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RESEARCH ARTICLE

Vestibular control of arterial blood pressure during head-down postural change in anesthetized rabbits

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Abstract This study was undertaken to elucidate neural control of the arterial blood pressure (ABP) in head-down postural change which causes both stimulation to the vestibular system and head-ward fluid shift. Experiments were carried out with urethane-anesthetized rabbits. The animal was mounted on a tilting table, tilted to 45° head-down in 5 s, and kept at the position for 5 min. The head-down rotation (HDR) induced a transient decrease in ABP (10 ± 3 mmHg; mean ± SE), and then the pressure gradually recovered toward the pre-HDR level during the 5 min at the head-down position. Pretreatment with hexamethonium bromide, a ganglionic transmission blocker, suppressed the HDR-induced drop of ABP, suggesting that the ABP drop was induced by an inhibition of autonomic neural outflows. Renal sympathetic nerve activity (RSNA) decreased considerably after 1.6 ± 0.2 s from the onset of HDR, which was followed by the ABP drop. Aortic depressor nerve activity (ADNA), an afferent for baroreceptor reflex, increased significantly during the rotation, but the peak of ADNA increase was 3.2 ± 0.5 s after the initiation of the HDR. Therefore, the suppression of RSNA seems to be induced mainly by a quicker mechanism than baroreceptor reflex. In order to test the possibility, we examined changes in ABP and RSNA during HDR using vestibular-lesioned rabbits. In these rabbits, RSNA and ABP did not change significantly during HDR. These results suggest that vestibular organs play a role in the transient drop in ABP induced by HDR through the suppression of sympathetic nerve outflows.

Keywords Head down rotation · Renal sympathetic nerve · Aortic depressor nerve · Arterial pressure · Rabbit

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Introduction

It is well known that baroreceptor reflexes play an important role in the regulation of arterial blood pressure (ABP) during postural change. Head down tilt (HDT) increases the ABP in the upper body due to a hydrostatic effect and head-ward fluid shift, which stimulates arterial and cardiopulmonary baroreceptors (Thames et al. 1982; Guo et al. 1982; Nagaya et al. 1995; Tanaka et al. 1999; Westerhof et al. 2006). The resultant baroreceptor reflexes induce an inhibition of sympathetic nerves (Thames et al. 1982; DiBona and Sawin 1985; Morita and Vatner 1985; Bishop and Hasser 1985; Nagaya et al. 1995; Badoer et al. 1998; Tanaka et al. 1999; Westerhof et al. 2006; Monahan 2007).

Postural change also stimulates the vestibular organs, semicircular canals and otolith, which are known to modulate a regulation of ABP through autonomic nervous system (Doba and Reis 1974; Yates 1992; Jian et al. 1999; Zhu et al. 2007). Stimulation of vestibular nerves, however, has been shown to produce various effects on sympathetic outflows; either excitation, inhibition or both. It has recently been shown that a natural vestibular stimulation using head-down neck flexions excited muscle sympathetic nerve activities (MSNA) in humans (Ray 2000, 2001; Ray and Monahan 2002; Kuipers et al. 2003). An experiment using

cats, on the other hand, demonstrated that a relatively weak stimulation of afferent component of the vestibular nerve inhibited the renal sympathetic nerve activity (RSNA; Uchino et al. 1970). Zakir et al. (2000) showed that electrical stimulation of otolith evoked a prominent inhibition of the sympathetic nerves which was followed by a rebound excitation in cats. Kerman and Yates (1998) examined vestibular influences on different sympathetic nerves innervating the head and abdominal viscera, using anesthetized and decerebrated cats. Interestingly, responses to electrical stimulation of the vestibular nerve were different between regionally different sympathetic nerves, i.e., the magnitude of the evoked responses of the renal sympathetic nerves was larger than that of external carotid nerves. In awake animals, vestibular inputs associated with postural alterations elicit regionally specific increases in vascular resistance that direct blood flow away from the tissues of the body where blood pooling occur (Wilson et al. 2006a, b), suggesting that the effect of vestibular input on vasoconstrictor sympathetic fibers is heterogeneous. Thus, the role of vestibulosympathetic reflex in ABP regulation during postural changes is complex and has not yet been fully understood. One of the very important points that should be addressed to clarify the interaction between the baroreflexes and the vestibulosympathetic reflexes is the time course of the both mechanisms during the postural change, because both of them use sympathetic vasoconstrictor fibers as a common efferent pathway to regulate the ABP.

