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Neuronal Activity of the Vestibular Nuclei Following Acute Hypotension in Rats

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The role of peripheral vestibular receptors in acute hypotension was investigated in anesthetized rats. Acute hypotension was induced by either intravenous infusion of sodium nitroprusside (SNP) or by experimental hemorrhage, and electrical activity and expression of cFos-like immunoreactive (cFL) protein were measured in the medial vestibular nuclei (MVN). Blood pressure decreased proportionately to the does of intravenous SNP and to the volume of the hemorrhage. Blood pressure decreased 10, 30, 50% for the 5, 10, 15 μg/kg SNP injection, respectively, and also decreased 30 and 50% after 1- and 2-ml blood loss, respectively, due to hemorrhage. In animals with intact labyrinths, acute hypotension induced by either intravenous infusion of SNP or hemorrhage produced different electrical activities with three different patterns in type I and II neurons of MVN. The responses of type I neurons showed excitatory in 2/3 of recorded neurons and inhibitory or no change in 1/3 of neurons, while the responses of type II neurons showed inhibitory in 2/3 of recorded neurons and excitatory or no change in 1/3 of neurons. In unilateral labyrinthectomized animals, 2/3 of type I neurons ipsilateral to the lesion showed an inhibitory response, and 2/3 of contralateral type I neurons showed an excitatory response after the induction of acute hypotension. The response patterns of type II neurons were opposite from those of the type I neurons. After 30% decrease in blood pressure, cFL protein expressed in the bilateral vestibular nuclei of control animals with intact labyrinths. Expression of cFL protein increased significantly proportionately to the reduction of blood pressure. The unilateral labyrinthectomized animals with acute hypotension produced expression of cFL neurons in contralateral vestibular nuclei to the lesion side, but not in ipsilateral vestibular nuclei. However, cFL protein was not expressed in bilateral vestibular nuclei after acute hypotension in bilateral labyrinthectomized animals. These results suggest that the peripheral vestibular receptors might play a significant role in controlling blood pressure following acute hypotension via activation of type I neurons and inhibition of type II neurons in the vestibular nuclei.

Key Words: Electrical activity, c-Fos, MVN, Acute hypotension, Peripheral vestibular receptor

INTRODUCTION

It is well known that the vestibular system controls posture and movement through vestibuloocular and vestibulospinal reflexes (Wilson & Melvill Jones, 1979). It also influences sympathetic outflow and blood pressure through vestibulo-autonomic reflex (Yates, 1992). However, abnormal stimulation of the vestibular system may evoke nausea, vomiting, vertigo, and tachycardia. Electrical stimulation of the vestibular nerve increases sympathetic activity, but loss of vestibular function impairs compensation for orthostatic hypotension during postural change (Doba & Reis, 1974; Yates, 1992; Park et al, 1999). The neural pathways involved in vestibulo-autonomic interactions include the nucleus tractus solitarius, the dorsal motor nucleus of the vagus nerve, the rostral ventrolateral medulla, and other brain stem nuclei (Yates et al, 1995; Balaban, 1998; Biaggioni et al, 1998).

Although many studies have addressed the influence of the peripheral vestibular system on autonomic functions, the effects of the changes in autonomic function on vestibular function are poorly understood. Excitation of peripheral vestibular receptors by postural changes produces functional changes in the cardiovascular system including blood pressure, pulse rate, baroreceptor reflex, and blood flow to the extremities (Kolev & Tibbling, 1992; Normand et al, 1997; Convertino, 1998). Conversely, patients with idiopathic hypertension, myocardial infarction, arrhythmia, or congestive heart failure, complain of vertigo, which could be explained by changes in blood flow to the peripheral vestibular system.

In the present study, to investigate a role of the peri-

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ABBREVIATIONS: UL, unilateral labyrinthectomy; BL, bilateral labyrinthectomy; MVN, medial vestibular nuclei; SVN, superior vestibular nuclei; IVN, inferior vestibular nuclei; SNP, sodium nitroprusside; cFL, c-Fos like immunoreactive protein.

pheral vestibular receptors on control of blood pressure, electrical activity and c-Fos protein which is considered to be useful marker for detecting changes in neuronal activities (Morgan & Curran, 1991), were measured in the vestibular nuclei after acute hypotension induced by sodium nitroprusside or hemorrhage in rats.

