

A comparison of autonomic responses in humans induced by two simulation models of weightlessness: lower body positive pressure and 6° head-down tilt

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Abstract

Six-degree head-down tilt (HDT) is well accepted as an effective weightlessness model in humans. However, some researchers utilized lower body positive pressure (LBPP) to simulate the cardiovascular and renal effects of a decreased gravitational stress. In order to determine whether LBPP was a suitable model for simulated weightlessness, we compared the differences between these two methods. Ten healthy males, aged 21–41 years, were subjected to graded LBPP at 10, 20 and 30 mm Hg, as well as 6° HDT. Muscle sympathetic nerve activity (MSNA) was microneurographically recorded from the tibial nerve along with cardiovascular variables. We found that MSNA decreased by 27% to a similar extent both at low levels of LBPP (10 and 20 mm Hg) and HDT. However, at a high level of LBPP (30 mm Hg), MSNA tended to increase. Mean arterial pressure was elevated significantly by 11% (10 mm Hg) at 30 mm Hg LBPP, but remained unchanged at low levels of LBPP and HDT. Heart rate did not change during the entire LBPP and HDT procedures. Total peripheral resistance markedly increased by 36% at 30 mm Hg LBPP, but decreased by 9% at HDT. Both stroke volume and cardiac output tended to decrease at 30 mm Hg LBPP, but increased at HDT. These results suggest that although both LBPP and HDT induce fluid shifts from the lower body toward the thoracic compartment, autonomic responses are different, especially at LBPP greater than 20 mm Hg. We note that high levels of LBPP (>20 mm Hg) activate not only cardiopulmonary and arterial baroreflexes, but also intramuscular mechanoreflexes, while 6° HDT only activates cardiopulmonary baroreflexes. We conclude that LBPP is not a suitable model for simulated weightlessness in humans. © 2000 Elsevier Science B.V. All rights reserved.

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1. Introduction

During spaceflight a cephalad redistribution of blood and fluid occurs due to loss of gravity. Six-degree head-down tilt (HDT) has been widely accepted as an effective simulated weightlessness model in humans by inducing a fluid shift from the lower body towards the thoracic compartment and loading the cardiopulmonary baroreceptor (Kakurin et al., 1976). Some researchers have utilized lower body positive pressure (LBPP) to simulate the cardiovascular and renal effects of a decreased gravitational stress since 1980s (Bennett et al., 1982; Kass and Moore-Ede, 1982; Geelen et al., 1989), because LBPP could also cause fluids to shift from the lower part of the

body to the thorax and result in a loading of cardiopulmonary baroreceptors. These researchers have anticipated that LBPP increased central blood volume in a manner similar to HDT.

However, Gaffney et al. investigated the central hemodynamic effects of LBPP in humans and observed unexpected decreases in stroke volume and cardiac output during LBPP of 40 and 100 mm Hg in supine subjects (Gaffney et al., 1981). Furthermore, Shi et al. found that LBPP caused reflex modulation of the cardiovascular system by stimulating not only cardiopulmonary and arterial baroreceptors but also intramuscular pressure-sensitive receptors (Shi et al., 1993a,b, 1997). However, 6° HDT only stimulates the cardiopulmonary baroreceptors without changes in systemic arterial blood pressure or heart rate (London et al., 1983; Goldsmith et al., 1985; Goldsmith, 1988, 1991).

The purpose of this study was to determine whether

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LBPP could be regarded as a suitable model for simulated weightlessness in humans. In order to conduct this purpose, we compared the differences in autonomic responses to LBPP and to 6° HDT.

2. Methods

2.1. Subjects

Ten healthy men aged from 21 to 41 years, weighing 58.6 ± 2.2 kg (body fat < 20%) and 170.1 ± 1.6 cm tall were selected. None had a history of cardiovascular, kidney or other diseases, and were not on any medication at the time of study. All had abstained from alcohol and caffeine use 24 hr prior to 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 this study and gave their consent to participate in the experiment. The 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.