The purpose of this study is to clarify the difference in time course between the baroreflex and the vestibulosympathetic reflex during postural change. A head-down rotation (HDR) immediately stimulates the vestibular system, whereas it increases ABP with a short delay because the elevation of ABP is attributable to combination of hydrostatic effect and head-ward fluid shift. In the present study, we investigated the time course of changes in ABP, RSNA, and aortic depressor nerve activity (ADNA) during HDR using control and vestibular-lesioned (VL) rabbits. We hypothesized that the change in ABP during HDR is smaller in VL rabbits than in control rabbits, and that the vestibulosympathetic reflex precedes the baroreceptor reflex.

Methods

Animal preparation

Experiments were performed on 18 Japanese white rabbits, weighing 2.5–3.3 kg. All surgical and experimental protocols were approved by the Animal Care Committee of the Tottori University and complied with the Institute for Laboratory Animal Research Guide for Care and Use of Laboratory Animals.

Two days (46 ± 5 h; mean $\pm$ SD) before the experiment, chemical labyrinthectomy was applied in seven rabbits by injecting 20 mg/kg sodium arsanilate (Sigma, Oakville, Ontario, Canada) dissolved in 0.9% saline into the bilateral intratympanic cavities (Chen et al. 1986) under anesthesia with 40 mg/kg sodium pentobarbital (Abbott Laboratories, Chicago, IL, USA). Subsequent to the injection of sodium arsanilate, each ear canal was packed with Gelfoam (Astellas Pharma Inc, Tokyo, Japan). This procedure caused horizontal nystagmus which disappeared a few minutes later. If the horizontal nystagmus was still observed 1 day after the injection, the rabbit was excluded from the study because the bilateral vestibular lesions seemed to be incomplete. Completion of the lesions was further confirmed by the absence of responses to caloric stimulation produced by irrigating cold water (20 ml, 4°C) into the inner part of the external canal. In seven control rabbits, the same amount of saline was injected to the bilateral intratympanic cavities instead of sodium arsanilate.

On experiment day both control ($n = 7$) and experimental ($n = 7$) animals were anesthetized by intraperitoneal injection of urethane (1.2–1.9 g/kg body weight, Wako, Tokyo, Japan), and then the aural vein was cannulated for intravenous administration. State of anesthesia was evaluated using the electrocardiogram and blood pressure (stable heart rate and blood pressure after minor noxious stimuli) (Kocsis and Gyimesi-Pelczer 2004). Supplementary doses (20% of initial dose) were intravenously administered as required. Another catheter was inserted from the right femoral artery, and the tip of the catheter was positioned in the aorta at the level of the heart to monitor blood pressure. The precise position of the catheter tip was confirmed by autopsy after the experiment. A pressure transducer (DT-4812; Viggo-Spectramed, FL) was attached to the animal's body on the thorax at fourth rib level so that its level relative to the heart did not change during HDR. The left renal sympathetic nerve was exposed via a retroperitoneal approach. Subsequently, the aortic depressor nerve in the left anterior neck was isolated from the surrounding tissues. The confirmation of the nerve was carried out by an electrical stimulation (SEN 3301; Nihon Koden,, Tokyo, Japan) that caused a drop of ABP. Rectangular train pulses (train duration, 5–10 s; pulse width, 1 ms; frequency, 50 Hz; intensity, 1–10 V) were transmitted through an isolator (SS104 J; Nihon Koden, Tokyo, Japan) to stimulate the nerve. For recording the activities of the renal sympathetic nerve and the depressor nerve, a stainless steel wire (50 μm in diameter, California Fine Wire, Grover Beach, CA, USA) insulated by silicon sheath was used. A small loop was made at the wire's tip where it was not insulated. Then, a piece of cellulose sheet (Data Sciences International, PA-PH,

St. Paul, MN, USA) was put between the nerve and surrounding tissues. The wire loop was attached to the nerve on the sheet. A loop of another wire was attached to the nerve about 2 mm proximal to the first loop. The pair of wires was then used as a bipolar electrode. The attached regions of both nerves were embedded with silicon gel. The incised skin and muscles were then sutured in each layer.

In the remaining four rabbits with *sham operation*, which was performed in a *similar* manner to the control animals, the other catheter was placed in the superior vena cava via jugular vein to record central venous pressure (CVP) during HDR.

