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Cardiovascular effects of static carotid baroreceptor stimulation during water immersion in humans

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Pump, Bettina, Makoto Shiraishi, Anders Gabrielsen, Peter Bie, Niels Juel Christensen, and Peter Norsk. Cardiovascular effects of static carotid baroreceptor stimulation during water immersion in humans. *Am J Physiol Heart Circ Physiol* 280: H2607–H2615, 2001.—We hypothesized that the more-pronounced hypotensive and bradycardic effects of an antiorthostatic posture change from seated to supine than water immersion are caused by hydrostatic carotid baroreceptor stimulation. Ten seated healthy males underwent five interventions of 15-min each of *1*) posture change to supine, *2*) seated water immersion to the Xiphoid process (WI), *3*) seated neck suction (NS), *4*) WI with simultaneous neck suction (−22 mmHg) adjusted to simulate the carotid hydrostatic pressure increase during supine (WI + NS), and *5*) seated control. Left atrial diameter increased similarly during supine, WI + NS, and WI and was unchanged during control and NS. Mean arterial pressure (MAP) decreased the most during supine (7 ± 1 mmHg, $P < 0.05$) and less during WI + NS (4 ± 1 mmHg) and NS (3 ± 1 mmHg). The decrease in heart rate (HR) by 13 ± 1 beats/min ($P < 0.05$) and the increase in arterial pulse pressure (PP) by 17 ± 4 mmHg ($P < 0.05$) during supine was more pronounced ($P < 0.05$) than during WI + NS (10 ± 2 beats/min and 7 ± 2 mmHg, respectively) and WI (8 ± 2 beats/min and 6 ± 1 mmHg, respectively, $P < 0.05$). Plasma vasopressin decreased only during supine and WI, and plasma norepinephrine, in addition, decreased during WI + NS ($P < 0.05$). In conclusion, WI + NS is not sufficient to decrease MAP and HR to a similar extent as a 15-min seated to supine posture change. We suggest that not only static carotid baroreceptor stimulation but also the increase in PP combined with low-pressure receptor stimulation is a possible mechanism for the more-pronounced decrease in MAP and HR during the posture change.

antidiuretic hormone; blood pressure; lower body negative pressure

THE DECREASE in mean arterial pressure (MAP) and heart rate (HR) is more pronounced during a posture change from seated to supine than during water immersion to the Xiphoid process (WI) (24), where low-pressure receptor stimulation is similar to that of the posture change (24) but with no simultaneous static carotid baroreceptor stimulation (4, 13, 17, 30). Thus the decrease in MAP and HR during the posture change could primarily be caused by the hydrostatic stimulation of high-pressure reflexes in the carotid sinus.

By static neck suction (NS), it is possible to stimulate carotid baroreceptors without affecting the filling of the heart and thereby the cardiopulmonary low-pressure receptors (8, 27). In this study, we utilized a combination of WI and NS, with the level of NS adjusted to simulate the hydrostatic pressure increase in the carotid sinus during a posture change. Thus, by application of mild NS on the seated subjects, we attempted to simulate the conditions of the supine position in regard to carotid baroreceptors. The hypothesis tested was that the effects of combined NS and WI would resemble those of an antiorthostatic posture change from seated to supine, because the more-pronounced decrease in MAP and HR during the posture change is induced by static carotid baroreceptor stimulation. We therefore anticipated that NS would augment the decrease in MAP and HR during WI to a very similar degree as during an antiorthostatic posture change.

MATERIALS AND METHODS

Ten male subjects [age 26 ± 1 (means ± SE) yr (range 22–31 yr), height 182 ± 2 cm (170–192 cm), and weight 82 ± 2 kg (72–91 kg)] completed the experiment. All had a negative history of cardiovascular and kidney diseases and were healthy, as indicated by medical history, normal physical examination, arterial blood pressure (<140/90 mmHg), electrocardiogram (unipolar), and urine strip test for glucose, leukocytes, erythrocytes, and protein. None of the subjects took any medication 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

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Ethics Committee of Copenhagen (KF 01–323/96) and was in compliance with the Declaration of Helsinki. No complications occurred. The experiment consisted of the following five interventions, each preceded and followed by 15 min with the subject in the seated position: *1*) 15 min in the seated position as control, *2*) 15 min of WI, *3*) 15 min of static NS in the seated position, *4*) 15 min of WI with simultaneous static NS (WI + NS), and *5*) a posture change to 15 min in the supine position. The level of NS was 21.8 ± 0.4 mmHg and was calculated so that it would simulate the effect of the hydrostatic pressure change when going from the seated to the supine position. This level of NS has previously been shown to induce similar effects on HR and MAP as carotid baroreceptor stimulation of a seated to supine posture change (unpublished observations). The calculation of the level of NS was done by measuring the distance from the carotid sinus to heart level (fourth intercostal space) on each subject in the seated position and by taking into account that only 64% of the NS pressure is transmitted to the carotid sinus (14). Thus the calculation was as follows: distance from carotid sinus to heart (in cm)/1.36 × (100/64) (see Ref. 10).

WI was carried out in a rectangular insulated plastic tank filled with tap water of 34.6–35.0°C. An adjustable chair was suspended from the ceiling over the tank in an electrical hoist so that the subject could be lowered into the water within 15 s. During control and the 15 min before and after each intervention, the subject was seated in the chair hovering over the tank with only the feet immersed. When changing position from seated to supine, the subjects was positioned horizontally on a plate, which was placed on top of the WI tank at level with the seat of the chair.