METHODS

Materials

Fifty-six Sprague-Dawley rats weighing 250~300 g were used, which were examined the vestibular function by rotatory test to select an intact labyrinthine animal. Animals were anesthetized with 300 mg/kg chloral hydrate intraperitoneally.

Measurement of blood pressure

A polyethylene tube was cannulated into the femoral artery in prone position and connected to the other end of the tube to preamplifier (Gould, USA). Blood pressure was analyzed using the Spike 2 program (Cambridge Electronic Design, UK), and mean arterial pressure was calculated as "diastolic pressure +1/3 pulse pressure".

Acute hypotension

Sodium nitroprusside was infused 0.5 ml for 10 min with 5, 10, 15 μg/kg/min by osmotic pump into the femoral vein. Also, acute hypotension was induced by depletion of 2 ml of blood for 30 sec from the femoral artery. The blood was then reperfused into the femoral vein to restore the pressure.

Labyrinthectomy

Surgical labyrinthectomy was performed as described in detail previously by Park et al (1995). Briefly, under chloral hydrate anesthesia, a small opening was made around the oval window using a small dental burr through a ventral approach under a surgical microscope. Through this opening, the membranous labyrinth was destroyed surgically with a small, right-angled hook, and aspirated with a suction pump. Unilateral labyrinthectomy (UL) was confirmed by the appearance of spontaneous nystagmus and postural asymmetry after recovery from anesthesia. Experiments in UL or bilateral labyrinthectomized rats were performed 14 days after surgery.

Electrophysiological recordings

The animals were anesthetized with thiopental sodium (ip, 30 mg/kg), secured in a head holder of stereotaxic device (Narishige, Japan), and mounted on a servo-controlled rotator, head centered over the axis of rotation with nose 30° down to bring the horizontal semicircular canals close to the horizontal plane of rotation. The body was supported in a horizontal position by a plastic plate hinged to the stereotaxic frame. Artificial respiration was achieved during rotation and body temperature was maintained by heating pad. Action potentials from single neurons were recorded extracellulary using stainless steel microelectrodes (A & M, USA) with impedence of 4~8 MΩ. Electrodes were positioned using a micromanipulator into MVN (AP: 11.0 mm, ML: 2.2 mm, DV: 5.8 mm from bregma) according to a stereotaxic atlas (Paxinos & Watson, 1986). Signals were amplified and filtered by signal processing system (SPS-8701, Australia) and displayed on an oscilloscope (Tektronix, 5113), which were analysed by data analysis program (Spike 2, Cambridge Electronic Design, UK).

Immunohistochemistry

Animals were deeply anesthetized with urethane (1 g/kg), transcardially perfused, fixed in 4% paraformaldehyde dissolved in 0.1 M phosphate buffer (PB) and decapitated. Then, brains were removed, post-fixed, rinsed in PB, and immersed in 30% sucrose solution for 1~2 days at 4°C. The tissue was sectioned with a thickness of 40 μm on a freezing microtome, incubated for 30 min with 6% hydrogen peroxide (H_2O_2), rinsed two times for 10 min with 0.1 M phosphate buffered saline (PBS) containing 5% dry milk, and incubated with 0.8% Triton X-100 dissolved in 0.1 M PBS containing 0.5% bovine serum albumin (PBS-BSA). After a brief wash, tissue was incubated overnight at room temperature with c-Fos polyclonal antibody (Ab-2; diluted 1 : 250; Oncogene, USA). On the next day, the tissue was rinsed with PBS-BSA, incubated with a biotinylated secondary antibody (goat anti-rabbit; DAKO, USA) and ABC Elite Kit (Vector Lab, USA). The neurons with c-Fos like immunoreactive nuclei were visualized by incubating the tissue with 0.05% diaminobenzidine HCl (DAB) and 0.003% H_2O_2. After DAB reaction, the tissue was rinsed with 0.1 M PB, mounted on gel coated slides, air-dried, dehydrated, coverslipped with Permount (Fisher Chemical, USA), and analyzed by brightfield microscopy. For quantification, only c-Fos like neurons in MVN were counted using a digital image analysis system (Image Pro Plus, USA).