Protocol

After the surgical preparation, the animal was placed on a tilting table in the prone position. The animal's head was fixed on the table by use of a splint during experiments. After stable ABP and nerve activities were recorded for 2 min at least, the animal was rotated to 45° head-down position in 5 s and kept at the position for 5 min. The axis of the rotation was placed at the rostral end of the sternum. HDR was repeated five to eight times, and the interval between each successive trial was at least 2 min. In three rabbits, hexamethonium bromide (Wako Pure Chemical Industries, Osaka, Japan) was injected intravenously (15 mg/kg) after the above-mentioned experimental protocol. Then, the HDR was repeated at 1, 10, 30, and 45 min after the pretreatment with hexamethonium.

Measurement and recording

The bipolar wire electrodes were connected to a differential amplifier with a band pass of 100–5,000 Hz during experiment. The amplified neural activity was integrated by a voltage integrator with a time constant of 0.05 s. The table position was monitored by a potentiometer which showed tilt angle as a DC voltage. ABP was measured using the pressure transducer attached to the body. These signals were connected to an amplifier (AP-601G; Nihon-Koden, Tokyo, Japan). Heart rate was calculated from the arterial pulse by off-line analysis.

Data analysis

Signals of ABP, nerve activity, integrated nerve activity and tilt angle were stored on DAT tape (TEAC RX832; Tokyo, Japan) for off-line analysis. The signal traces were digitized at 2 kHz with an analog-to-digital converter (Interface Corp. PCI-3153; Hiroshima, Japan) via a low-pass filter with a cutoff at 8 kHz and subsequently analyzed with MATLAB (MathWorks, Natick, MA, USA). Mean ABP was calculated as diastolic pressure plus one third of the pulse pressure for each beat. The data for mean ABP, CVP, and nerve activities were averaged over either 5-s interval (Fig. 1) or 1-s interval (Figs. 3, 4, 5) in each HDR. The data from two to four HDR trials were averaged in each animal. Except in Fig. 1A and Fig. 5, the values for these data were expressed as normalized values, the baseline value before HDR being taken as 100% in each experiment. These results were presented as mean ± SE (standard errors of the mean).

Analysis of variance with Tukey–Kramer multiple comparison test was used to determine statistical significance in experiments with more than two groups. Student's *t* test was used in comparison between two groups. Differences were considered statistically significant at $P < 0.05$.

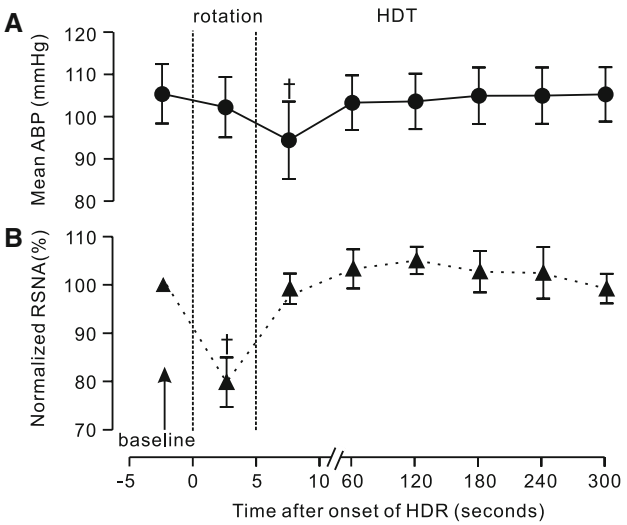

Fig. 1 Changes in mean ABP and RSNA during head down tilt ($n = 7$). Each trace shows time course of the mean ABP (*solid line*) and RSNA (*dotted line*) during and after HDR. *Vertical dotted lines* indicate the onset and the end of rotation. *Daggers* indicate $P < 0.05$ versus baseline

Results

Changes in ABP and RSNA during and after HDR in control rabbits

Figure 1 shows changes in mean ABP and RSNA during and after HDR in control anesthetized rabbits ($n = 7$). Average of mean ABP in control rabbits was 105 ± 6 (mean ± SE) mmHg at the horizontal prone position. The mean ABP began to decrease during the rotation, reached the lowest level (96 ± 9 mmHg) right after HDR (time = 0), then recovered toward the pre-HDR level within 1 min, and remained a plateau at the pre-HDR level during the rest of 5 min head-down period (Fig. 1A). The RSNA decreased significantly during the rotation and recovered quickly to the baseline level right after the HDR (Fig. 1B).