The sessions were separated by 15 min of being seated and performed with the sequence in balanced randomized order between the subjects. The subject spent the night at the laboratory, fasted for 15 h before the experiment, and was awakened at 7:45 AM on the day of study. Each subject dressed in a bathing suit and was weighed, and a short catheter (Venflon 2, 1.2 mm, length 45 mm) was placed in a cubital vein for blood sampling. Between 8:00 and 9:00 AM, the subject rested in the seated position while the rebreathing procedure for measurement of cardiac output (see below) was exercised. The subject was then instrumented with cuffs around the right upper arm and left index finger for determination of brachial and peripheral arterial pressures, respectively, and a NS device was placed around the whole circumference of the neck (10, 14).

The experiment started at 9:00 AM. Systolic (SAP) and diastolic arterial pressures (DAP) were measured at the 6th and the 14th min of every 15-min period in the right brachial artery by conventional sphygmomanometry. Arterial pulse pressure (PP) was calculated from SAP minus DAP, and MAP was calculated from DAP + ⅓ PP. In addition, arterial pressures and HR were measured continuously by a photopletysmographic method (Finapres, 2300 Finapres, Ohmeda) in the left index finger, with the pressure signal stored in a computer (LabView) for later analysis. Peripheral MAP in the finger (MAP_p) was estimated from the pressure signal as the electronic mean. The cuffs for arterial pressure determinations were, at all times, kept at heart level (level of the fourth intercostal space when the subject was in the seated position and level with the midaxillary line when the subject was supine). HR and MAP_p were determined as mean values over 5-min periods and over the initial consecutive 0.5-, 1.5-, and 2.5-min periods at the begining of the interventions and right after them.

Left atrial diameter was measured by echocardiography (Aloka SSD 500, Simonsen & Weel) according to the criteria of Feigenbaum (5) at the fourteenth minute of each 15-min period during end expiration as an average of measurements from 3 M-mode pictures (printouts from a video recorder, Sony SVO-9500 MDP) obtained from the parasternal long-axis view. All the measurements were performed in a blind fashion.

Nineteen milliliters of blood were sampled at the thirteenth minute of every 15-min period and immediately transferred into various chilled tubes. The catheter was thereafter flushed with 19 ml of isotonic saline. Samples for determination of concentrations of plasma norepinephrine (NE) and plasma epinephrine were transferred to polyethylene tubes containing 20-μl/ml blood a mixture of reduced glutathione and EGTA (0.195 mol/l glutathione, 0.250 mol/l EGTA) adjusted to pH 6–7 with NaOH. The samples were immediately placed on ice and subsequently centrifuged at 4°C at 1,500 *g* for 10 min. Plasma was thereafter transferred to polyethylene tubes and frozen at −30°C for later analysis by a radioenzymatic assay (11).

The tubes for determination of plasma concentration of arginine vasopressin (AVP) and atrial natriuretic peptide (ANP) contained EDTA and aprotinine, and those for determination of plasma osmolality contained 15 ± 2.5 IU lithium-heparin/ml blood. Plasma concentrations of AVP and ANP were measured by radioimmunoassay as previously described by Emmeluth et al. (3) To increase accuracy, the mean value of two plasma AVP measurements from two blood samples taken on same experimental point in time was used. For the AVP assay, the detection limit was 0.15 pg/ml, and the recovery of unlabeled AVP added to plasma was within 72 ± 4%. The intraassay coefficient of variation was 3.0% at 5.2 pg/ml, and the interassay coefficient of variation was 7.9% at 2.4 pg/ml and 16.7% at 0.4 pg/ml. Results were not corrected for incomplete recovery. For the ANP assay, the detection limit was 1.5 pg/ml, recovery was 67%, and intraassay and interassay coefficients of variation were 5.8 and 8.2%, respectively. Plasma osmolality was measured on fresh samples by freezing point depression (Advanced Instruments 3MO Plus).

At the end of every 15-min period, after the other measurements were performed, cardiac output was measured by rebreathing inert blood-soluble (freon 22) and -insoluble (SF_6) gases, which were analyzed in a photo- and magneto-acoustic multigas analyzer (AMIS 2001, Innovision A/S, Odense) (1, 2). Total peripheral vascular resistance and stroke volume were calculated from conventional formulas using the MAP_p and HR values obtained during the rebreathing maneuvers (by using the brachial MAP value obtained before the cardiac output measurement; however, the same conclusion was reached).

Room temperature was kept between 25.6 and 26.7°C, and humidity was kept between 27 and 49%.

An 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 15 min. Differences between mean values were evaluated by post hoc multiple range tests (Newman-Keuls or least significant difference test when indicated). Furthermore, an ANOVA with the variable as main variate and intervention (control, supine, WI, WI + NS, and NS, respectively) and subject as factors was used to detect differences between series at selected similar points in time. Differences between mean values were evaluated by post hoc multiple range tests (Newman-Keuls or least significant difference test when indicated). 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. Statistics were always performed on absolute values, although relative values are sometimes used in the presentation.

