and plasma NE content. In the present study, the control plasma NE level in the hyperbaric environment was reduced; however, plasma NE response to LBNP was not significantly attenuated at 3 atm abs. Increase in NE in response to LBNP became significant only at higher LBNP ($-40$ mmHg) at hyperbaria. These results may indicate a blunt response of plasma NE level to hypovolemic stress in hyperbaric environment. On the other hand, the LBNP-induced enhancement of MSNA was attenuated at 3 atm abs. It is not clear why a similar response did not occur in NE and MSNA in the present study. We speculate that MSNA is a sensitive measure of sympathetic activity in hyperbaric environment. Although we have no evidence, there would be a possibility that the clearance rate of NE was altered in the hyperbaric environment. Further investigation is warranted.

Bradydardia in a high-pressure environment is a consistent observation in accordance with the present study. The mechanism underlying this HR reduction (hyperbaric bradycardia) is not completely understood. It may be attributed to both oxygen-dependent and oxygen-independent factors (17). The bradycardia is attributable to either increased parasympathetic activity (36) and/or reduced sympathetic activity during exposure to hyperbaria (18). We cannot exclude the possibility that direct effects of hyperoxia and/or hyperbaria at the sinus node reduce heart rate. The oxygen independent factors for contributing to bradycardia may include gas density and pressure per se (28). These factors, individually or in combinations, may also be responsible for producing hyperbaric bradycardia.

The reduction of baseline FBF along with increased FVR at 3 atm abs indicates cutaneous and/or muscle

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**Table 2. Changes in cardiovascular and leg volume during LBNP**

<table>
<thead>
<tr>
<th>LBNP</th>
<th>Control</th>
<th>$-20$ mmHg</th>
<th>$-40$ mmHg</th>
<th>Recovery</th>
</tr>
</thead>
<tbody>
<tr>
<td>HR, beats/min</td>
<td>$1$ atm</td>
<td>$3$ atm</td>
<td>$1$ atm</td>
<td>$3$ atm</td>
</tr>
<tr>
<td></td>
<td>$62 \pm 3$</td>
<td>$70 \pm 3^+$</td>
<td>$92 \pm 7^+$</td>
<td>$57 \pm 3$</td>
</tr>
<tr>
<td></td>
<td>$57 \pm 3^+$</td>
<td>$66 \pm 7^+$</td>
<td>$86 \pm 6^+$</td>
<td>$53 \pm 2^+$</td>
</tr>
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<td>$\Delta$ HR, beats/min</td>
<td>$1$ atm</td>
<td>$3$ atm</td>
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<td></td>
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<td>$8 \pm 1^+$</td>
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<tr>
<td></td>
<td>$0$</td>
<td>$9 \pm 2^+$</td>
<td>$29 \pm 3^+$</td>
<td>$-4 \pm 1$</td>
</tr>
<tr>
<td>MAP, mmHg</td>
<td>$1$ atm</td>
<td>$3$ atm</td>
<td>$1$ atm</td>
<td>$3$ atm</td>
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<tr>
<td></td>
<td>$78 \pm 3$</td>
<td>$78 \pm 3$</td>
<td>$74 \pm 5$</td>
<td>$77 \pm 3$</td>
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<td>$81 \pm 4$</td>
<td>$76 \pm 6$</td>
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<td>$70 \pm 8^+$</td>
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<td>Thigh volume,</td>
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<td>$1$ atm</td>
<td>$3$ atm</td>
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<td>ml</td>
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<td>$1,694 \pm 99^+$</td>
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<td>Calf volume,</td>
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<td>$1$ atm</td>
<td>$3$ atm</td>
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<td>$1,590 \pm 46$</td>
<td>$1,573 \pm 46^+$</td>
<td>$1,590 \pm 46^+$</td>
<td>$1,560 \pm 46^+$</td>
</tr>
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</table>

Values are means ± SE. HR, heart rate; MAP, mean arterial pressure; SV, stroke volume; LBNP, lower body negative pressure. $^*P < 0.05$ vs. 1 atm abs. $^\dagger P < 0.05$ vs. control value.
vasoconstriction (24). Decreased limb blood flow in resting humans was observed during exposure to hyperbaria (22), and this effect was attributed to an influence of hyperoxia on vascular smooth muscle (2, 3). This mechanism probably played a contributing role in the decreased FBF in the hyperbaric environment of the present study; however, the hyperoxia-induced reduction in MSNA probably did not play a major role in changing the vasomotor activity in the cutaneous vasculature. It is unlikely that a discrepant sympathetic outflow between the leg and the arm occurred in the present study, because it is generally recognized that the response of MSNA in the peroneal nerve and the radial nerve is identical during LBNP (21, 33). However, evidence exists that circulatory response in the leg and the arm is incompatible during head-up tilt (12). Therefore, we need further observation to determine whether discordant circulatory responses occur in the hyperbaric environment. The other factor of increased FVR may be related to altered sensitivity of the adrenoreceptors. This notion is based on the inverse relationship between circulating NE and adrenoreceptor sensitivity, because adrenoreceptor hypersensitivity has been reported in patients with dysautonomias in which circulating catecholamines are absent or reduced (23).

Changes in intrathoracic blood volume cause reflex changes in blood flow in the human forearm. A decrease in the intrathoracic blood volume by the application of LBNP causes reflex constriction of these vessels. Current evidence indicates that the reflex control of FBF and FVR during LBNP is primarily under the control of cardiopulmonary baroreflexes, although an interaction with high-pressure arterial baroreceptors is possible at higher levels of LBNP (9).

Changes in leg volume in response to LBNP were independent of ambient pressure, suggesting that venous compliance in the lower extremities was not altered during the acute exposure at 3 atm abs.

There are at least three important findings in the present study. First, because responsiveness of MSNA to hypovolemic stress was found to be independent of ambient pressure during LBNP, SNA contributed to maintenance of BP during acute hyperbaric exposure. Second, the reduction of baseline FBF with a concurrent increase in FVR at 3 atm abs indicated a substantial cutaneous and/or muscle vasoconstriction in a hyperbaric environment. Third, MAP was found to be independent of ambient pressure, but HR was reduced at 3 atm abs. Orthostatic intolerance during a long-term exposure to a hyperbaric environment observed in earlier observations may be attributed, in part, to attenuated SNA. The reduced baseline SNA at 3 atm abs suggests that an enhanced SNA response is needed to support cardiovascular requirements of orthostasis, as indicated by increased total peripheral resistance.
(24). However, in the present study, the response at 3 atm abs was the same as at 1 atm abs, which therefore contributed to reduce orthostatic tolerance (LBNP) in hyperbaria.

In conclusion, the present study reveals that hyperbaria attenuates SNA, but that its responsiveness to hypovolemic stress may not be affected by increased atmospheric pressure in humans.

Perspectives

It is not certain whether the present observation indicates an attenuation of SNA in deeper dives, because the PO2 of the inspiratory gas mixture during deeper dives is usually controlled at near 0.4 atm abs by breathing the artificially composed gas mixture. To identify the major contributing factor for altered SNA response, MSNA should be studied in hyperoxic normoxic environments as well as in hyperbaric normoxic environments. It is also not certain whether deep water diving differs from the present experimental condition. We know of a single observation that suggests there is no change in forearm blood flow during deep water diving (13), because this study observed that tissue insulation of the forearm during immersion at 15-m depth in the critical water temperature was identical to that of surface diving.

Although the present study revealed the data in men, it is not clear whether the present results are applicable to women during similar conditions.

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