2.2. Experimental protocol and procedures

We used the system for local negative and positive pressure loading (Kawasaki Heavy Industries) at the Space Medicine Research Center, affiliated with the Research Institute of Environmental Medicine, Nagoya University. The ambient temperature of the experimental room was kept at 25–27°C using an air conditioner. All experiments were carried out with the subject supine on the tilt table. MSNA was recorded microneurographically from the tibial nerve at the popliteal fossa. Respiration curves derived from nasal airflow with a thermistor, precordial electrocardiogram (ECG) from a CM5 lead, and blood pressure (mm Hg) waves obtained using tonometry (model BP-508S, Colin Electronics, Komaki, Japan) were simultaneously recorded. Impedance plethysmography (model AI-601G, Nihon Kohden, Tokyo, Japan) was used to measure transthoracic impedance (Z_0) for the estimation of fluid shift and stroke volume (SV, ml beat⁻¹). After having rested for >30 min, the subject was asked to breathe synchronously to an electronic metronome set at a frequency of 0.25 Hz. After recording the control data for MSNA, ECG, blood pressure, respiration, and Z_0 , along with dZ/dt (differential of Z_0) for 6 min, LBPP and HDT were applied to the subjects. LBPP was progressively increased to 10, 20 and 30 mm Hg, while HDT was progressively increased to 6°. Each step lasted for 6 min. All variables were monitored continuously throughout the procedures and stored on a DAT recorder (model PC216Ax, 8-channel, double-speed, Sony Precision Technology, Tokyo, Japan).

2.3. LBPP and HDT

Graded LBPP was applied distally to the subject's iliac crests 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 the 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 up and down hydraulically, and a 6° HDT was utilized.

2.4. Recording of muscle sympathetic nerve activity

MSNA was recorded from the tibial nerve at the popliteal fossa by a microneurographic technique using a tungsten microelectrode with a tip diameter of about 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 500–5000-Hz band-pass filter. MSNA was then full-wave rectified and integrated with a time constant of 0.1 sec. The identification of MSNA was based on the presence of the following discharge characteristics reported previously elsewhere (Vallbo et al., 1979): (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 skin touch; (3) modulation by respiration; and (4) enhancement by maneuvers increasing intrathoracic pressure, such as the Valsalva maneuver.

2.5. Data collection and analysis

Data from the last 5 min of the resting period and for each stage were selected for analysis. The integrated MSNA trace was displayed along with the ECG 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) and the number of bursts per 100 heartbeats (burst incidence) were used as quantitative indexes. SV was calculated from the equation $SV = \rho(L/Z_0)^2(dZ/dt)_{\min}T$, where ρ is a constant with a value of 135 Ω cm, L is the distance between the two inner circular electrodes, Z_0 is the total impedance of the thorax, $(dZ/dt)_{\min}$ is the differential of Z_0 per minute, and T is the left ventricular ejection time. Cardiac output (CO, l min⁻¹) was obtained as the product of SV and the heart rate (HR, beats min⁻¹). Mean arterial pressure (MAP, mm Hg) was calculated as diastolic blood pressure (mm Hg) plus one-third of pulse pressure (mm Hg). Total peripheral resist-

Table 1

A comparison of the effects of lower body positive pressure and head-down tilt on muscle sympathetic nerve activity and systemic hemodynamic variables^a

	LBPP				Control-2	HDT (6°)
	Control-1	10 mm Hg	20 mm Hg	30 mm Hg		
MAP (mm Hg)	82.1±2.1	80.6±2.3	84.9±2.4	91.3±3.2*	84.0±1.6	85.4±1.8
HR (beats min ⁻¹)	59.6±2.6	58.8±2.5	58.5±2.2	58.7±2.5	59.1±2.5	56.9±2.0
SV (ml beat ⁻¹)	71.9±11.2	70.2±9.3	60.8±7.1	58.3±9.4	70.8±8.2	77.9±8.9*
CO (l min ⁻¹)	4.2±0.6	4.1±0.5	3.5±0.4	3.4±0.5	4.1±0.5	4.4±0.6*
Z0 (Ω)	26.2±1.3	25.8±1.2	25.5±1.2	25.6±1.2	26.0±1.3	25.2±1.1*
TPR (PRU)	22.6±2.8	22.4±2.8	26.2±2.3	30.7±3.3*	22.5±2.6	20.6±2.0*
MSNA						
BR (bursts min ⁻¹)	14.2±1.5	10.3±1.2*	10.3±1.4*	12.9±1.4	14.7±1.3	10.7±1.3*
BI (bursts 100 beats ⁻¹)	24.1±2.7	17.8±2.2*	17.6±2.4*	22.0±2.0	25.2±2.3	18.5±2.1*

^a Values are mean±SE. LBPP, lower body positive pressure; HDT, head-down tilt; MAP, mean arterial pressure; HR, heart rate; SV, stroke volume; CO, cardiac output; Z0, transthoracic impedance; TPR, total peripheral resistance; PRU, peripheral resistance unit; MSNA, muscle sympathetic nerve activity; BR, burst rate; BI, burst incidence. *, $P<0.05$ vs. control.

ance [TPR, mm Hg sec ml⁻¹, i.e. peripheral resistance unit] was the ratio of MAP to CO.