RESULTS

MAP decreased compared with prevalues and those found during control at similar time points, during supine from 92 ± 3 to 84 ± 3 mmHg, during WI + NS from 93 ± 3 to 88 ± 3 mmHg, and during NS from 92 ± 2 to 89 ± 2 mmHg ($P < 0.05$; Table 1 and Fig. 1). During WI and control, there were no significant changes. The initial decrease in MAP during supine was more pronounced than those of the other interventions, and, thereafter, the MAP of supine and WI + NS interventions were more decreased than those of control, NS, and WI ($P < 0.05$; Table 1 and Fig. 1). Because the start values vary, although insignificantly, between the interventions, the relative changes compared with preintervention are depicted in Fig. 1. In accordance with the values of MAP, peripheral MAP_p decreased by 3.9 ± 3.1 to 7.5 ± 2.2 mmHg during supine, by up to 4.9 ± 0.6 mmHg during WI + NS, and only during the initial 5 min of NS by up to 4.6 ± 1.0 mmHg compared with the mean value of preintervention measurements ($P < 0.05$). The acute changes (over the initial 2.5 min) of MAP_p during NS are depicted in Fig. 2. No significant changes occurred during control and WI. SAP increased during supine and initially

Table 1. *Cardiovascular and neuroendocrine variables in subjects during seated control, supine, WI, WI +NS, and NS*

	Seated		Intervention		Seated	
	6 min	15 min	21 min	30 min	36 min	45 min
SAP, mmHg						
Control	118 ± 2	116 ± 2	118 ± 2	117 ± 2	116 ± 2	117 ± 2
Supine	118 ± 2	117 ± 3	122 ± 3§	122 ± 3§	117 ± 3	117 ± 3
WI	116 ± 3	116 ± 2	120 ± 2§	118 ± 2	116 ± 2	115 ± 2
WI + NS	118 ± 2	119 ± 3	120 ± 2	118 ± 2	118 ± 3	115 ± 3
NS	117 ± 3	117 ± 3	114 ± 3†*	113 ± 3†‡	117 ± 2	117 ± 3
DAP, mmHg						
Control	81 ± 4	78 ± 4	79 ± 4	80 ± 4	78 ± 3	77 ± 4
Supine	80 ± 3	79 ± 4	65 ± 4*†	68 ± 4†	80 ± 3	77 ± 3
WI	78 ± 4	78 ± 3	74 ± 4	75 ± 4	79 ± 3	76 ± 3
WI + NS	80 ± 3	81 ± 3	74 ± 4†	73 ± 4†	80 ± 3	78 ± 4
NS	79 ± 3	79 ± 3	76 ± 3	77 ± 3	80 ± 3	79 ± 3
MAP, mmHg						
Control	93 ± 3	91 ± 3	92 ± 3	92 ± 3	91 ± 2	90 ± 3
Supine	92 ± 3	92 ± 3	84 ± 3†	86 ± 3†	92 ± 3	90 ± 3
WI	90 ± 3	91 ± 2	89 ± 3	89 ± 3	91 ± 2	89 ± 3
WI + NS	92 ± 3	93 ± 3	89 ± 3†	88 ± 3†	92 ± 3	91 ± 3
NS	92 ± 2	91 ± 3	89 ± 2†	89 ± 2	93 ± 2	91 ± 3
CO, l/min						
Control		4.7 ± 0.3		4.6 ± 0.3		4.4 ± 0.3
Supine		4.5 ± 0.2		6.1 ± 0.2†		4.2 ± 0.2
WI		4.5 ± 0.2		6.4 ± 0.2†		4.3 ± 0.3
WI + NS		4.6 ± 0.3		6.4 ± 0.2†		4.5 ± 0.2
NS		4.3 ± 0.2		4.3 ± 0.1		4.4 ± 0.1
TPR, mmHg·min·l^{-1}						
Control		18 ± 1		18 ± 1		19 ± 1
Supine		18 ± 1		13 ± 1†		20 ± 1
WI		18 ± 1		13 ± 1†		20 ± 1
WI + NS		20 ± 1		13 ± 1†		19 ± 1
NS		19 ± 1		18 ± 1		20 ± 1
SV, ml						
Control		63 ± 4		64 ± 4		63 ± 4
Supine		63 ± 4		97 ± 5†		60 ± 4
WI		62 ± 3		95 ± 3†		62 ± 5
WI + NS		63 ± 4		97 ± 3†		62 ± 3
NS		61 ± 3		60 ± 2		61 ± 3
Epinephrine, pg/ml						
Control		21 ± 3		22 ± 5		22 ± 6
Supine		20 ± 4		8 ± 3†		22 ± 5
WI		19 ± 3		9 ± 2†		16 ± 3
WI + NS		24 ± 4		13 ± 3†		23 ± 5
NS		17 ± 4		24 ± 5		26 ± 4

Values are means ± SE; $n = 10$ subjects [9 subjects for cardiac output (CO), total peripheral vascular resistance (TVR), and stroke volume (SV)]. SAP, DAP, and MAP, systolic, diastolic, and mean arterial pressure, respectively. Subjects were studied during: *1*) seated control, *2*) posture change to supine (supine), *3*) water immersion to the Xiphoid process (WI), *4*) neck suction (NS), and *5*) WI with simultaneous NS (WI + NS). *Significant differences compared with other interventions at similar time points. †Significant differences ($P < 0.05$) compared with initial 15 min. ‡Significant differences compared with other interventions at similar time points by least significant difference test. §Significant difference ($P < 0.05$) compared with initial 15 min by least significant difference test.

