

Central volume expansion is pivotal for sustained decrease in heart rate during seated to supine posture change

BETTINA PUMP,¹ TSUTOMU KAMO,⁴ ANDERS GABRIELSEN,¹ PETER BIE,²
NIELS JUEL CHRISTENSEN,³ AND PETER NORSK¹

¹Danish Aerospace Medical Centre of Research, Rigshospitalet 7805, DK-2200 Copenhagen;

²Department of Physiology, University of Odense, DK-5000 Odense C; ³Department of Internal Medicine and Endocrinology, Herlev Hospital, DK-2730 Herlev, Denmark; and

⁴Neurology Division, St. Marianna University, Kanagawa, 216-8511 Kawasaki, Japan

Received 3 May 2001; accepted in final form 30 May 2001

Pump, Bettina, Tsutomu Kamo, Anders Gabrielsen, Peter Bie, Niels Juel Christensen, and Peter Norsk.

Central volume expansion is pivotal for sustained decrease in heart rate during seated to supine posture change. *Am J Physiol Heart Circ Physiol* 281: H1274–H1279, 2001.—During prolonged, static carotid baroreceptor stimulation by neck suction (NS) in seated humans, heart rate (HR) decreases acutely and thereafter gradually increases. This increase has been explained by carotid baroreceptor adaptation and/or buffering by aortic reflexes. During a posture change from seated to supine (Sup) with similar carotid stimulation, however, the decrease in HR is sustained. To investigate whether this discrepancy is caused by changes in central blood volume, we compared ($n = 10$ subjects) the effects of 10 min of seated NS (adjusted to simulate carotid stimulation of a posture change), a posture change from seated to Sup, and the same posture change with left atrial (LA) diameter maintained unchanged by lower body negative pressure (Sup + LBNP). During Sup, the prompt decreases in HR and mean arterial pressure (MAP) were sustained. HR decreased similarly within 30 s of NS (65 ± 2 to 59 ± 2 beats/min) and Sup + LBNP (65 ± 2 to 58 ± 2 beats/min) and thereafter gradually increased to values of seated. MAP decreased similarly within 5 min during Sup + LBNP and NS (by 7 ± 1 to 9 ± 1 mmHg) and thereafter tended to increase toward values of seated subjects. Arterial pulse pressure was increased the most by Sup, less so by Sup + LBNP, and was unchanged by NS. LA diameter was only increased by Sup. In conclusion, static carotid baroreceptor stimulation per se causes the acute (<30 s) decrease in HR during a posture change from seated to Sup, whereas the central volume expansion (increased LA diameter and/or arterial pulse pressure) is pivotal to sustain this decrease. Thus the effects of central volume expansion override adaptation of the carotid baroreceptors and/or buffering of aortic reflexes.

antidiuretic hormone; baroreceptors; blood pressure; lower body negative pressure; neck suction

HEART RATE (HR) is decreased throughout a posture change from upright seated to supine (Sup), during which arterial high-pressure and cardiopulmonary low-pressure receptors are stimulated (20, 21). During

prolonged static neck suction (NS), which stimulates only carotid baroreceptors, there is an acute decrease in HR, but thereafter it increases toward control levels (8, 15, 32).

The gradual increase in HR over time during NS after the prompt decrease is probably caused by baroreceptor adaptation and/or buffering from the aortic receptors (4, 16, 26). Thus, the question arises why these mechanisms do not induce a gradual increase in HR during a seated to Sup posture change.

The discrepancy in duration of the HR response to NS versus a posture change from seated to Sup could be due to the increase in central blood volume that takes place immediately when the posture is changed to Sup or to other factors activated by movement of the upper body. Vestibular stimulation, which probably occurs to some degree by the posture change, has been shown to affect HR and sympathetic nervous activity (2, 23, 24). Activation of intra-abdominal receptors (1) or changes in intracranial pressure might also cause hemodynamic effects. Thus these factors and/or central volume expansion could be causes for the sustained decrease in HR in the Sup position.

In this study, we compared the effects of a posture change from seated to Sup, seated NS with the level adjusted to simulate the hydrostatic pressure increase of a posture change in the carotid sinus, and a posture change combined with low-level lower body negative pressure (Sup + LBNP) adjusted so that low pressure receptor stimulation was prevented by keeping left atrial (LA) diameter unchanged (19, 20). NS and Sup + LBNP would in this way cause the same degree of carotid high- and cardiopulmonary low-pressure receptor stimulation, with and without movement of the upper body. During Sup and Sup + LBNP, however, there would be similar body movements and hydrostatic carotid baroreceptor stimulation, with and without simultaneous central blood volume expansion.