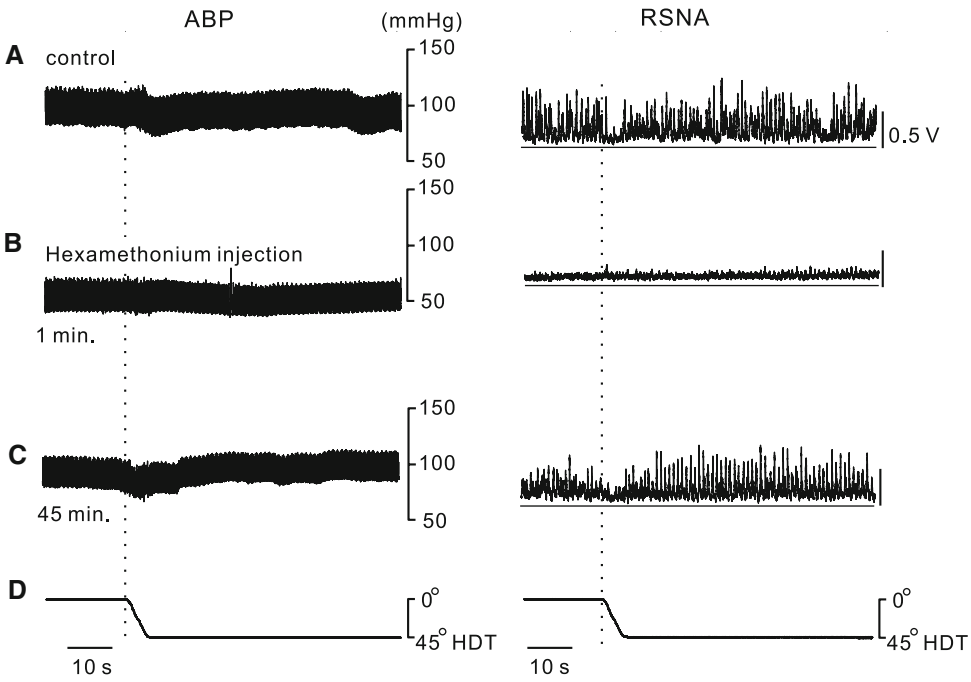

Fig. 2 Effect of pretreatment with hexamethonium on ABP (*left panel*) and RNSA (*right panel*) during HDR. Traces show, from *top to bottom*, control (**A**) and two conditions with different periods of 1 and 45 min (**B** and **C**) after intravenous injection of hexamethonium. All traces are aligned on the onset of tilting (*vertical dotted lines*). *Bottom traces* indicate body position of the animal (**D**)

Effect of hexamethonium injection

A possibility that the ABP drop was caused by other mechanisms than autonomic nerves was tested using hexamethonium, an autonomic ganglion blocker. After injection of hexamethonium, RSNA immediately disappeared as shown in Fig. 2B (right panel). Mean ABP significantly decreased from 108 ± 4 to 69 ± 7 mmHg ($n = 3$, $P < 0.01$; Fig. 2B, left panel). After 45 min from the injection of hexamethonium, the mean ABP recovered to 91 ± 2% ($n = 3$) of the control level before hexamethonium injection (Fig. 2C). HDR induced a significant decrease in ABP before injection of hexamethonium (Fig. 2A) and after recovery (Fig. 2C), but did not 1 min after the pretreatment of hexamethonium (Fig. 2B). The average decrease in the HDR-induced mean ABP drop was significantly greater before injection of hexamethonium (6 ± 2 mmHg) than that (− 2 ± 1 mmHg) after the injection ($n = 3$, $P < 0.01$).

Time course of changes in ABP, RSNA, and ADNA in control rabbits

We described here a temporal relationship between ABP, RSNA, and ADNA during HDR. Figure 3A shows typical changes in ABP and RSNA during HDR in a control rabbit. RSNA was identified as phasic heartbeat-related firings which corresponded to falling phases in ABP. HDR produced an inhibition of the RSNA (Fig. 3Ab, c) which preceded a reflex drop in ABP (Fig. 3Aa).

Figure 3B shows percent changes in mean ABP and RSNA in seven control rabbits. All rabbits showed a transient suppression of RSNA in the HDR period. Latency of the peak suppression from onset of HDR was 1.6 ± 0.2 s. Then, the activity increased gradually toward the baseline level and resumed the pre-HDR baseline level after 7.4 ± 0.5 s. The peak suppression of RSNA preceded the initiation of ABP drop, suggesting that the ABP drop is produced by inhibition of sympathetic vasoconstrictor nerves. Heart rate did not change significantly during HDR (Table 1).