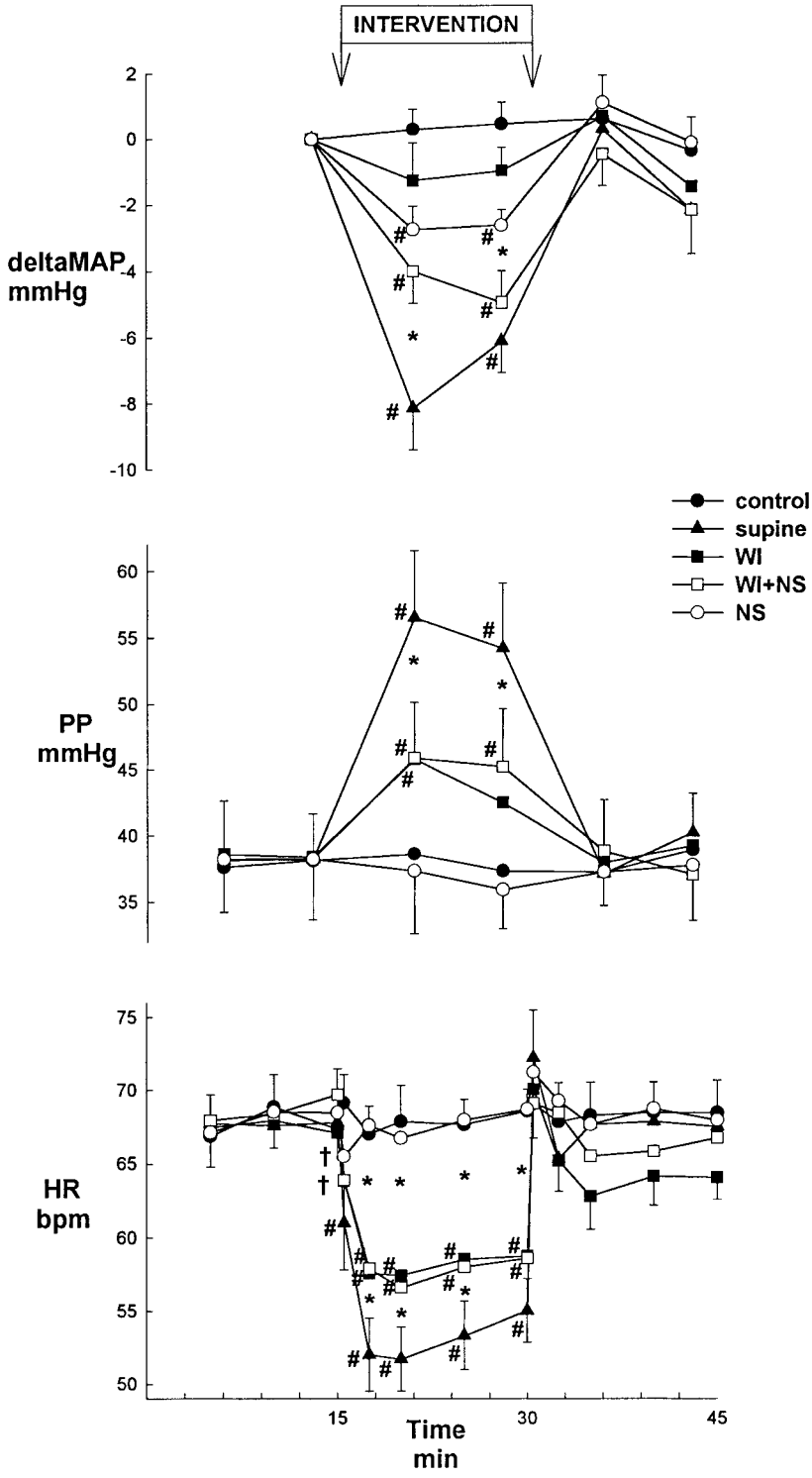

Fig. 1. Mean arterial pressure (MAP; changes from mean of preintervention), arterial pulse pressure (PP), and heart rate (HR) during the following five 15-min interventions: *1*) seated control, *2*) a posture change to the supine position (supine), *3*) seated water immersion to the Xiphoid process (WI), *4*) application of neck suction in the seated position adjusted to counteract the hydrostatic pressure from heart to the carotid sinus (NS), and *5*) NS during simultaneous seated WI (WI + NS). Each intervention is preceded and followed by 15 min of being seated. Values are means ± SE; n = 10 subjects. #Significant differences compared with values of initial 15 min in the seated position, ($P <$ 0.05). †Significant differences compared with initial 15 min (least significant difference test, $P < 0.05$) *Significant difference between the two sessions ($P < 0.05$). bpm, Beats/min.

during WI and decreased during NS (Table 1). During supine and WI + NS, DAP decreased ($P < 0.05$, Table 1). PP increased similarly by 5.7 ± 1.4 to 7.3 ± 2.2 mmHg during WI + NS and WI ($P < 0.05$) and more so during supine, by 17.2 ± 3.5 mmHg ($P < 0.05$; Fig. 1). During control and NS, PP was unchanged.