In this way, we tested the hypothesis that central blood volume expansion by a seated to Sup posture

Address for reprint requests and other correspondence: B. Pump, Rigshospitalet 7805, 9 Blegdamsvej, DK-2100 Copenhagen, Denmark (E-mail: bpump@post.uni2.dk).

The costs of publication of this article were defrayed in part by the payment of page charges. The article must therefore be hereby marked "advertisement" in accordance with 18 U.S.C. Section 1734 solely to indicate this fact.

change overrides the effect on HR of adaptation of carotid baroreceptors and/or buffering of the aortic reflexes and that it is pivotal for the sustained bradycardic response.

MATERIALS AND METHODS

Ten male subjects aged 24 ± 1 yr (range 21–28 yr), with a height of 182 ± 2 cm (174–196 cm), and weight of 80 ± 3 kg (62–94 kg), completed the experiment. All were nonsmokers, had a negative history of cardiovascular and kidney diseases, and were healthy as indicated by a normal physical examination, arterial blood pressure, electrocardiogram, and urine strip test for glucose, leukocytes, erythrocytes, and protein. None of the subjects took any medication for at least 1 mo before the study. Informed consent was obtained after the subjects had read a description of the experimental protocol, which was approved by the Ethics Committee of Copenhagen (KF 01–323/96) and was in compliance with the Declaration of Helsinki. No complications occurred.

The patient spent the night at the laboratory and fasted for 12 h before the experiment. He was instrumented with a short venous catheter (1.2×45 mm, Venflon 2), arterial pressure cuffs, and a NS device around the whole circumference of the neck (11, 13) and rested seated with the legs placed horizontally in an LBNP box (19) for 30 min before start of the experiment at 8:30 AM.

The experiment consisted of four sessions, each lasting 30 min: 1) a control session in which the subject was seated with his trunk vertical with back and neck support and the legs placed horizontally for 30 min; 2) a session (Sup) with 10 min of being seated (with legs horizontal), 10 min in the Sup position, and then again 10 min of being seated; 3) a session with 30 min of being seated but with simultaneous application of NS during the middle 10 min; and 4) a session with posture changes similar to during session 2, but with application of LBNP when the subject was in the Sup position (Sup + LBNP) (19). The sessions were separated by 30 min of being seated and performed with the sequence in a balanced, randomized order between the subjects.

The level of NS was adjusted (22.2 ± 0.4 mmHg) so that it would resemble the effect of the hydrostatic pressure when going from the seated to the Sup position (11). The adjustment was done by measuring the distance from the carotid sinus to the heart level (fourth intercostal space) on each subject in the seated position and by taking into account that only 64% of the NS is transmitted to the carotid sinus (13).

Blood (18 ml) was sampled at 10-min intervals for determination of plasma concentrations of norepinephrine (NE), epinephrine (E), arginine vasopressin (AVP), and plasma osmolality as previously described (5, 12, 20). The catheter was thereafter flushed with 18 ml of isotonic saline.

Arterial pressures were measured every 5 min by conventional sphygmomanometry as previously described (20), and peripheral mean arterial pressure (MAPp) was additionally measured continuously by a photoplethysmographic method (19). HR was registered continuously with chest electrodes (19).

Left atrial (LA) diameter was measured at 5-min intervals by echocardiography from the parasternal long-axis view (6), as previously described (20). During Sup + LBNP, however, LA diameter was measured continuously (19, 20). Room temperature was kept between 24.1° and 26.4°C and humidity between 35 and 55%.

Analysis of variance software (ANOVA; Statgraphics Plus for Windows, version 3.0) for repeated measures with the

variable as main variate and time and subject as factors was used to evaluate the effects on a variable over time within each series of experiment compared with the initial 10 min. Differences between mean values were evaluated by a post hoc