2.6. Statistical analysis

The group data were averaged and expressed as mean±standard errors (S.E.). One-way factorial ANOVA and multiple comparison test using Fisher's least-significant difference were undertaken to determine the effects of LBPP on the MSNA responses and systemic hemodynamic variables. The paired Student's *t*-test was used to determine the effects of 6° HDT on MSNA and cardiovascular responses. $P<0.05$ was considered significant. All analyses were conducted using a statistical analysis program (StatView J-4.5, Power PC version, 1992–95 Abacus Concepts).

3. Results

Complete data were obtained in all studies. There were no untoward effects from the study, and none of the subjects complained of any discomfort during the experi-

ment. The results are shown in Tables 1 and 2 and Figs. 1–4.

MSNA was suppressed during low levels of LBPP (10 and 20 mm Hg) and 6° HDT, burst rate declined by 27.5% ($P<0.05$) during low levels of LBPP and by 27.2% ($P<0.05$) at 6° HDT. However, MSNA tended to increase at 30 mm Hg LBPP. MAP was elevated significantly by 11% (10 mm Hg) at 30 mm Hg LBPP ($P<0.05$), but remained unchanged at low levels of LBPP and 6° HDT. HR remained unchanged during the entire procedures of LBPP and 6° HDT. TPR markedly increased by 36% at 30 mm Hg LBPP ($P<0.05$) but decreased by 9% at 6° HDT ($P<0.05$). Both SV and CO tended to decrease at 30 mm Hg LBPP, but increased at 6° HDT ($P<0.05$). Z0 was decreased slightly during LBPP, but significantly ($P<0.05$) during 6° HDT.

4. Discussion

In the present study, we found that the effects of LBPP on vasomotor sympathetic activity and cardiovascular responses were quite different from those of 6° HDT, especially at 30 mm Hg LBPP.

Table 2

Deviations in mean arterial pressure, heart rate, stroke volume, cardiac output, total peripheral resistance and muscle sympathetic nerve activity (burst rate) during graded lower body positive pressure and 6° head-down tilt^a

	LBPP			HDT
	10 mm Hg	20 mm Hg	30 mm Hg	
MAP (mm Hg)	N.S.	N.S.	+9.2	N.S.
HR (beats min ⁻¹)	N.S.	N.S.	N.S.	N.S.
SV (ml beat ⁻¹)	N.S.	N.S.	N.S.	+7.1
CO (l min ⁻¹)	N.S.	N.S.	N.S.	+0.3
TPR (PRU)	N.S.	N.S.	+8.1	-1.9
MSNA-BR (bursts min ⁻¹)	-3.9	-3.9	N.S.	-4

^a LBPP, lower body positive pressure; HDT, head-down tilt; MAP, mean arterial pressure; HR, heart rate; SV, stroke volume; CO, cardiac output; TPR, total peripheral resistance; PRU, peripheral resistance unit; MSNA, muscle sympathetic nerve activity; BR, burst rate; N.S., not significant.