Changes in ADNA and ABP of a control rabbit during HDR are shown in Fig. 3C. ADNA was identified as phasic heartbeat-related discharges, synchronizing with rising phases in ABP (Kobayashi et al. 1999). Electrical stimulation of the aortic depressor nerve decreased the blood pressure and the heart rate (not illustrated). HDR produced an excitation of the aortic depressor nerve. Figure 3D shows average data of changes in ADNA obtained from seven control rabbits. Latency to the peak increase in ADNA from onset of HDR was 3.2 ± 0.5 s. The peak of the ADNA excitation occurred before the decrease in mean ABP, but it was significantly later than the peak suppression of RSNA ($P < 0.05$). Interestingly, the RSNA began to resume their discharges before the ADNA reached the maximum level.

Changes in ABP and RSNA during HDR in VL rabbits

Average of mean ABP in VL rabbits was 89 ± 5 mmHg ($n = 7$) in the horizontal prone position. The mean ABP was not significantly different from that of control rabbits. The HDR-induced drop of ABP was not observed in a VL rabbit (Fig. 4A). No obvious suppression of RSNA was recorded

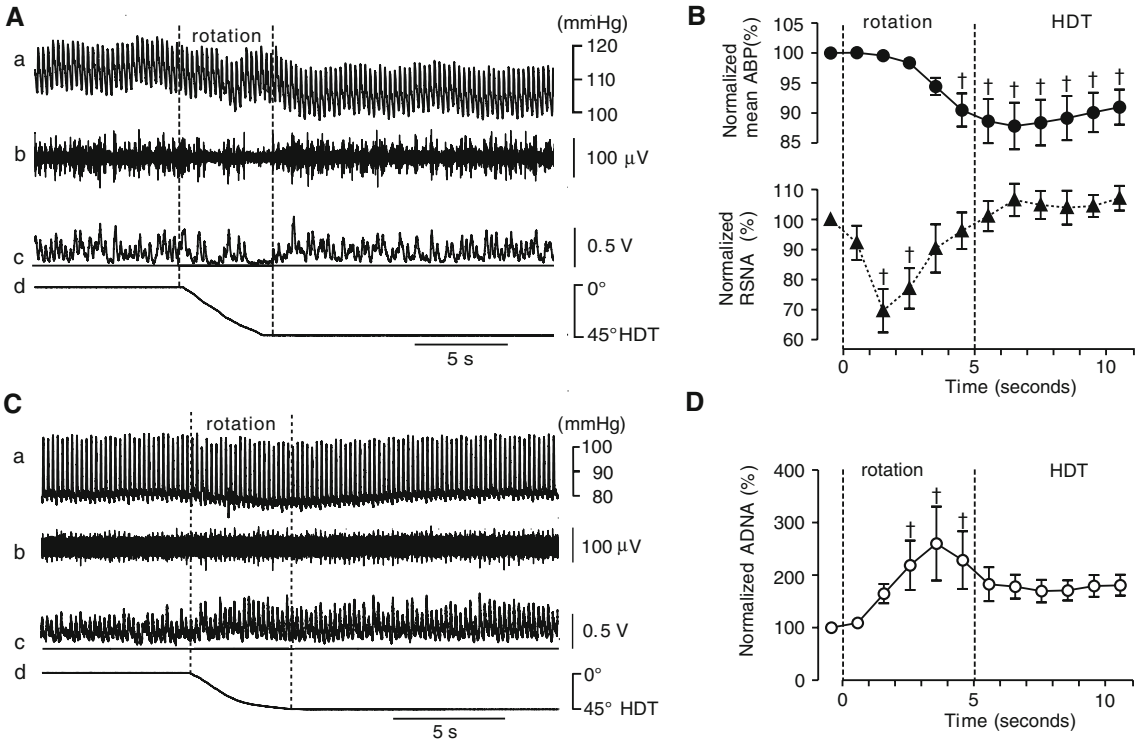

Fig. 3 Changes in ABP, RSNA, and ADNA during HDR. **A** Traces show, from *top to bottom*, ABP (*a*), RSNA (*b*), integrated RSNA (*c*) and body position signals from a potentiometer(*d*). **B** Summarized results of changes in RNSA (*closed triangles*) and mean ABP (*closed circles*) with one-second resolution ($n = 7$). *Vertical dotted lines* indicate the onset and the end of rotation. *HDT* head down tilt. *Daggers* indicate $P < 0.05$ vs. baseline level. **C** Traces show, from *top to bottom*, ABP (*a*), aortic depressor nerve activity (ADNA) (*b*), integrated ADNA (*c*), and body position (*d*). **D** Summarized results of changes in ADNA (*open circles*) during the early period of HDR ($n = 7$). *Vertical dotted lines* indicate the onset and the end of rotation. *Daggers* indicate $P < 0.05$ versus baseline level