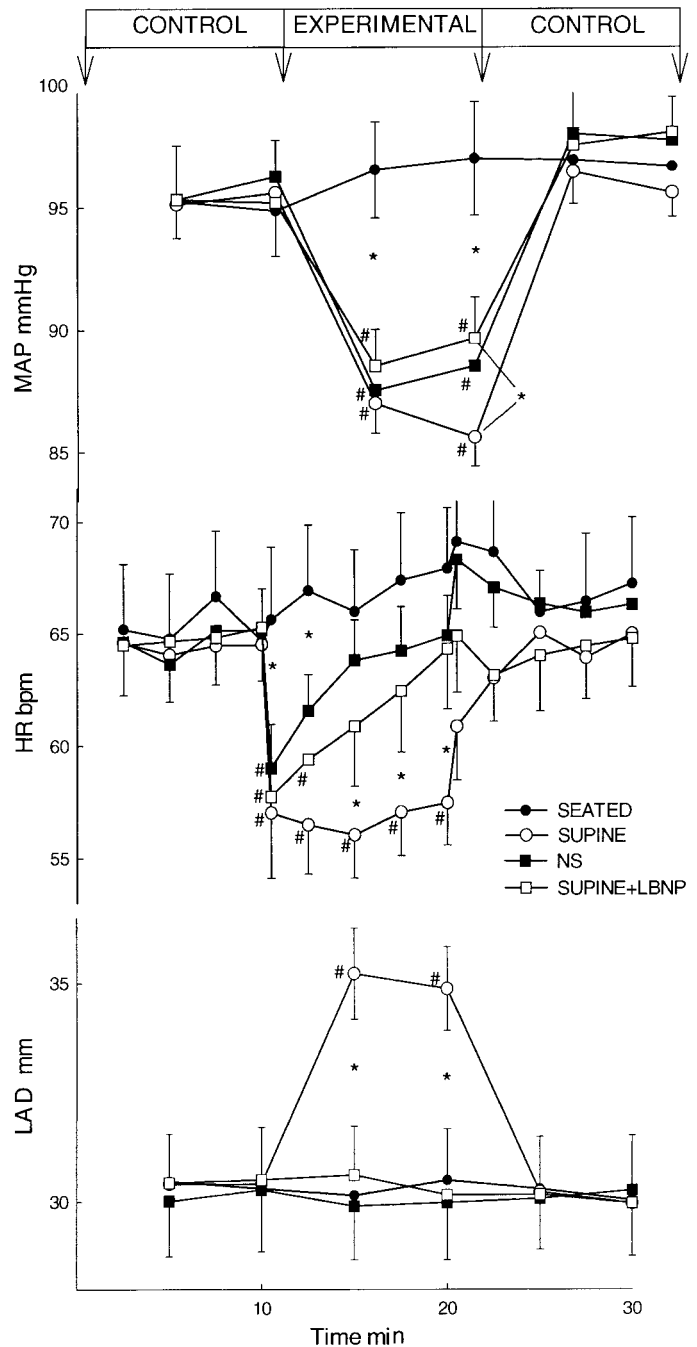


Fig. 1. Mean arterial pressure (MAP), heart rate (HR), and left atrial (LA) diameter during 10 min of being seated without and with simultaneous application of neck suction (NS) adjusted to counteract the pressure of the hydrostatic column from heart to carotid sinus, during supine (10 min of being supine) without and with simultaneous lower body negative pressure (Supine + LBNP) adjusted to keep LA diameter unchanged compared with that of the seated position. Each intervention is preceded and followed by 10 min in the seated position. Values are means \pm SE, $n = 10$ subjects. # $P < 0.05$, significant difference compared with values of initial 10 min in the seated position. * $P < 0.05$, between sessions indicates significant difference between the two.

multiple-range test (Newman-Keuls). Furthermore, ANOVA software (GB-stat for Windows, version 5.3) was used to detect differences within and between the sessions, respectively. A paired Student's *t*-test was used to detect whether means differed at selected points in time of two series. *P* < 0.05 was chosen as the level of significance.

RESULTS

During NS, Sup + LBNP, and Sup, HR decreased similarly within 30 s from 65 ± 2 to between 57 ± 2 and 59 ± 2 beats/min. During Sup + LBNP and NS, however, HR increased gradually toward the values of the seated position, whereas the decrease was sustained during Sup (*P* < 0.05, Fig. 1).

When MAP was measured after 5 min of intervention it was decreased similarly during Sup from 96 ± 2 to 87 ± 1 mmHg, during NS from 96 ± 1 to 88 ± 2 mmHg, and during Sup + LBNP from 95 ± 1 to 89 ± 2 mmHg (*P* < 0.05, Fig. 1). At *minute 20*, however, values of Sup were below those of Sup + LBNP (*P* < 0.05), thus MAP tended to increase toward the values of seated subjects. Arterial pulse pressure (PP) increased during Sup from 47 ± 2 to 56 ± 3 mmHg and less during Sup + LBNP from 46 ± 2 to between 51 ± 3 and 53 ± 3 mmHg (*P* < 0.05, Table 1). At *minute 20* PP during Sup was above that of Sup + LBNP (*P* < 0.05, Table 1). During seated control and NS there were no significant changes in PP. Systolic arterial pressure decreased during NS (*P* < 0.05) and during *minute 20* of Sup (*P* < 0.05), whereas no significant changes occurred during seated control and Sup + LBNP (Table 1). Diastolic arterial pressure decreased during Sup, NS, and Sup + LBNP and at *minute 20* it was more decreased during Sup than during NS and Sup + LBNP (*P* < 0.05, Table 1).