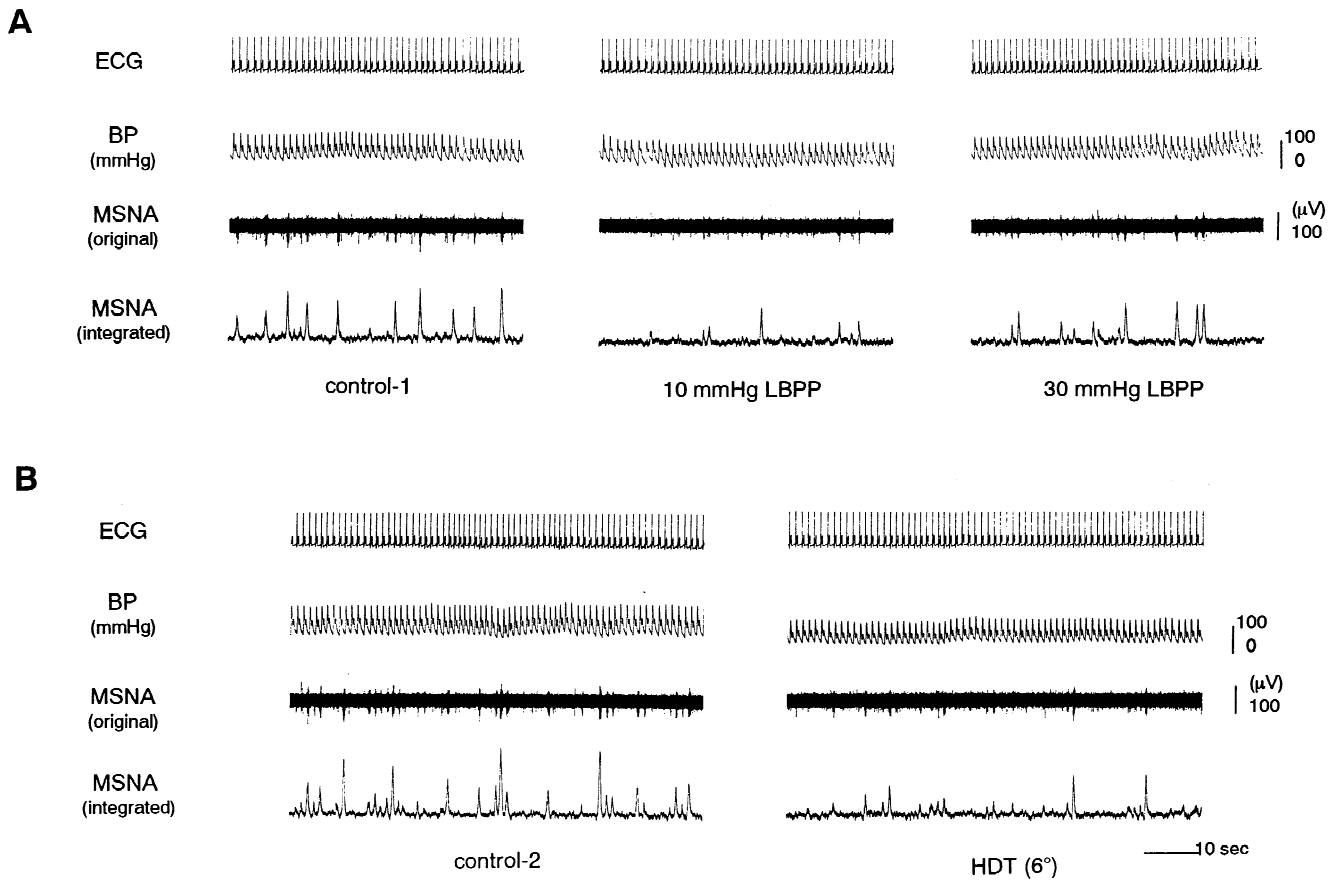


Fig. 1. Original tracings of electrocardiogram (ECG), blood pressure (BP), and muscle sympathetic nerve activity (MSNA, original and integrated) during lower body positive pressure (LBPP) (A), and 6° head-down tilt (HDT) (B) in one subject.

4.1. A comparison between low levels of LBPP and 6° HDT

MSNA was significantly suppressed while systemic blood pressure and heart rate did not change during low

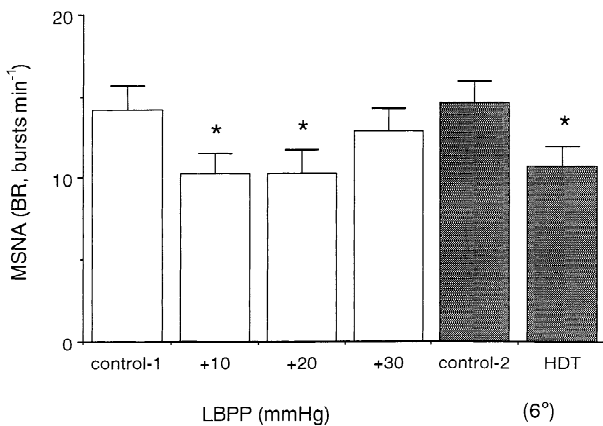


Fig. 2. A comparison of muscle sympathetic nerve activity responses to lower body positive pressure and 6° head-down tilt in humans. MSNA, muscle sympathetic nerve activity; BR, burst rate; LBPP, lower body positive pressure; HDT, head-down tilt. *, $P < 0.05$ vs. control.