The decrease in HR was most pronounced during supine, where it decreased from a mean value of 68 ± 2 beats/min to a nadir of 52 ± 3 beats/min ($P < 0.05$; Fig. 1). During WI + NS and WI, HR decreased less but similarly from between 68 ± 2 and 69 ± 2 beats/min to a nadir of 57 ± 2 beats/min ($P < 0.05$; Fig. 1). During NS, there was only a transient decrease from a mean value of 68 ± 2 to 65 ± 2 beats/min at the initial 0.5 min ($P < 0.05$; Figs. 1 and 2). No significant changes occurred during control.

Left atrial diameter increased similarly during supine, WI, and WI + NS from between 29 ± 1 and 30 ±

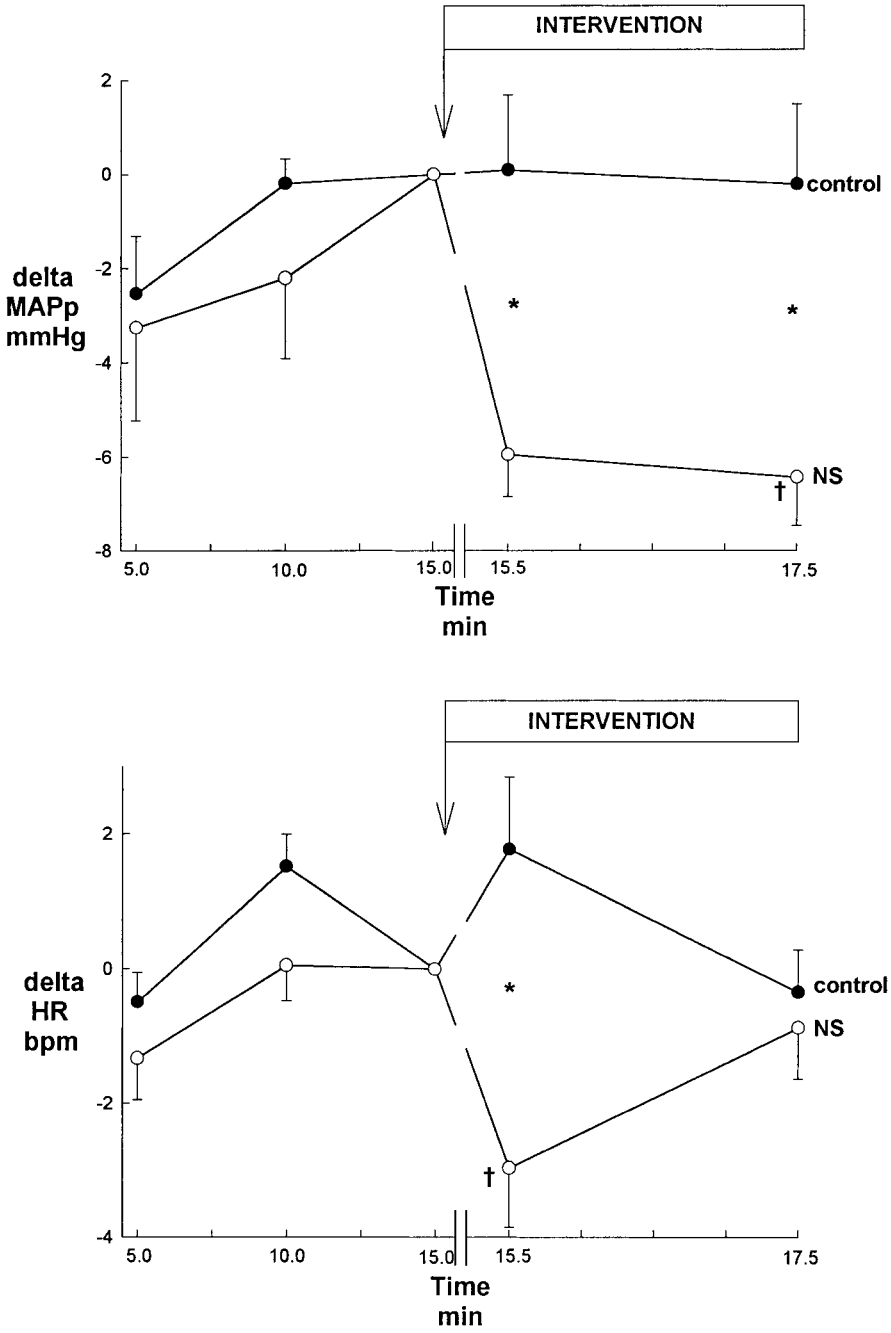

Fig. 2. Acute (over initial 2.5 min) relative changes in peripheral MAP (MAP_p) and HR during NS (○) and seated control (●). †Significant difference from initial 15 min (least significant difference test, $P < 0.05$). *Significant difference between sessions ($P < 0.05$).

1 to 35 ± 1 mm ($P < 0.05$; Fig. 3), whereas no significant changes occurred during control and NS. The same pattern was observed for cardiac output and stroke volume with similar and significant increases during supine, WI, and WI + NS ($P < 0.05$; Table 1). Total peripheral vascular resistance decreased similarly during supine, WI, and WI + NS ($P < 0.05$; Table 1). There were no significant changes during NS and control.