MAPp was decreased throughout Sup and was unchanged during seated control (*P* < 0.05, Table 1). During NS, there was a prompt decrease (within 30 s) in MAPp in the index finger (*P* < 0.05), after which it increased slightly toward the values of seated. During Sup + LBNP there was a gradual decrease reaching a significant level from after 2.5 min of intervention (*P* < 0.05, Table 1). MAPp during NS and Sup + LBNP were very similar after *minute 2.5*.

During Sup, LA diameter increased from 30 ± 1 to 35 ± 1 mm (*P* < 0.05), whereas it varied insignificantly between 30 ± 1 and 31 ± 1 mm during seated control, NS, and Sup + LBNP (Fig. 1). During Sup + LBNP, LA diameter at *minute 12.5* and *minute 17.5* did not differ from values of seated subjects either.

Plasma concentration of NE decreased during Sup from 165 ± 11 to 117 ± 13 pg/ml (*P* < 0.05). During seated control, NS, and Sup + LBNP, there were no significant changes in plasma NE (Fig. 2). Plasma concentration of E followed a pattern very similar to that of NE with a significant decrease during Sup from 34 ± 6 to 18 ± 4 pg/ml and with no significant changes during the other sessions (varying insignificantly between 29 ± 5 and 39 ± 6 pg/ml).

Plasma concentration of AVP likewise decreased during Sup from 0.8 ± 0.2 to 0.6 ± 0.1 pg/ml (*P* < 0.05, Fig. 2). During seated control, NS, and Sup + LBNP no significant changes occurred (Fig. 2). The slightly higher level of plasma AVP during the end of NS and Sup + LBNP was due to an increase in plasma AVP concentration in one subject (from 2.17 to 5.21 and from 1.78 to 4.76 pg/ml, respectively). Plasma osmolality varied insignificantly during all four sessions between 285 ± 1 and 287 ± 1 osmol/kg.

Table 1. Arterial pressures in seated subjects without and with simultaneous application of NS, and during a posture change from seated to supine without and with simultaneous application of lower body negative pressure

	Seated, min				Seated/Supine ± LBNP/NS, min					Seated, min				
	2.5	5	7.5	10	10.5	12.5	15	17.5	20	20.5	22.5	25	27.5	30
SAP, mmHg														
Seated		127 ± 2		126 ± 2					127 ± 2				128 ± 3	127 ± 3
Supine		126 ± 2		127 ± 2					125 ± 3				127 ± 2	126 ± 2
NS		126 ± 2		126 ± 2					118 ± 2*‡				128 ± 2	128 ± 2
Supine + LBNP		126 ± 2		126 ± 2					124 ± 2				129 ± 2	128 ± 2
DAP, mmHg														
Seated		80 ± 3		79 ± 2					81 ± 3‡				82 ± 2	82 ± 2
Supine		80 ± 2		80 ± 2					68 ± 1*				81 ± 2	80 ± 1
NS		80 ± 2		81 ± 2					72 ± 2*				83 ± 2	82 ± 2
Supine + LBNP		80 ± 2		80 ± 1					71 ± 2*				82 ± 2	83 ± 2
PP, mmHg														
Seated		47 ± 3		46 ± 3					45 ± 3				46 ± 3	45 ± 3
Supine		46 ± 3		47 ± 2					56 ± 3*†				46 ± 3	46 ± 3
NS		45 ± 3		45 ± 2					46 ± 3				44 ± 2	46 ± 2
Supine + LBNP		46 ± 2		46 ± 2					53 ± 3*†				47 ± 2	45 ± 2
MAPp, mmHg														
Seated	88 ± 3	88 ± 3	89 ± 3	89 ± 3	89 ± 3	89 ± 3	90 ± 3	90 ± 3	90 ± 3	91 ± 3	91 ± 3	91 ± 3	92 ± 3	90 ± 2
Supine	87 ± 2	86 ± 2	88 ± 2	89 ± 1	81 ± 3*	81 ± 2*†	81 ± 2*†	80 ± 2*†	80 ± 2*†	91 ± 4	89 ± 3	88 ± 3	89 ± 3	89 ± 3
NS	90 ± 3	90 ± 2	91 ± 2	91 ± 2	82 ± 2*†	84 ± 2*	85 ± 2*	86 ± 2	86 ± 2	93 ± 2	95 ± 2	96 ± 2	95 ± 2	95 ± 2
Supine + LBNP	90 ± 2	89 ± 2	91 ± 3	90 ± 3	87 ± 3	87 ± 3	84 ± 3*†	84 ± 3*	85 ± 3*†	91 ± 3	93 ± 3	91 ± 3	91 ± 3	90 ± 3

Values are means ± SE; *n*, 10 subjects. LBNP, lower body negative pressure; NS, neck suction; systolic (SAP) and diastolic (DAP) arterial pressure and arterial pulse pressure (PP); brachial artery, peripheral mean arterial pressure (MAPp, index finger). **P* < 0.05, significant difference compared with initial 10 min. †*P* < 0.05, significant difference compared with seated at similar point in time. ‡*P* < 0.05, significant difference compared with other 3 sessions at similar points in time.