Statistical analysis

All data are represented as the mean$\pm$SD. The statistical significance of differences was assessed using Statview 4.0 (Abacus Concepts, USA). Values of $p<0.05$ were considered significant.

RESULTS

Changes in blood pressure by SNP or hemorrhage

Mean arterial blood pressure was 97.3$\pm$3.4 mmHg in animals with intact labyrinths, and 96.8$\pm$4.2 mmHg in UL animals. However, SNP infusion decreased the blood pressure within 2 min of the beginning of the injection, and hypotension continued for 2 min after the injection. Blood pressure decreased proportionately to does of intravenous SNP and to the volume of hemorrhage. Blood pressure was 87.2$\pm$3.8 (10% decrease), 68.4$\pm$4.2 (30% decrease), 49.2$\pm$3.1 mmHg (50% decrease) for the 5, 10, and 15 μg/kg/min SNP injected, respectively. Blood pressure also decreased 30 and 50% after 1- and 2-ml blood loss due to hemorrhage, respectively. When the hemorrhaged blood was replaced by perfusion, the blood pressure has been restored to the control levels. In UL animals, the decrease in blood pressure after injection of SNP was similar to that in intact labyrinthine animals. In this experiment, we injected SNP

at 15 μg/kg and removed 2 ml of blood to induce acute hypotension (Fig. 1).

Responses following acute hypotension in intact labyrinthine animals

Electrical activity: In order to classify the type of neurons in MVN, the animals on turntable were rotated sinusoidally. Neurons were classified as type I if their firing rate increased with ipsilateral angular acceleration and decreased with contralateral acceleration and type II if they responded in an inverse pattern (Wilson & Melvill Jones, 1979). The electrical activities of type I and type II neurons at rest were 22.8±26.6 and 21.0±17.3 spikes/sec, respectively. And the number of neurons recorded was more in type I than in type II. Electrical activity in MVN was not affected by a 10% decrease in blood pressure, but a 30% decrease in blood pressure did affect neuronal activity. A 50% decrease in blood pressure elicited 3 patterns of responses in neuronal activity. In type I neurons, 62% of the recorded neurons showed increased activity (excitation), 26% showed decreased activity (inhibition), and there was no change in 12% (no response). The responses of type II neurons following acute hypotension were also 3 patterns; inhibition in 68% of recorded neurons, excitation in 19%, and no response in 13% (Table 1). Figure 2-A shows that acute hypotension induced by SNP injection increased electrical activity of type I neurons and decreased activity of type II neurons in right MVN. Changes in neuronal activities began at the time of maximum depression of blood pressure and the activities returned to the control levels after recovery of blood pressure.

Acute hypotension induced by hemorrhage also produced 3 patterns of response in MVN neurons which were similar to the responses caused by SNP. Type I neurons showed excitation in 68% of recorded neurons and inhibition or no response in 32%. Type II neurons showed inhibition in 67% and excitation or no response in 33%. Changes in neuronal activity following acute hypotension induced by hemorrhage were maintained during hypotension, and the activity returned to control levels after recovery of the blood pressure by reperfusion. Figure 2-B shows that electrical activity of type I neurons increased by hemorrhage and the increased activity was maintained during hypotension and returned to the control levels by reperfusion. Response of type II neurons was opposite to that of type I neurons.

Expression of cFL protein: Few numbers of cFL immunoreactive neuron were expressed in MVN of intact labyrinthine animals, but acute hypotension induced by SNP injection of 15 μg/kg showed expression of 104.8±27.1