Plasma AVP decreased during supine from 1.5 ± 0.2 to 1.2 ± 0.2 pg/ml and during WI from 1.6 ± 0.2 to 1.4 ± 0.1 pg/ml ($P < 0.05$; Fig. 3). During the other interventions, there were no significant changes. The level of AVP was slightly (insignificantly) higher during NS than during the other interventions, mainly due to a higher level in one subject. Plasma ANP varied insignificantly between 21 ± 2 and 26 ± 3 pg/ml except for during NS, where it decreased from 24 ± 2 to 21 ± 2 pg/ml ($P < 0.05$). Forearm venous plasma NE decreased similarly during supine, WI, and WI + NS from between 207 ± 25 and 221 ± 37 pg/ml to between 130 ± 16 and 140 ± 21 pg/ml ($P < 0.05$; Fig. 3). During control and NS, no significant changes occurred. Plasma epinephrine exhibited a pattern very similar to that of NE, with a decrease during supine, WI, and WI + NS ($P < 0.05$; Table 1).

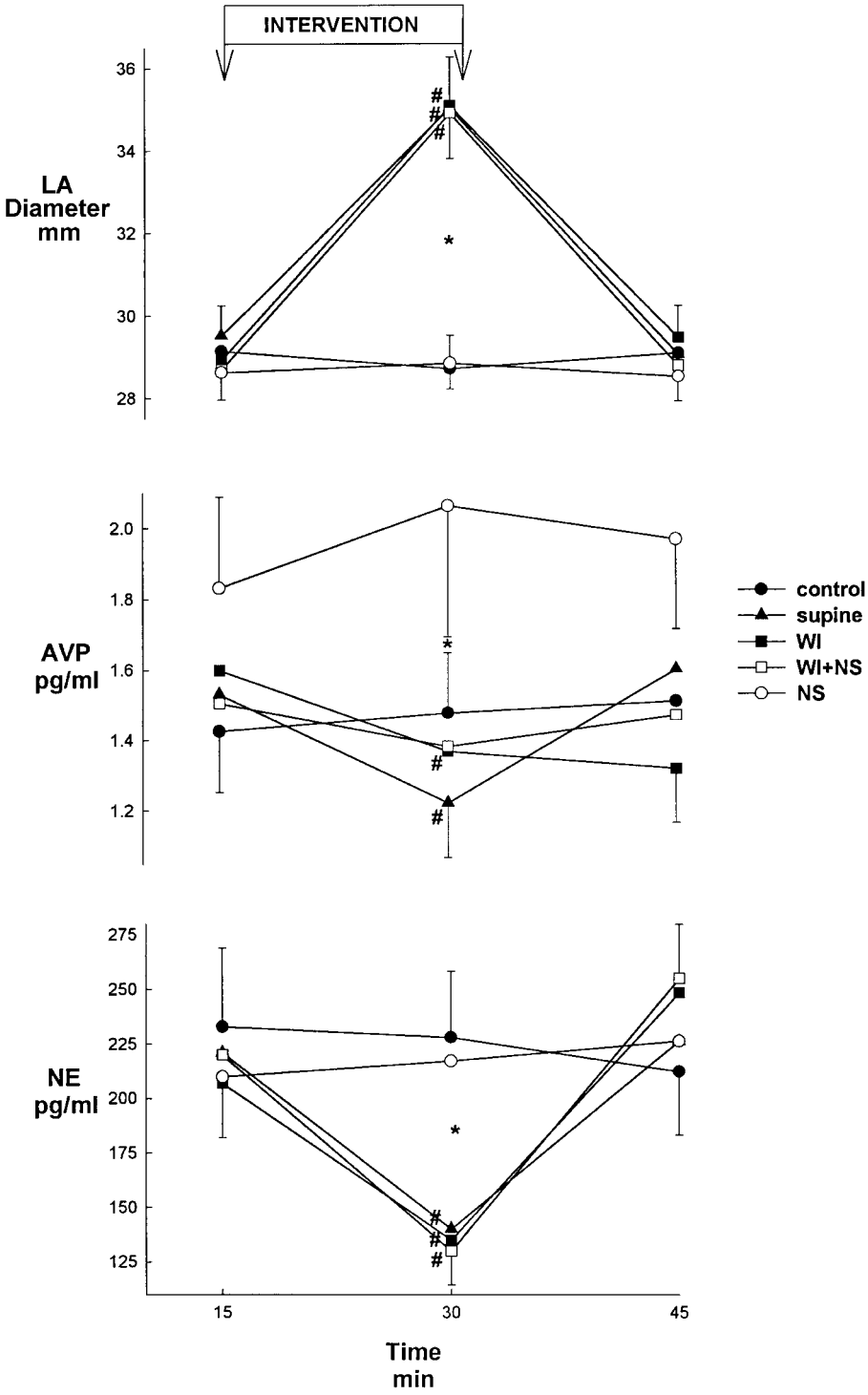

Fig. 3. Left atrial (LA) diameter and plasma concentrations of arginine vasopressin (AVP) and norepinephrine (NE) during control, supine, WI, NS, and WI + NS. Values are means ± SE; n = 10 subjects. #Significant differences from values of initial 15 min in the seated position ($P < 0.05$). *Significant differences between the two sessions ($P < 0.05$).