Table 1 Effect of HDR on heart rate in control and VL rabbits

	Heart rate, beats/min		
	Before HDR	During HDR	After HDR[a]
Control ($n = 7$)	268 ± 10	267 ± 9	266 ± 9
VL ($n = 7$)	251 ± 13	252 ± 13	252 ± 13

[a] Values after HDR during which the posture was kept at 45° head-down position

in the VL rabbit after onset of HDR. Figure 4B shows the average changes in mean ABP and the average RSNA in VL ($n = 7$) and control ($n = 7$) rabbits, respectively. The RSNA in VL rabbits did not change significantly during HDR. The mean ABP in VL rabbits ($n = 7$) did not change significantly, while the mean ABP in controls ($n = 7$) started to decrease at 4 s after the onset of HDR ($P < 0.05$).

Changes in CVP during HDR

Changes in CVP during HDR in control rabbits ($n = 4$) are shown in Fig. 5. Average of CVP was 1.8 ± 1.3 mmHg at the horizontal prone position. The CVP tended to elevate slightly to 2.9 ± 0.9 mmHg at 3.0 ± 1.0 s (Fig. 5) from the onset of HDR, but this change was statistically not significant.

Discussion

During HDR, ABP was lowered in anesthetized control rabbits. The decrease in ABP was induced 3.0 s after the onset of HDR, it reached the lowest level at 6.2 s from the onset, then it recovered to the baseline level by 1 min from the onset (Figs. 1, 3B). The reduction of ABP was associated with suppression of RSNA (Figs. 1, 3B). Pretreatment with a ganglion-blocking agent extinguished RSNA and the HDR-induced depression of ABP (Fig. 2), suggesting that the drop of ABP is due to a suppression of sympathetic vasoconstrictor nerve activity. HDR seems to have induced the suppression of RSNA possibly through two mechanisms in the present experiments, i.e., baroreceptor reflexes and/or a vestibulosympathetic reflex.

Exposure to HDR causes head-ward fluid shift (Nixon et al. 1979), elevates ABP in the upper body and stimulates baroreceptors located at the aortic arch and the carotid sinuses, which increases ADNA (Moffitt et al. 1999). If the baroreceptor reflexes are the main cause of the ABP drop

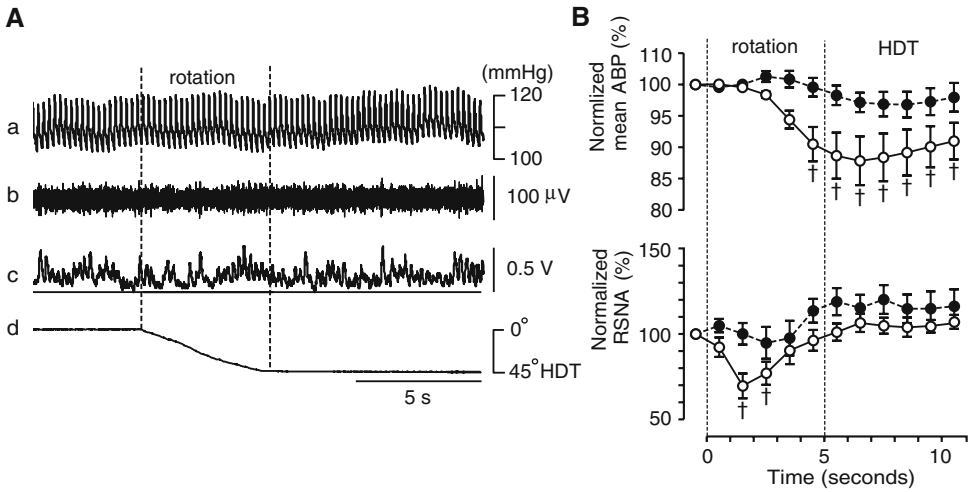

Fig. 4 Effect of HDR on ABP and RSNA in VL rabbits. **A** Traces show, from *top to bottom*, ABP (*a*), RSNA (*b*), integrated RSNA (*c*) and body position signals (*d*). **B** Summarized results of changes in mean ABP (*upper panel*) and changes in RSNA (*lower panel*) during HDR in control (*open circles*, $n = 7$) and VL rabbits (*closed circles*, $n = 7$). *Vertical dotted lines* indicate the onset and the end of rotation. *Daggers* indicate $P < 0.05$ versus each baseline

