Otolithic and tonic neck receptors control of limb blood flow in humans

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Normand, Hervé, Olivier Etard, and Pierre Denise. Otolithic and tonic neck receptors control of limb blood flow in humans. J. Appl. Physiol. 82(6): 1734–1738, 1997.—The aim of this study was to evaluate the role of otolithic receptors and neck mechanoreceptors on the control of the cardiovascular system. We measured calf (CBF) and forearm blood flow (FBF) by strain-gauge plethysmography, mean arterial pressure (MAP), and heart rate (HR) in 12 healthy subjects in two body positions (lying prone and on the left side) and three head positions (reference, flexion, and extension). When the subjects were lying prone, CBF and FBF were lower in head flexion than in reference position (5.8 ± 0.4 and 3.8 ± 0.3 ml·min⁻¹·100 ml⁻¹, respectively) than in reference position (5.8 ± 0.4 and 3.8 ± 0.3 ml·min⁻¹·100 ml⁻¹, P < 0.05), with no significant difference in MAP and HR. When the subjects were lying on the side, changing the head position from reference to flexion significantly increased FBF (from 3.7 ± 0.2 to 4.2 ± 0.4 ml·min⁻¹·100 ml⁻¹, MAP (from 97.2 ± 3.3 to 102.4 ± 5.8 mmHg), and HR (from 63.7 ± 1.4 to 65.9 ± 2.5 beats/min; P < 0.05).

Because otolithic receptors and neck mechanoreceptors are involved when the subjects are lying prone, and otolithic receptors are not involved when the subjects are lying on the side, the results suggest that otolithic and neck mechanoreceptors exert significant influences over the cardiovascular system.

The immediate response to orthostatism is a generalized vasconstriction by a-adrenergic stimulation, linked to a deactivation of cardiopulmonary receptors and a decrease in arterial baroreceptor activity when arterial pressure drops (4). The respective importance of the two types of receptors and their interaction in the control of vascular resistances (VRs) is still debated (11, 15, 17), and it is also possible that other receptors may participate in orthostatic reflexes. In animals, the vestibular system can modulate the sympathetic activity (24, 25), and it was shown that bilateral vestibular nerve section in cat impairs the orthostatic reflexes (5).

To our knowledge, there has been only one study showing a possible influence of the otolithic system on the cardiovascular system in humans (8). In subjects lying prone, a complete head flexion from extension was accompanied by a decrease in limb blood flow (BF). The change in head position relative to gravity induces not only otolithic stimulation but also a redistribution of cephalic fluids, which, in turn, could indirectly stimulate other receptors, e.g., via face congestion or changes in carotid transmural pressure. However, the cardiovascular changes observed were not the result of a stimulation of carotid baroreceptors, cephalic congestion, or increased thoracic pressure. Thus it was suggested that vestibular stimulation may play a role (8). If this is the case, the fact that the response was long lasting precludes a role of semicircular canals, leaving only the otolithic receptors as possible sensors.

Lower body negative pressure (LBNP) and head-up tilt induce a deactivation of the cardiopulmonary baroreceptors, which, in turn, increases sympathetic activity. However, whereas LBNP does not modify the increase in R-R interval obtained by carotid baroreceptor activation (2, 3, 16), this increase in R-R interval is higher with subjects in the upright than in the supine position, at least when sympathetic influences on the sinus node are removed (6). Because LBNP does not involve otolithic activation, in contrast to a change from the supine to upright position, a role of the otoliths might explain the observed difference.

In static conditions, two types of receptors are stimulated by head flexion on the trunk. The otolithic receptors sense the position of the head in space, and the neck tonic receptors sense its position in relation to the trunk. It is known that the two receptors interact, as shown by a number of studies on the convergence of otolithic and tonic neck receptor pathways on vestibular nuclei and other brain stem structures (23). Thus the absence of change in BF observed by Essandoh et al. (8) during head flexion with subjects lying supine cannot exclude the possibility of either a role of the tonic neck receptors or a mechanical effect of the position of the neck because of the possible interaction of the two receptors. Indeed, tonic neck mechanoreceptor stimulation in a subject lying supine with the neck flexed is similar to that seen in a subject in the prone position, whereas stimulation of otolithic receptors is the reverse. In other words, neck receptors and otolithic responses add up in one case and subtract in the other. In addition, a cardiovascular response can be induced by neck flexion in patients in a state of cerebral death (thus without vestibular reflexes), whereas the same maneuver does not evoke a response in patients in a state of coma (12). In the first case, the response would only be of neck origin, and in the second, it would be counterbalanced by an otolithic response in the opposite direction.

The aim of this study was to assess separately the effect of otolithic receptor and neck mechanoreceptor stimulation on the cardiovascular system. We quantified the effect of head movements in subjects lying on the side, compared with prone. With subjects lying on the side, only the neck mechanoreceptors are stimulated because there is no otolithic reorientation relative to gravity, whereas otoliths are stimulated with the subjects lying prone. We will refer to the first situation as neck stimulation and the second as neck + otolith stimulation. In our experimental conditions, we could not stimulate the otoliths independently of the neck.
However, the difference between the effects of neck + otolith stimulation and neck stimulation allowed us to approximate the effect of a stimulation of the otoliths alone.