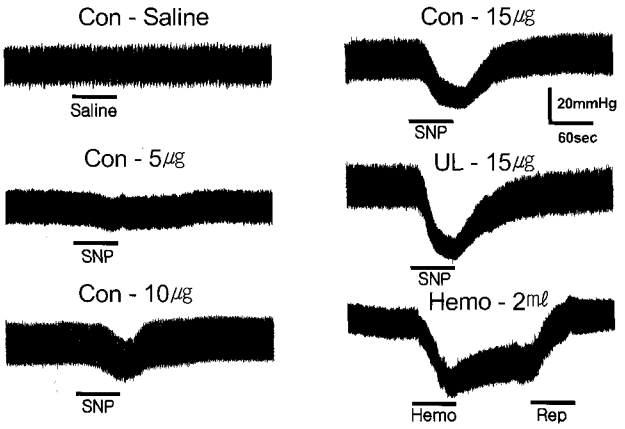

Fig. 1. Representative recordings showing changes in arterial blood pressure induced by intravenous infusion of sodium nitroprusside (SNP) or hemorrhage (Hemo). Control rats (Con) received 0.5 ml of SNP with 5, 10, 15 μg/kg/min, and the same volume of saline to the control. Unilateral labyrinthectomized rat (UL) was given 15 μg/kg/min of SNP. Two ml of blood was removed from the femoral artery for 1 min (Hemo) and the hemorrhaged blood was reinfused into the femoral vein (Rep).

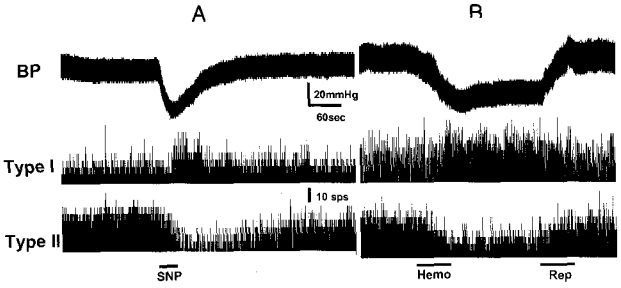

Fig. 2. Responses of type I and II neurons in right medial vestibular nuclei following acute hypotension induced by sodium nitroprusside (A) or hemorrhage (B) in animals with intact labyrinths. BP, blood pressure; SNP, injection of sodium nitroprusside at 15 μg/kg; Hemo, hemorrhage of 2 ml; Rep, reperfusion of 2 ml.

Table 1. Responses of vestibular neurons following acute hypotension induced by infusion of SNP

			Excitation		No response		Inhibition	
			% Change	No of neuron	% Change	No of neuron	% Change	No of neuron
Control		Type I	+34.3±39.0	65 (62%)	0	13 (12%)	−27.2±20.4	27 (26%)
		Type II	+44.6±61.3	14 (19%)	0	10 (13%)	−27.2±19.5	51 (68%)
UL	Ipsi	Type I	+51.7±29.0	6 (10%)	0	6 (10%)	−31.4±22.2	48 (80%)
		Type II	+42.7±38.7	30 (59%)	0	6 (12%)	−22.2±17.4	15 (29%)
	Contra	Type I	+58.1±52.5	45 (72%)	0	9 (14%)	−19.3±10.5	9 (14%)
		Type II	+14.2±11.5	7 (13%)	0	8 (15%)	−16.9±12.4	38 (72%)

Control, intact labyrinthine rats; UL, unilateral labyrinthectomized rats; Ipsi, ipsilateral MVN to the injured vestibular side; Contra, contralateral MVN to the injured vestibular side; % change, % changes of response from resting activity; No of Neuron, number of neurons recorded. Values are means±SD.