levels of LBPP and 6° HDT. Translocation of fluid volume from the lower body to the thorax was suggested by a reduction of thoracic impedance (Z0). It is well known that maneuvers to increase venous return decrease MSNA by loading the cardiopulmonary baroreceptors, since the cardiopulmonary baroreceptors convey tonic afferent nerve traffic to the cardiovascular center and inhibit efferent sympathetic nerve activity to muscle (Deliuss et al., 1972; Mancia et al., 1976; Thoren, 1979). The suppression of MSNA during low levels of LBPP and 6° HDT is thought to buffer the hypertensive effect of the increased venous return by reducing peripheral vascular resistance.

In general, an increase in MSNA is associated with increases in vascular tone and a decrease in MSNA is associated with decreases in vascular tone in peripheral circulation (Vallbo et al., 1979). Therefore, reduction in MSNA can cause a decrease in TPR. This relationship was observed during 6° HDT in our study. In normotensive subjects at HDT, a decrease in venous tone has been also found (London et al., 1983). However, TPR did not decrease during LBPP, despite a reduction in MSNA. The extramural pressure of the vessels in the lower part of the body increases in parallel with the pressure levels of the chamber. The increase in local extramural pressure may

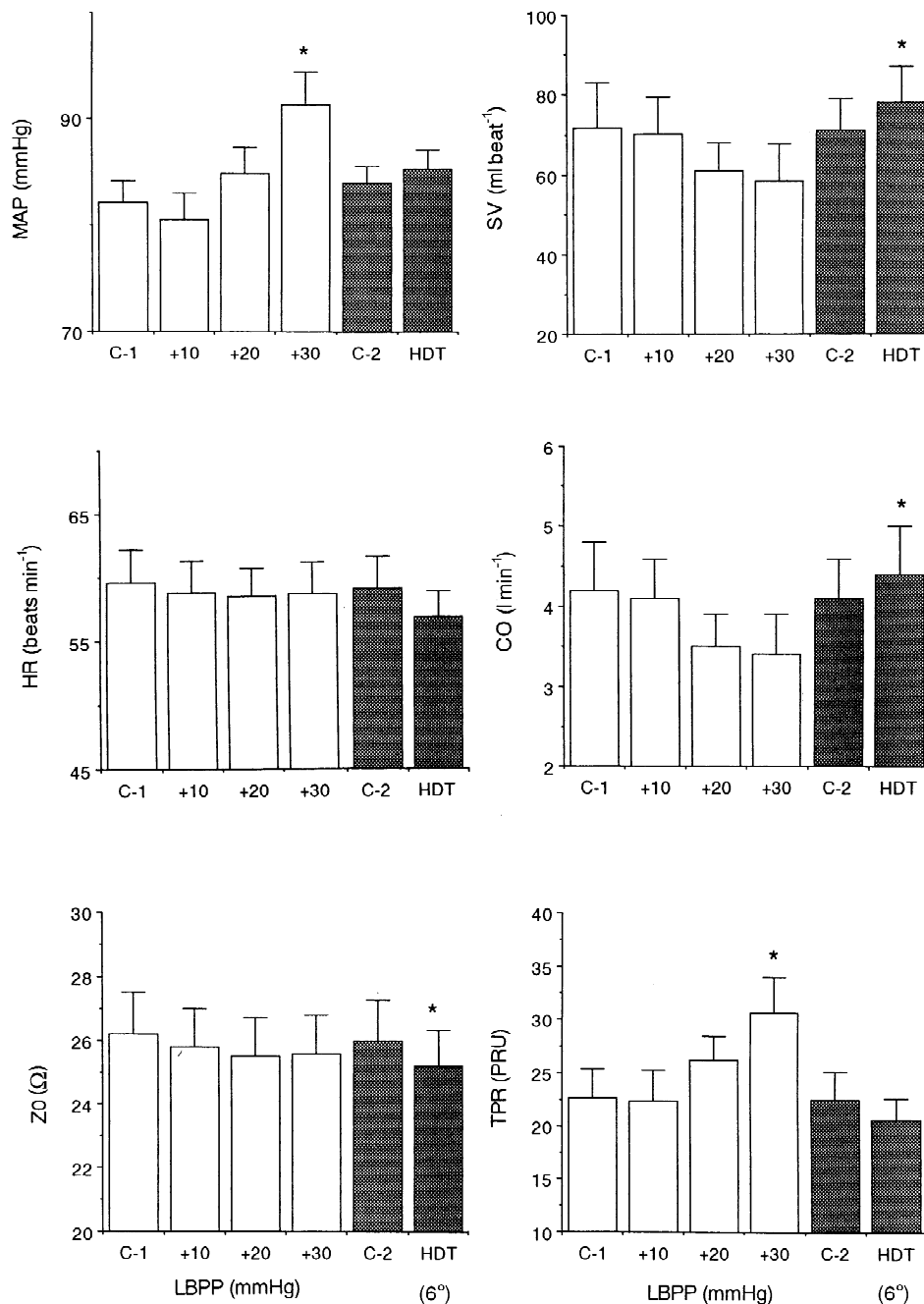


Fig. 3. Different systemic hemodynamic responses to lower body positive pressure and 6° head-down tilt. LBPP, lower body positive pressure; HDT, head-down tilt; MAP, mean arterial pressure; HR, heart rate; Z0, transthoracic impedance; SV stroke volume; CO, cardiac output; TPR, total peripheral resistance; PRU, peripheral resistance unit; C-1, control-1; C-2, control-2. *, $P < 0.05$ vs. control.

compress the venous system. This mechanical compression of the venous system may increase venous tone according to Laplace's law, possibly causing an increase in peripheral vascular tone in the lower extremities.

4.2. A comparison of high level LBPP and 6° HDT

Unlike at low levels of LBPP and 6° HDT, MSNA tended to be enhanced at a high level of LBPP (30 mm Hg), possibly because of the intramuscular mech-

anoreflexes. It has been reported that $LBPP > 20$ mm Hg can activate the intramuscular pressure-sensitive receptors (Shi et al., 1993a). The activation of these receptors increases afferent nerve traffic to the cardiovascular center (Mitchell et al., 1983; McWilliam and Yang, 1991) via the group III and/or IV afferent nerve fibers, through dorsal spinal root pathways (McCloskey and Mitchell, 1972; Kumazawa and Mizumura, 1977). The afferent activity results in a sustained rise in both TPR (Kumada et al., 1975; Gaffney et al., 1981; Williamson et al., 1994) and