METHODS

Subjects. Twelve male subjects (age 22–31 yr) without previous cardiovascular, cochlear, vestibular, or neurological pathological conditions participated in this study. They were informed of the protocol and familiarized with the instruments and recording procedures before giving their written consent.

Table position and head support. The subjects lay in the desired position with the head resting comfortably on a mobile support at the edge of the examining table. The support allowed us to place the head at the desired height and at different positions for examination. To ensure good venous drainage, an articulated system was used to maintain the subject's right forearm and leg stable and above heart level. The table was covered with a soft mattress to ensure the subject's comfort.

BF. Right forearm BF, (FBF) and calf BF (CBF) were measured with a venous occlusion strain-gauge plethysmograph (10) with the gauges placed around the region of maximal circumference of the segment of limb studied. Venous occlusion was simultaneously ensured by cuffs adapted to the size of the right thigh and arm and rapidly inflated to 50 mmHg with a single compressor. BF was calculated by using the initial part of the plethysmographic curve and expressed in milliliters per minute per 100 ml.

Arterial pressure and heart rate (HR). Continuous arterial pressure and HR measurements were done with an automatic arterial pressure monitor (Finapres 2300e) placed on the middle finger at heart level. Pressure values provided by this system do not significantly differ from those taken directly from the radial artery in subjects in various physiological conditions (18), and there is good agreement in the evaluation of beat-to-beat variations (14). Mean arterial pressure (MAP) was calculated as the sum of the diastolic arterial pressure and one-third of the difference between systolic and diastolic arterial pressures. Forearm VR (FVR) and calf VR (CVR) were calculated as MAP divided by FBF and CBF, respectively (13).

Protocol. The experiments were performed at 2 or 4 PM in a room at 24.2 ± 0.8°C. Each subject was studied lying prone and on his left side (Figs. 1 and 2). The head support was adjusted to place the head in the reference position, defined as horizontal to the body axis, without rotation. After the cuffs and sensors were set in place, the subject remained in the initial reference position for 10 min before measurements were taken. The studies of the two body positions were separated by 10 min.

At each body position, five measurement sequences were done based on head position, with each extension or flexion measurement sequence preceded and followed by a measurement sequence in the reference position. During each sequence, FBF and CBF were measured four times, namely, 90, 135, 180, and 225 s after the new head position was taken. All four values of BF were identical in each sequence and thus were averaged. MAP and HR were averaged from the overall sequence of measurements.

It has been shown that in the prone position, BF in limbs decreases with time (1). To control for this variable, the order in which the effects of body and head position were studied was randomized.

Effect of otolithic stimulation. For each subject, the effect of otolithic stimulation alone was calculated by subtracting, at each head position, the value obtained with the subject lying
on the side from that obtained with the subject lying prone. Differences obtained in head flexion are referred to as head-down values and those in head extension as head-up values.

Statistical analysis. The overall calculations were carried out by using the statistical software SAS 6.08. Values are expressed as means ± SE. For each body position (prone, on left side, and prone minus on left side), the data were compared by two-way analysis of variance, testing for head position (flexion, extension, reference) and subject variability. The Dunnett’s test was used to compare head positions.

RESULTS

Baseline data at each body and head position are given in Table 1. Results in Fig. 3 are presented in terms of differences relative to the reference position.

With the subjects lying prone (neck + otolith stimulation), MAP and HR did not change with head position, whereas CBF was affected (P < 0.01). It was lower when the head was in flexion compared with the...
reference position (5.2 ± 0.6 ml·min⁻¹·100 ml⁻¹; reference 5.8 ± 0.4 ml·min⁻¹·100 ml⁻¹; P < 0.05) and tended to increase when the head was in extension (P < 0.1). FBF was less affected by head position (P = 0.07), and this only occurred in head flexion compared with the reference position (3.2 ± 0.4 ml·min⁻¹·100 ml⁻¹; reference 3.8 ± 0.3 ml·min⁻¹·100 ml⁻¹; P < 0.05). CVR was significantly increased in head flexion and decreased in head extension, whereas FVR was not affected by head position.

With the subjects lying on the side (neck stimulation), MAP, HR, and FBF were significantly higher when the head was in flexion (MAP: 102.4 ± 5.8 mmHg; reference 97.2 ± 3.3 mmHg; HR: 65.9 ± 2.5 beats/min; reference 63.7 ± 1.4 beats/min; FBF: 4.2 ± 0.4 ml·min⁻¹·100 ml⁻¹; reference 3.7 ± 0.2 ml·min⁻¹·100 ml⁻¹; P < 0.05), whereas CBF, FVR, and CVR did not change. Head extension had no effect on any of the cardiovascular parameters.

Head-down otolithic stimulation significantly decreased MAP (P < 0.05) and FBF (P < 0.01). It tended to decrease CBF (P < 0.1) and increase FVR (P < 0.1). Head-up otolithic stimulation had no significant effect on cardiovascular parameters.