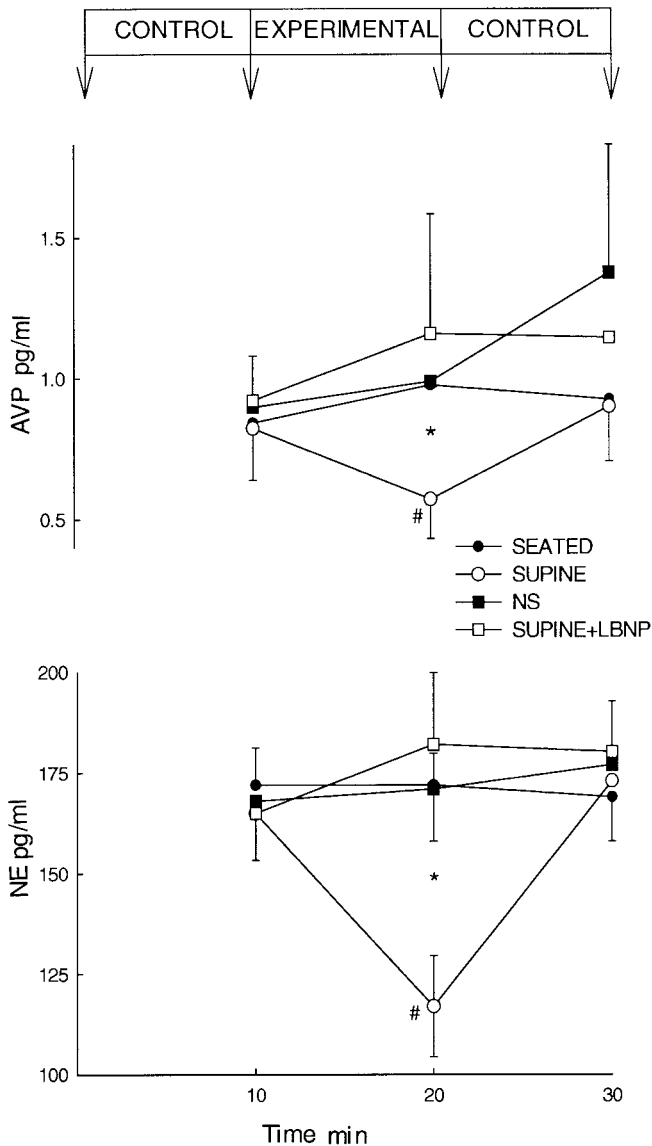


Fig. 2. Plasma concentrations of arginine vasopressin (AVP) and norepinephrine (NE) during seated, supine, supine + LBNP, and NS (see Fig. 1). Values are means \pm SE, $n = 10$ subjects. # $P < 0.05$, significant difference from value of initial 10 min in the seated position. * $P < 0.05$, between sessions indicates significant difference between the two.

DISCUSSION

As expected, we observed a sustained decrease in HR during Sup (19, 20), whereas there was an acute decrease during NS and Sup + LBNP, followed by a gradual increase toward the level of seated. Therefore during Sup, static carotid baroreceptor stimulation per se causes the acute (<30 s) decrease in HR, whereas the central blood volume expansion (increased LA diameter and/or arterial PP) is pivotal to sustain this decrease. Thus the effects of central blood volume expansion override those of baroreceptor adaptation and/or buffering of the aortic reflexes. Because Sup + LBNP could have affected HR by other mechanisms than those initiated by baroreceptors due to movement of the upper body (e.g., vestibular), our results indicate

that such factors play little or no role for the cardiovascular adjustments.