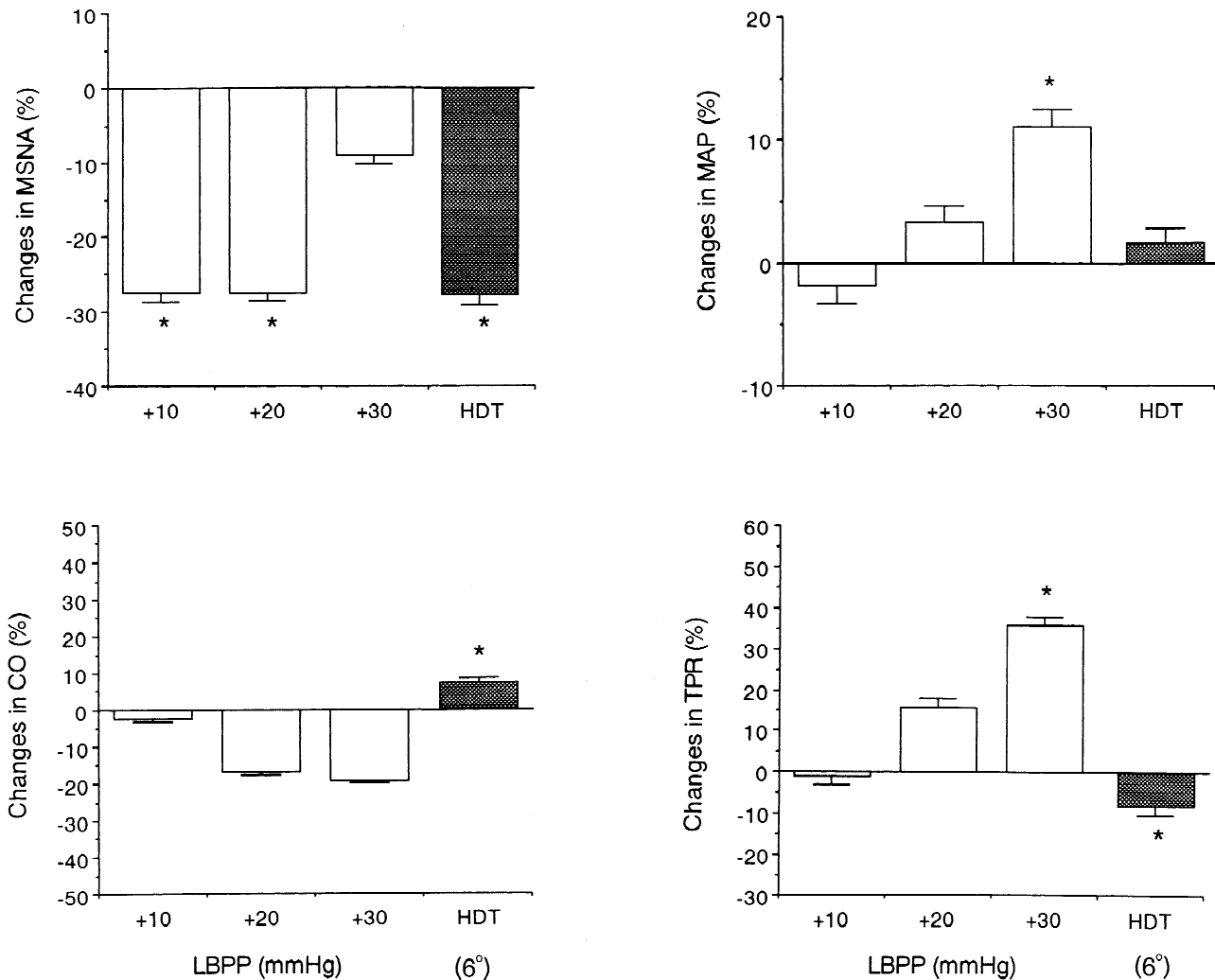


Fig. 4. Comparisons of changes in muscle sympathetic nerve activity, mean arterial pressure, cardiac output, and total peripheral resistance during lower body positive pressure and 6° head-down tilt. MSNA, muscle sympathetic nerve activity; MAP mean arterial pressure; CO, cardiac output; TPR, total peripheral resistance. *, $P < 0.05$ vs. control.

arterial pressure (Julius et al., 1982; Osterziel et al., 1984; Julius, 1986, 1988; Williamson et al., 1994). Though high levels of LBPP cause cardiopulmonary and arterial baroreceptor loading, which has a suppressive effect on MSNA, the baroreflex-mediated suppressive response of MSNA could be counteracted by the excitatory effect of the intramuscular pressure-sensitive receptor activation (Fu et al., 1998).

Another difference was a marked increase in TPR during high levels of LBPP in contrast with a significant reduction in TPR during 6° HDT. One possibility is an enhancement of vasomotor sympathetic nerve activity. However, in the present study, MSNA at 30 mm Hg LBPP was still close to the control value. Therefore, the increase in TPR during 30 mm Hg LBPP can not be fully explained by an increase in vasomotor sympathetic nerve activity. In addition to the neural-mediated increase in TPR, high levels of LBPP may cause a mechanical increase in TPR based on Laplace's law and a hormone-related increase in