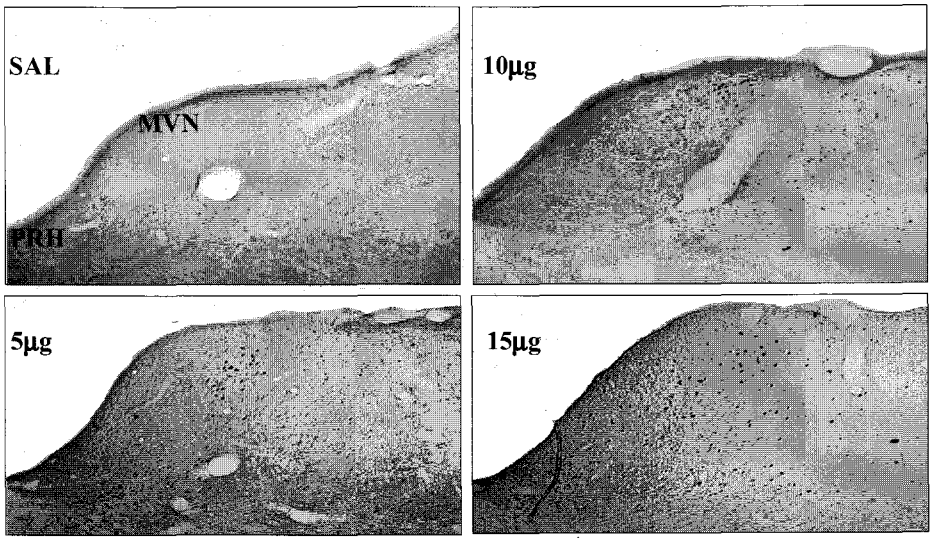

Fig. 3. Photomicrograhs showing expression of cFL protein in medial vestibular nucleus (MVN) of animals with intact labyrinths 2 hours after saline (SAL) or intravenous infusion of sodium nitroprusside with different doses of 5, 10, 15 μg/kg. A few number of cFL protein appear in prepositus hypoglossal nucleus (PrH) following SNP injection. Horizontal solid bar indicates 200 μm.

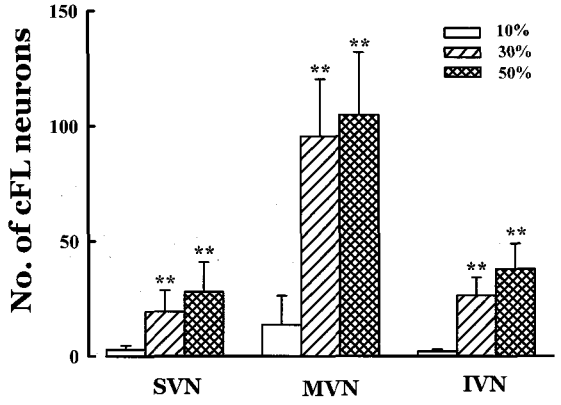

Fig. 4. Bar histographs showing changes in cFL protein expression in superior vestibular (SVN), medial vestibular (MVN), and inferior vestibular nuclei (IVN) following 10, 30, 50% decrease in blood pressure by infusion of nitroprusside with 5, 10, 15 μg/kg, respectively. *Denotes significant difference between 10% and 30% or 50% (**$p<0.01$). Number of rats in each condition of blood pressure is 5.

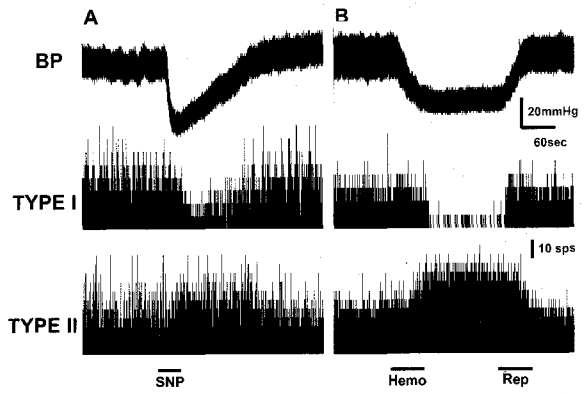

Fig. 5. Responses of type I and II neurons in left medial vestibular nuclei following acute hypotension induced by SNP (SNP) or hemorrhage (Hemo) in left unilateral labyrinthectomized animals. Notations are the same as the previous figures.

cFL immunoreactive neuron in MVN, which was a similar response in bilateral MVN. cFL protein was also expressed in superior and inferior vestibular nuclei after acute hypotension induced by SNP. Number of cFL immunoreactive neuron increased proportionately to a decrease of blood pressure. Also expression of cFL protein following hemorrhage was similar to the expression by SNP (Figs. 3, 4).

Responses following acute hypotension in UL animals

Electrical activity in ipsilateral MVN: lectrical activity of type I neurons ipsilateral to the lesion side at rest was 17.1±14.9 spikes/sec 14 days after UL, which was slightly lower compared to intact labyrinthine animals. Acute hypotension induced by SNP produced 3 patterns of response; inhibition in 80% of recorded neurons, excitation in 10%, and no response in 10%. This was the opposite of the response seen in intact labyrinthine animals. The activity of type II neurons ipsilateral to the lesion at rest was 25.2±24.6 spikes/sec 14 days after UL, which increased slightly comparing to the intact labyrinthine animals. Acute hypotension induced by SNP evoked excitation in 59% of recorded neurons, inhibition in 29%, and no response in 12% (Fig. 5, Table 1).