DISCUSSION

The results show that the decrease in MAP and HR is more pronounced during a 15-min moderate anti-orthostatic posture change from seated to supine than during WI. In addition, WI combined with NS (WI + NS) further decreased MAP but had no further effect on HR. NS did not, however, decrease MAP as much as the posture change. We therefore suggest that the additional increase in PP during supine is a possible mechanism for the further decrease in MAP and HR compared with the effects of WI + NS. Furthermore, the release of AVP and NE seems independent of static carotid baroreceptor stimulation and is probably governed by an interaction of cardiopulmonary low-pressure and pulsatile arterial (PP) baroreceptor stimulation.

From the results of previous studies, we know that MAP is less decreased during WI (4, 6, 13, 24) than

during an antiorthostatic posture change from seated to supine (21, 22, 25), even though the increase in central blood volume is similar. During the posture change, carotid baroreceptors are also stimulated due to the hydrostatically increased pressure. Therefore, we hypothesized that static carotid baroreceptor stimulation by application of NS during WI would decrease MAP further and lead to the same decrease as that of the antiorthostatic posture change. It turned out, however, that PP increased similarly during WI + NS and WI but significantly more so during the posture change from seated to supine. Thus, in the supine position, the pulsatile stimulation of the arterial high-pressure receptors (carotid and aortic) was more pronounced than during WI + NS, whereas the low-pressure and static carotid receptor stimulation were similar (Table 2). Therefore, we suggest that the increase in PP during an antiorthostatic posture change could be the stimulus for the more-pronounced decrease in HR and MAP.

As depicted in Fig. 1 and Table 2, MAP was unchanged during stimulation of low-pressure reflexes combined with some increase in PP during WI. Static stimulation of the carotid sinus by NS decreased MAP (Fig. 1 and 2), but the decrease was more pronounced when both high- and low-pressure receptors were stimulated, as during WI + NS (Table 2). The maximal decrease in MAP was obtained during a combination of high- and low-pressure receptor stimulation and with a further pulsation (the posture change to supine; Table 2). Thus the combined static and pulsatile arterial and cardiopulmonary baroreceptor stimulation caused the most pronounced hypotensive effect. When comparing the effects of WI and WI + NS, left atrial diameter and PP were similar, but static carotid stimulation differed (Table 2). The augmented carotid baroreceptor stimulation during WI + NS most probably further decreased MAP. This is in accordance with the observation that MAP also decreased during carotid baroreceptor stimulation by NS alone.

As previously observed (9, 18, 24), the changes in HR during the posture change, WI + NS, and WI were reciprocal and parallel to those of PP (Table 2). This supports the notion that the adaptation of HR to more long-term antiorthostatic stimuli is primarily governed by arterial baroreflexes through changes in PP. During NS, we, like others (10, 16, 20, 32), observed an acute decrease in HR (Fig. 2), which was caused by acute static carotid baroreceptor stimulation. This is in accordance with previous results from our laboratory (21, 22), where a model for selective carotid stimulation by a posture change combined with lower body negative pressure was used. It was demonstrated that HR is promptly decreased by static carotid stimulation but that a simultaneous increase in left atrial diameter and/or PP prolongs the bradycardic effect.

The lesser increase in PP during WI than during the posture change, even though stroke volume increased similarly, merits comments. One explanation could be the altered pulse wave reflection due to bending of the vascular tree at the hip in the seated position during WI. Another reason could be effects on the arterial system of the front-to-back compression of the thorax caused by the transverse gravitational stress during supine. These explanations are, however, speculative and need further investigation.

As expected from the results of previous investigations, plasma AVP was suppressed during the posture change and during WI (7, 17, 22). During WI + NS, however, the small numeric decrease in plasma AVP did not reach a significant level. When comparing the effects of the posture change to supine with those of WI + NS, the additional increase in PP (combined with an increased low-pressure receptor stimulation; Table 2) could have accounted for the decrease in AVP release during supine. This is in accordance with our previous findings from a model including a posture change combined with lower body negative pressure demonstrating that suppression of AVP is critically dependent on an increase in PP, left atrial diameter, or both (22).

During WI, plasma AVP also decreased. When the results of WI + NS are compared with those of WI, PP and left atrial diameter increased very similarly (Figs. 1 and 3). The only difference in baroreceptor stimulus comparing WI + NS with WI was the static carotid receptor stimulation during WI + NS. Thus, even though static carotid receptor stimulation was added to the low-pressure receptor stimulation during WI + NS, plasma AVP was not significantly suppressed. Therefore, the results show that during low-pressure receptor stimulation, AVP release is not suppressed by static carotid high-pressure stimulation. Accordingly, Weh-

Table 2. *Degree of changes in static (carotid) or pulsatile (arterial PP) arterial high-pressure and cardiopulmonary low-pressure (LA diameter) baroreceptor stimulation compared with seated position during supine, WI, NS, and WI+NS interventions*

	Stimuli			Effect	
Intervention	Static carotid stimulation	Cardiopulmonary stimulation (LA diameter)	Pulsatile arterial stimulation (PP)	MAP	HR
Supine	↑	↑	↑↑	↓↓↓	↓↓↓
WI+NS	↑	↑	↑	↓↓	↓↓
NS	↑	→	→	↓	↓→*
WI	→	↑	↑	→	↓↓

LA diameter, left atrial diameter; PP, pulse pressure; HR, heart rate. Arrows indicate the degree of increase (↑) or decrease (↓). →, unchanged. *Only acute change.

berg et al. (33) observed no AVP suppression during an increased perfusion pressure of up to 200 mmHg in isolated carotid sinuses in dogs, and the results of other experiments in dogs have likewise shown no effect on AVP release during sustained loading of the carotid sinus (31).