TPR, such as an enhancement of the renin–angiotensin–aldosterone axis, which has a vasoconstrictive effect (Mannix et al., 1996).

4.3. Different SV and CO responses to LBPP and 6° HDT

We found that both LBPP and 6° HDT increased preload because of a cephalad fluid shift. However, SV and CO changed differently in these two procedures. Both SV and CO had a tendency to decrease at 30 mm Hg LBPP, while they increased during 6° HDT. TPR increased during LBPP, especially at high levels of LBPP, indicating an increase in afterload. Since afterload also plays an important role in determining stroke volume, the increase in preload under the graded LBPP could be completely offset by the opposing effect of increased afterload, resulting in a decrease in SV (Julius et al., 1982). In contrast, during 6° HDT, the decreased TPR indicated a reduction of after-

load. Thus, the increase in preload resulted in increases in SV and CO.

4.4. Conclusion

In this study, we compared the different autonomic responses to LBPP and to 6° HDT in healthy humans. Though either LBPP or 6° HDT produced a fluid shift from the lower body towards the thoracic compartment, responses of vasomotor sympathetic activity and cardiovascular variables such as TPR, SV and CO were quite different, especially at high levels of LBPP. Thus, we conclude that LBPP is not a suitable model for simulating weightlessness in humans, especially at LBPP greater than 20 mm Hg.

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