**DISCUSSION**

Effect of neck and otolith receptors on BF. Consistent with the finding of Essandoh et al. (8), we found that the combined stimulation of the otolithic and tonic neck receptors resulted in a change in CBF (P < 0.01) attributable to a change in CVR (P < 0.001). This effect appears mainly due to the otoliths because neck stimulation alone has no effect on CBF (Fig. 3). In the forearm, the combined stimulation of the otolithic and tonic neck receptors affected BF to a lesser extent (P = 0.07), and FBF only decreased in head flexion (P < 0.05). However, neck flexion alone significantly increased FBF (P < 0.05). Therefore, otoliths probably affect FBF as well as CBF. These observations support the possibility that the absence of changes in BF observed by Essandoh et al. in subjects during head flexion while lying supine could be the result of an opposite effect of otolithic and tonic neck receptor activation on sympathetic activity. However, it is difficult to compare the present study with that of Essandoh et al. because Essandoh et al. studied this maneuver only in three subjects, probably as a control.

Hydrostatic pressure variations at the level of the carotid baroreceptors cannot explain the changes in BF with subjects in the prone position. Indeed, if there were a sufficient increase in transmural pressure at the carotid level to activate the baroreflex during head flexion in prone position, this would result in a peripheral vasodilation. Similarly, if there were a sufficient blood redistribution toward the head and a change in the cardiopulmonary receptor stimulation, this would preferentially act on the upper limb (9).

Comparison of the effects on upper and lower limbs. The lower limb seemed preferentially affected by the changes in VR. Several factors could explain this observation. First, because of the length of the experiments, we measured BF without exclusion of the hand and foot circulation. However, Essandoh et al. (8) excluded circulation to the extremities and showed that the reduction in CBF during head flexion was the same whether or not the circulation to the ankle was excluded. Accounting for the increase in skin fraction relative to muscle mass toward the extremities, they also concluded that the reduction in BF essentially affected muscular circulation. Thus, because the surface-to-volume ratio is greater in the upper than in the lower limb, the fraction of FBF directed to the skin is also expected to be greater. This could explain why the change in BF may be significant only in the lower limb, where circulation of the distal extremity is not excluded. Second, several studies have shown differences in calf and forearm vascular response in different conditions. Mental stress, breathing against a resistance, and cough increase BF only in the upper limb, whereas the Valsalva maneuver affects circulation in the upper and lower limb equally (21). Both LBNP <20 mmHg and a change from a supine to a sitting position decrease BF in the upper limb without affecting that in lower limb (7, 9). However, it must be noted that the differential effect of LBNP on the upper and lower limb circulation does not depend on a different sympathetic activation. It has been shown that sympathetic nerve activity in arm and leg muscles during LBNP was identical (19). Third, the changes in neck position affect the anatomic relationships between subclavian arteries and surrounding muscles (in particular scalenus), and this could explain the changes in BF, independent of adrenergic stimulation. Head flexion alone, which decreases scalenus tension, could increase FBF, and head extension could decrease it.

Source of the change in limb BF. In the prone position, combined neck and otolith stimulation by changes in the head position affected BF without significantly altering MAP and HR. This indicates that it is the effect of head position on VR that explains the change in BF. These results are consistent with the observation of Essandoh et al. (8) on MAP and CVF. With the subjects lying on the left side, neck stimulation alone by changing the head position affected FBF, MAP, and HR, without any change in CBF. The change in FBF does not seem to be due to a change in VR, because BF increased in proportion to MAP. Thus we can conclude that otolithic stimulation alone affected CBF, FBF, and MAP without significant changes in VR. Significant changes in vasomotion are only obtained in the lower limb through a combined stimulation of otolithic and tonic neck mechanoreceptors.

What is the role of otoliths and neck mechanoreceptors on blood pressure control? Cardiac response to carotid baroreceptors' stimulation of vagal origin is fast (~0.5 s; Ref. 6), but the sympathetic response is slower. The peak of the muscle sympathetic activity in response to the carotid compression occurs 2–3 s after the onset of stimulation (19), and the delay between sympathetic activation and change in arterial pressure is ~5–6 s (22). Thus the otolithic and neck mechanorecep-
neck extension has no effect on BF and MAP (Fig. 3), includes a neck extension and a head-up orientation. The neck flexion induces an increase in FBF and CBF (Fig. 3C), the effects of both receptors contributing to cardiovascular adaptation.

The same movement from prone instead of supine includes a neck extension and a head-up orientation. Neck extension has no effect on BF and MAP (Fig. 3B), whereas the head-up orientation still produces an increase in CBF (Fig. 3C). Thus, whatever the position of the body when lying, a change to standing can be associated with in increase in CBF. From a teleological point of view, this appears beneficial, because orthostatism necessarily increases metabolic needs, at least in the lower limb, even if it is not followed by a locomotor activity.

In summary, this study shows that peripheral BF's are differently affected by head movements, depending on the head position in space. The difference could account for a differential effect of otoliths and neck mechanoreceptors on cardiovascular control.

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