Several investigators (3, 16, 25, 28, 31) have used NS as a tool to investigate the acute effects (within seconds) of carotid baroreceptor stimulation on HR, arterial pressures, and sympathetic nervous activity. Only a few studies (8, 15, 26, 32), however, have focused on the effects of longer-lasting (>2 min) static NS in humans. All of these investigators observed temporary sinus node inhibition and a decrease in MAP during NS similar to the results of the present study. The duration and magnitude of the decrease in HR and MAP vary with the level of the NS stimulus and with the posture of the subjects. In this study, however, we have for the first time investigated the cardiovascular effects of a static NS stimulus within the normal physiological range because we applied NS in seated humans at a level with the change in hydrostatic pressure in the carotid sinus during a seated to Sup posture change. We observed an acute decrease in HR (within 30 s) very similar to that of Sup, but the decrease was reverted from between *minute 2.5* and *minute 5*. Therefore, static carotid baroreceptor stimulation is pivotal for the prompt decrease in HR during Sup.

When comparing the temporal effects of NS and Sup + LBNP, the pattern of HR and brachial MAP responses are very similar. HR decreased within 30 s during NS and Sup + LBNP and thereafter gradually increased toward the level of seated subjects. The buffering effect from inhibition of aortic baroreceptors by the decrease in MAP and/or carotid baroreceptor adaptation (resetting) probably caused the gradual increase in HR (26). During Sup, however, the decrease in HR and MAP was sustained during the whole 10-min period. This suggests that the effects of low-pressure receptor stimulation and increased PP during the Sup posture override the aortic buffering effect and/or carotid baroreceptor adaptation.

The degree of peripheral vasodilatation apparently differed when we compared the acute effects of NS with those of Sup + LBNP because MAP_p in the index finger did not decrease during the initial 2.5 min of Sup + LBNP, whereas it did so during NS (Table 1). Movement of the upper body during Sup + LBNP could have caused the attenuated peripheral vasodilatation, which is in accordance with results of Cui et al. (2), who observed increased sympathetic nervous activity after vestibular stimulation. Therefore, whereas HR and brachial MAP (after 5 min) seem independent of vestibular factors, the peripheral vasodilatation could have been affected.

Theoretically, a small increase in intracranial pressure after the posture change from seated to Sup could also have affected cardiovascular variables. Grady et al. (7) observed a gradual increase in arterial pressure and an increase in HR during small gradual increments in intracranial pressure in anesthetized dogs. Furthermore, Jones (10) measured a rise in mean intracranial pressure after posture changes in subjects with the potential for intracranial pressure increase. Therefore, it is a theoretical possibility that a slightly

increased intracranial pressure induced by the posture change from seated to Sup could elicit small HR and MAP changes through a mild degree of Cushing reflex (26). Likewise, a small change in abdominal pressure due to the antiorthostatic posture change could have influenced cardiovascular variables. Saleh et al. (27) observed increased sympathetic output and decreased baroreflex sensitivity after stimulation of gastric afferents in rats. Furthermore, Halliwill et al. (9) found an attenuated increase in forearm vascular resistance during strong (-60 mmHg) LBNP in healthy humans wearing medical antishock trousers, when trouser legs and the abdominopelvic region were inflated, compared with during inflation of the trouser legs alone. These results suggest that venous pooling in the abdomen (which probably occurs during an antiorthostatic posture change) affects cardiovascular variables. The similarity between the cardiovascular effects of NS and Sup + LBNP suggests, however, that factors other than baroreflexes (e.g., vestibular, intraabdominal, or intracranial) play little or no role for the more long-term cardiovascular and neuroendocrine adjustments to moderate antiorthostasis.

Because NE and AVP can modulate arterial pressures and HR (4), plasma concentrations of AVP and NE were measured, and as expected from previous studies (20, 22), they were decreased by Sup. No significant changes occurred during Sup + LBNP and NS. Thus our results confirm (14, 19, 20, 22) that NE release into forearm venous blood is governed by low-pressure receptor stimulation and is unaffected by isolated carotid baroreceptor stimulation. We (22) have observed that carotid baroreceptor stimulation during simultaneous low-pressure receptor stimulation (water immersion combined with NS) does not suppress AVP release. The present results show that AVP release is not suppressed by isolated static carotid baroreceptor stimulation (Sup + LBNP and NS). This is in compliance with results of Wehberg et al. (33), who induced huge increases in perfusion pressure of isolated carotid sinuses in dogs with no subsequent suppression of AVP release. As expected, plasma osmolality did not change during any of the interventions. Thus such changes could not have accounted for the AVP results.

Suppression of AVP release during an antiorthostatic posture change is critically dependent on an increase in LA diameter, PP, or both (20). Thus we did not know before initiation of this study whether plasma AVP could be suppressed by an isolated increase in LA diameter or PP, respectively. In the present study, however, we observed an increase in PP during Sup + LBNP, although the increase was smaller than during Sup. Because plasma AVP was not suppressed during Sup + LBNP, where LA diameter was unchanged and PP increased, it seems that an increase in PP without stimulation of cardiopulmonary receptors is not sufficient to suppress AVP release. Results of previous studies (17, 18, 29) suggest that AVP release is unaffected by isolated low-pressure receptor unloading by LBNP. Thus, when our results are compared with those of other studies, it leads to the

suggestion that a combined increase in LA diameter and PP is required to suppress the release of AVP.