Plasma AVP increased when going from supine to seated, whereas no changes occurred during the 15 min after WI. These results suggest that not only less distension of the heart but also a decrease in PP and/or carotid pressure is important for the AVP release during moderate orthostasis. This notion is supported by the results of Norsk et al. (18), who observed increased plasma AVP during 50 mmHg of lower body negative pressure with a concomitant narrowing of PP, whereas plasma AVP was unchanged during a lower level of lower body negative pressure, when central venous pressure and left atrial diameter decreased and PP remained unchanged. Kamegai et al. (10) observed that static carotid baroreceptor stimulation by NS during passive whole body head-up tilt attenuated AVP release in humans. Also, the results of experiments in dogs suggest that inhibition of arterial baroreceptors is pivotal for the stimulation of AVP release (29, 31). Thus, when our results are compared with those of other studies, we suggest that during antiorthostasis, a combined increase in PP and left atrial diameter is required to suppress AVP release, whereas static carotid baroreceptor stimulation is of less importance. During a moderate orthostatic maneuver, however, the increase in AVP release is probably more dependent on hydrostatic carotid baroreceptor inhibition but possibly augmented by less pulsatile arterial baroreceptor stimulation.

Plasma NE decreased during simultaneous increase in left atrial diameter only, and the decreases were similar during supine, WI + NS, and WI despite different levels of static and pulsatile arterial baroreceptor stimulation (Table 2). These results confirm that forearm sympathetic nervous activity is primarily governed by low-pressure reflexes and is apparently unaffected by carotid baroreceptor stimulation (15, 21, 22).

The increase in cardiac output and stroke volume and the decrease in total peripheral vascular resistance were very similar during supine, WI + NS, and WI. Cardiac output was, however, only measured at the end of the 15-min interventions, where MAP during supine and WI + NS did not differ significantly. Thus it is possible that the decrease in total peripheral vascular resistance was in fact more pronounced during the initial phase of the posture change compared with during WI. This notion needs further investigation with more frequent cardiac output measurements.

Limitations. It could be argued that the insufficient effects of WI + NS on HR and MAP compared with supine were due to too low a level of NS. This is, however, unlikely, because previous results from our laboratory (unpublished observations) show that the effects of carotid baroreceptor stimulation obtained by a posture change from seated to supine can be simulated quite accurately by a NS of the same magnitude as in this study.

Theoretically, another explanation for the weaker effects of WI + NS than of the posture change could be that the movement of the upper body, which did not occur during WI + NS, affected vestibular, intraabdominal, or intracranial receptors. We have, however, previously observed that other factors than baroreflexes seem to play little or no role for the cardiovascular adjustments to antiorthostasis (unpublished observations). Thus it is likely that increased pulsatile baroreceptor stimulation (PP) caused the more pronounced cardiovascular responses during supine than during WI + NS.

Because peripheral PP is increased compared with PP in the aorta (12, 19, 28), the aortic baroreceptors probably sensed lower pressures than those indicated by our brachial PP measurements. In addition, the central to peripheral pressure difference is enhanced by upright tilt (12) so that the changes in aortic PP during the seated to supine posture change was underestimated by our brachial measurements. Taking these discrepancies in pressure in the brachial artery and the aorta into account does not, however, change the conclusions of the study.

We used WI to obtain cardiopulmonary low-pressure receptor stimulation similar to that of the posture change to supine. Even though the changes in left atrial diameter were similar, it can, however, not be excluded that stretch receptors in the other chambers of the heart and/or in the large intrathoracic vessels were stimulated differently by the two interventions. Furthermore, WI is not a specific stimulus for cardiopulmonary low-pressure receptor stimulation, because, e.g., total plasma volume increases (4). Our study design takes this inadequacy into account by comparing the effects of WI with those of WI + NS.

In conclusion, static carotid baroreceptor stimulation by NS during WI is not sufficient to decrease MAP and HR to the same extent as during a posture change from seated to supine. We suggest that the additional increase in PP, which causes pulsatile arterial baroreceptor stimulation, during the posture change is a possible mechanism for the further decrease in MAP and HR. Furthermore, the release of AVP and NE seems independent of static carotid baroreceptor stimulation and is probably governed by an interaction of cardiopulmonary low-pressure and pulsatile arterial baroreceptor stimulation.

Perspectives. In this study, we compared the cardiovascular and neuroendocrine effects of a posture change from seated to supine with those of similar low- and static high-pressure baroreceptor stimulation by WI with and without simultaneous NS. During the posture change, we observed more pronounced decreases in MAP, HR, and plasma AVP, which were probably due to the difference in pulsatile arterial baroreceptor input. Therefore, in future studies, it is not only important to distinguish between effects of arterial high- and cardiopulmonary low-pressure reflexes but also between the static and the pulsatile

components of arterial baroreceptor stimulation. A further insight into the relative importance and interaction of baroreflexes might lead to better understanding and treatment of diseases with cardiovascular and volume homeostatic disorders.

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