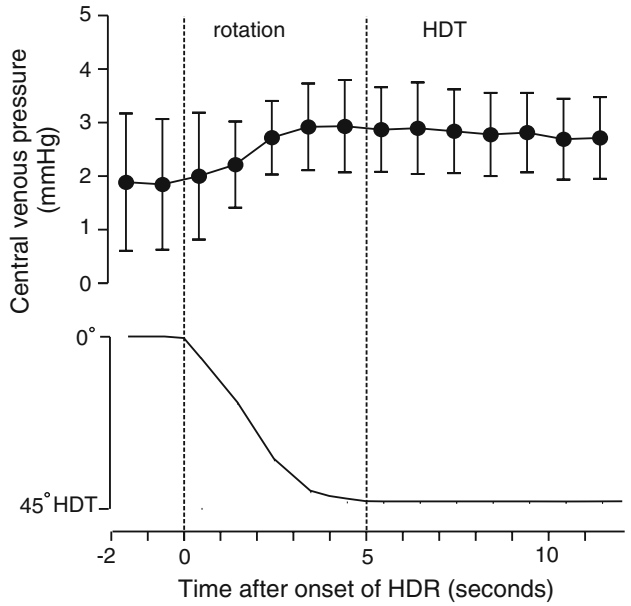

Fig. 5 Changes in CVP during HDR. Traces show time course of change in CVP (*upper panel*) and body position (*lower panel*). *Vertical dotted lines* indicate the onset and the end of rotation

during HDR, the activation of ADNA should have preceded the suppression of RSNA. The present results, however, showed that the peak activation of ADNA occurred later than the peak suppression of RSNA (Fig. 3). Moreover, the RSNA began to recover when the ADNA was still going up, and the RSNA recovered to the pre-HDR level 5–10 s after the onset of HDR even though the ADNA kept higher activity than its baseline during that period (Fig. 3). These results suggest that another mechanism that is quicker than the baroreceptor reflexes should be involved in the response of ABP during HDR.

There are a number of studies that demonstrated a significant role of vestibulosympathetic reflex in the regulation of ABP during postural changes. Doba and Reis (1974) showed that bilateral lesions of the rostral fastigial nucleus resulted in impairment of the reflex changes in blood pressure evoked by head-up tilting and suggested that the vestibular apparatus participated in concert with the baroreceptors in the initiation and maintenance of the orthostatic reflexes. Yates and colleagues demonstrated that vestibular stimulation induced by nose-down rotation reduced splanchnic nerve activity (Yates and Miller 1994), that vestibular inputs evoked by head-up tilt elicited regionally specific increase in vascular resistance (Wilson et al. 2006a, b), and that bilateral vestibular lesions altered orthostatic responses to nose-up rotation in cats (Jian et al. 1999). Zhu et al. (2007) demonstrated otolith specific influences on cardiovascular system in alert rats. Ray and colleagues found that a head-down neck flexion induced a vestibulosympathetic reflex which was identified as an increase of MSNA (Ray 2000, 2001), that the vestibular reflex was additive to the baroreflex (Ray 2000), and that the vestibular reflex was attenuated with increasing age (Kuipers et al. 2003; Ray and Monahan 2002). In the present experiments, HDR reduced the RSNA and ABP in the vestibular-intact control rabbits but did not in the VL rabbits (Fig. 4). These results are consistent with previous reports and suggest that HDR activates the vestibular nerves, which in turn suppresses the RSNA in control rabbits.