Limitations. Following the study by Ludbrook et al. (13), we made the assumption that 64% of the NS pressure is transmitted to the carotid sinus. Thron et al. (30), however, suggested a higher transmission rate. Therefore, it is possible that the carotid baroreceptor stimulus in our case was stronger during NS than during Sup + LBNP. Similar cardiovascular effects of the two interventions (Fig. 1) indicate, however, that the magnitude of carotid baroreceptor stimulation was very similar when comparing results of the two models.

In conclusion, static carotid baroreceptor stimulation per se causes the acute (<30 s) decrease in HR during a posture change from seated to Sup, whereas the central blood volume expansion (increased LA diameter and/or arterial PP) is pivotal for the sustained decrease. Thus central blood volume expansion overrides baroreceptor adaptation and/or buffering of the aortic reflexes. Furthermore, the bradycardic response seems unaffected by other factors (e.g., vestibular) activated by movement of the upper body.

We gratefully acknowledge the technical assistance of Birthe Lynderup and Inge H. Pedersen.

This study was supported by Danish Research Council Grants 9602455 and 9802910.

REFERENCES

1. **Brenner BM and Rector F.** Peritoneal dialysis. In: *The Kidney* (5th ed.). Philadelphia, PA: Saunders, 1996.
2. **Cui J, Mukai C, Iwase S, Sawasaki N, Kitazawa H, Mano T, Sugiyama Y, and Wada Y.** Response to vestibular stimulation of sympathetic outflow to muscle in humans. *J Auton Nerv Syst* 66: 154–162, 1997.
3. **Eckberg DL.** Adaptation of the human carotid baroreceptor-cardiac reflex. *J Physiol (Lond)* 269: 579–589, 1977.
4. **Eckberg DL and Sleight P.** Afferent baroreceptor activity. Effector responses to baroreceptor forcings. In: *Human Baroreflexes in Health and Disease*. Oxford, UK: Clarendon, 1992, p. 136–153 and 255–299.
5. **Emmeluth C, Goetz KL, Drummer C, Gerzer R, Forssman WG, and Bie P.** Natriuresis caused by increased carotid Na^+ concentration after renal denervation. *Am J Physiol Renal Fluid Electrolyte Physiol* 270: F510–F517, 1996.
6. **Feigenbaum H.** *Echocardiography* (4th ed.). Philadelphia, PA: Lea and Febiger, 1986, p. 621–639.
7. **Grady PA and Blaumanis OR.** Physiologic parameters of the Cushing reflex. *Surg Neurol* 29: 454–461, 1988.
8. **Hainsworth R and Al-Shamma YMH.** Cardiovascular responses to stimulation of carotid baroreceptors in healthy subjects. *Clin Sci (Lond)* 75: 159–165, 1988.
9. **Halliwill JR, Lawler LA, Eickhoff TJ, Joyner MJ, and Mulvagh SL.** Reflex responses to regional venous pooling during lower body negative pressure in humans. *J Appl Physiol* 84: 454–458, 1998.
10. **Jones B.** The effects of patient repositioning on intracranial pressure. *Aust J Adv Nurs* 12: 32–39, 1994.
11. **Kamegai M, Kristensen MS, Warberg J, and Norsk P.** Carotid baroreflexes and plasma vasopressin in humans during head-up tilt. *Am J Physiol Regulatory Integrative Comp Physiol* 263: R318–R323, 1992.
12. **Knudsen JH, Christensen NJ, and Bratholm P.** Lymphocyte norepinephrine and epinephrine, but not plasma catecholamines predict lymphocyte cAMP production. *Life Sci* 59: 639–647, 1996.

13. **Ludbrook J, Mancía G, Ferrari A, and Zanchetti A.** The variable-pressure neck-chamber method for studying the carotid baroreflex in man. *Clin Sci Mol Med* 53: 165–171, 1977.
14. **Mancía G, Ferrari A, Gregorini L, Leonetti G, Parati G, Picotti GB, Ravazzani C, and Zanchetti A.** Plasma catecholamines do not invariably reflect sympathetically induced changes in blood pressure in man. *Clin Sci (Lond)* 65: 227–235, 1983.
15. **Mancía G, Ferrari A, Gregorini L, Valentini R, Ludbrook J, and Zanchetti A.** Circulatory reflexes from carotid and extracarotid baroreceptor areas in man. *Circ Res* 41: 309–315, 1977.
16. **Mancía G and Mark AL.** Arterial baroreflexes in humans. In: *Handbook of Physiology. The Cardiovascular System. Peripheral Circulation and Organ Blood Flow*. Bethesda, MD: Am Physiol Soc, 1983, sect. 2, vol. III, pt. 2, chapt. 20, p. 755–791.
17. **Norsk P, Bonde-Petersen F, and Warberg J.** Influence of central venous pressure change on plasma vasopressin in humans. *J Appl Physiol* 61: 1352–1357, 1986.
18. **Norsk P, Ellegaard P, Vidbaek R, Stadeager C, Jessen F, Johansen LB, Kristensen M, Kamegai M, Warberg J, and Christensen NJ.** Arterial pulse pressure and vasopressin release in humans during lower body negative pressure. *Am J Physiol Regulatory Integrative Comp Physiol* 264: R1024–R1030, 1993.
19. **Pump B, Christensen NJ, Videbaek R, Warberg J, Hendriksen O, and Norsk P.** Left atrial distension and antithrostatic decrease in arterial pressure and heart rate in humans. *Am J Physiol Heart Circ Physiol* 273: H2632–H2638, 1997.
20. **Pump B, Gabrielsen A, Christensen NJ, Bie P, Bestle M, and Norsk P.** Mechanisms of inhibition of vasopressin release during moderate antithrostatic posture change in humans. *Am J Physiol Regulatory Integrative Comp Physiol* 277: R229–R235, 1999.
21. **Pump B, Schou M, Gabrielsen A, and Norsk P.** Contribution of leg vasculature to hypotensive effects of an antithrostatic posture change in humans. *J Physiol (Lond)* 519: 623–628, 1999.
22. **Pump B, Shiraishi M, Gabrielsen A, Bie P, Christensen NJ, and Norsk P.** Cardiovascular effects of static carotid baroreceptor stimulation during water immersion in humans. *Am J Physiol Heart Circ Physiol* 280: H2607–H2615, 2001.
23. **Radtke A, Popov K, Bronstein AM, and Gresty MA.** Evidence for a vestibulo-cardiac reflex in man. *Lancet* 356: 736–737, 2000.
24. **Ray CA, Hume KM, and Short TL.** Skin sympathetic outflow during head-down neck flexion in humans. *Am J Physiol Regulatory Integrative Comp Physiol* 273: R1142–R1146, 1997.
25. **Rea RF and Eckberg DL.** Carotid baroreceptor-muscle sympathetic relation in humans. *Am J Physiol Regulatory Integrative Comp Physiol* 253: R929–R934, 1987.
26. **Rowell LB.** Reflex control during orthostasis. Control of regional blood flow during dynamic exercise. In: *Human Cardiovascular Control*. New York: Oxford University Press, 1993, p. 62–64 and 245–247.
27. **Saleh TM, Connell BJ, and Allen GV.** Visceral afferent activation-induced changes in sympathetic nerve activity and baroreflex sensitivity. *Am J Physiol Regulatory Integrative Comp Physiol* 276: R1780–R1791, 1999.
28. **Shi X, Foresman BH, and Raven PB.** Interaction of central venous pressure, intramuscular pressure, and carotid baroreflex function. *Am J Physiol Heart Circ Physiol* 272: H1359–H1363, 1997.
29. **Thrasher TN.** Baroreceptor regulation of vasopressin and renin secretion: low-pressure versus high-pressure receptors. *Front Neuroendocrinol* 15: 157–196, 1994.
30. **Thron HL, Brechmann W, Wagner J, and Keller K.** Quantitative Untersuchungen über die Bedeutung der Gefäßdehnungsrezeptoren im Rahmen der Kreislaufhomöostase beim wachen Menschen. *Pflügers Arch* 293: 68–99, 1967.
31. **Tushar HD, Collins JC, Snell M, and Mosqueda-Garcia R.** Modeling of arterial and cardiopulmonary baroreflex control of heart rate. *Am J Physiol Heart Circ Physiol* 272: H2343–H2352, 1997.
32. **Van Tilborg KA, Rabelink TJ, van Rijn HJM, Boomsma F, and Koomans HA.** Arterial baroreflex control of renal hemodynamics in humans. *Circulation* 90: 1883–1890, 1994.
33. **Wehberg KE, Gala GJ, and Brunner MJ.** Comparison of carotid baroreflex control of plasma AVP concentration in conscious and anesthetized dogs. *Am J Physiol Regulatory Integrative Comp Physiol* 261: R950–R956, 1991.