The new findings in the present study are (1) suppression of the RSNA occurred prior to excitation of ADNA during HDR in the control rabbits, and (2) the HDR-induced suppression of RSNA and reduction of ABP were almost completely abolished by bilateral vestibular lesions. These data suggest that the drop of ABP is mainly produced by vestibulosympathetic reflex and that the baroreflex does not play a significant role in this case. In order to confirm the latter, however, further experiments using animals with baroreceptor denervation will be needed. The reason that HDR failed to induce RSNA and ABP responses in VL rabbits, in

which the baroreceptors should have been stimulated, is unclear. One possible explanation is that the baroreflex was not strong enough to decrease the ABP. Morita et al. (2001) showed that exposure to microgravity, a free-drop, increased aortic nerve activity with no significant change in ABP in anesthetized rats. In the present experiments, 45° HDR elevates intravascular pressures of rabbits at the aortic baroreceptors theoretically by 3–4 mmHg due to a hydrostatic effect because distance between the heart and the baroreceptors is 6–7 cm. This increase might be not enough to elicit a suppression of the RSNA even though it increases the ADNA. Nagaya et al. (1995) also suggested that 3.4 mmHg elevation of hydrostatic pressure at the carotid sinus during 15 (degree) HDT in humans was not enough to stimulate the carotid sinus baroreceptors.

Wilson et al. (2003) suggested that the vestibulosympathetic reflex during postural change played an important role in the regulation of cerebral circulation. Orthostatic hypotension reduces a cerebral blood flow and occasionally causes syncope. Combination of the vestibulosympathetic reflex and the baroreflex seems to play an important role to prevent the orthostatic hypotension induced by a gravitational stress (Gotoh et al. 2004) or head-up tilt (Wilson et al. 2006a, b). In our previous studies, HDT increased cerebral blood flow velocity in humans (Kawai et al. 1993) and elevated intracranial pressure in rats (Kawai et al. 1997) and rabbits (Tatebayashi et al. 2003). However, the cerebral blood flow rate was kept constant during HDT (Asai et al. 2002) and no remarkable edema was found in the brain tissues in rabbits (Shimoyama et al. 2000), suggesting that some compensatory mechanisms were working for the homeostasis in the cerebral circulation. The HDR-induced vestibulosympathetic reflex might be one of the compensations at the beginning of the postural change.

Head-down rotation may also stimulate cardiopulmonary baroreceptors (Nagaya et al. 1995; Badoer et al. 1998; Tanaka et al. 1999) because it causes head-ward fluid shift from the lower extremities and expands blood volume in the thorax. Inputs from the cardiopulmonary baroreceptors also cause an inhibition of SNA (Thames et al. 1982; DiBona and Sawin 1985; Morita and Vatner 1985; Bishop and Hasser 1985; Nagaya et al. 1995; Badoer et al. 1998; Tanaka et al. 1999; Westerhof et al. 2006; Monahan 2007). Nagaya et al. (1995) demonstrated that an exposure to 15° HDT caused 2.16 mmHg elevation of CVP and 37% decrease in MSNA, suggesting that the MSNA was reduced in response to the cardiopulmonary baroreceptors. The decrease in MSNA was kept during 10 minutes of HDT, which forms a contrast to our result that the HDR-induced decrease in RSNA has recovered to the baseline level within a minute. In the present experiments, CVP tended to increase during HDR, but the change in CVP was small and statistically not significant. These findings suggest that cardiopulmonary baroreceptors play a role in maintaining the change in SNA but not in initiating the change. On the other hand, vestibulosympathetic reflex plays an important role in initiating the decrease in SNA at beginning of the postural change but not in maintaining the suppression of SNA.

The ABP drop observed in the present study could be attributable to inhibition of sympathetic activity and/or enhancement of cardiac vagal tone. The latter does not seem to play an important role in the ABP drop because the HDR did not change the heart rate significantly (Table 1). Thus, in the present study, we did neither record the vagal activity nor use vagotomized animals. Shimokawa et al. (1998) reported that anesthesia by urethane decreased the gain of baroreceptor reflex control of heart rate but did not affect the ABP-RSNA relationship. Kerman and Yates (1998) suggested that the gain of vestibular-mediated reflexes were heightened when ABP was below normal values. Therefore, decreases in ABP induced by urethane may increase the gain. Further study is needed to clarify the effect of anesthetics, using alert animals.

In conclusion, HDR induced a transient decrease of ABP in control urethane-anesthetized rabbits. The ABP drop was abolished by pretreatment with hexamethonium, a ganglion-blocking agent, and was preceded by inhibition of RSNA that occurred prior to excitation of ADNA during HDR. The HDR-induced suppression of RSNA and reduction of ABP were almost completely abolished by bilateral vestibular lesions. These results suggest that the drop of ABP is mainly produced by vestibulosympathetic reflex and that the baroreflex does not play a significant role in this case.

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