Electrical activity in contralateral MVN: The resting activity of type I neurons contralateral to the lesion side was 24.9±19.7 spikes/sec 14 days after UL, which implied vestibular compensation following UL. Acute hypotension induced by SNP evoked excitation in 72% of the recorded neurons, inhibition in 14%, and no response in 14%. The resting activity of type II neurons was 19.0±9.4 spikes/sec 14 days after UL. SNP-induced acute hypotension produced inhibition in 72% of recorded neurons and excitation or no response in the remainder of the neurons. The electrical activity of MVN neurons following acute hypotension induced by hemorrhage in UL animals was similar to the activity induced by SNP infusion (Fig. 6, Table 1).

cFL protein expression: Number of cFL immunoreactive neuron was 12.7±4.9 in ipsilateral MVN to the lesion side

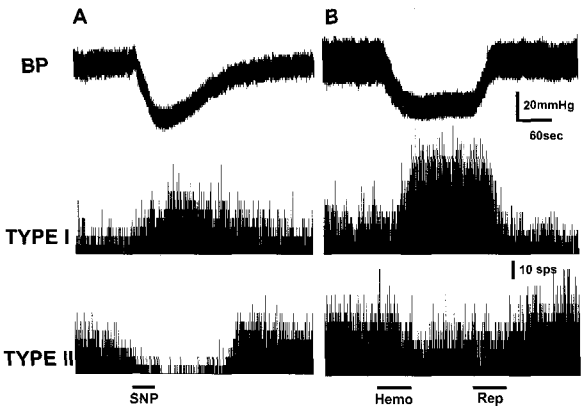

Fig. 6. Responses of type I and II neurons in right medial vestibular nuclei following acute hypotension induced by SNP (SNP) or hemorrhage (Hemo) in left unilateral labyrinthectomized animals. Notations are the same as the previous figures.

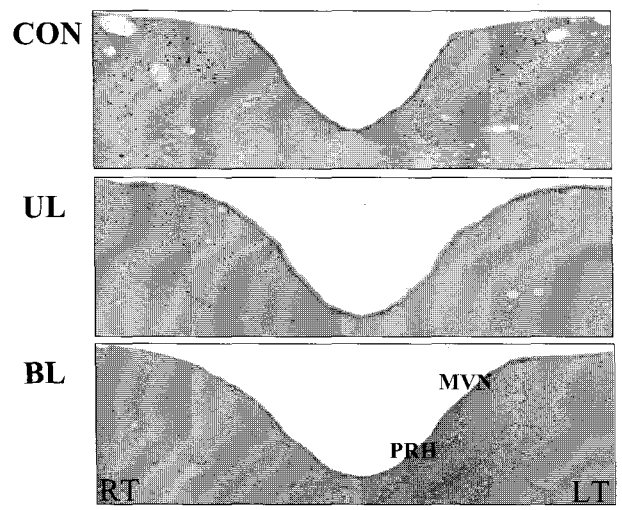

Fig. 7. Photomicrograhs showing effect of left unilateral (UL) and bilateral (BL) labyrinthectomy on cFL protein expression in medial vestibular nucleus (MVN) following 50% decrease in blood pressure by sodium nitroprusside. INTACT and LESION represent intact side and lesion side of peripheral vestibular receptors in UL animal, respectively. CON, control animal with intact labyrinths; PrH, prepositus hypoglossal nucleus; horizontal solid bar, 200 μm.

and 82.3±20.7 in contralateral MVN following SNP-induced acute hypotension 14 days after UL, which showed significantly asymmetric expression between bilateral MVN ($p < 0.01$). Acute hypotension induced by hemorrhage also produced more expression of cFL protein in contralateral MVN to the lesion side than in ipsilateral MVN. However, in bilateral labyrinthectomized animals, cFL protein was not expressed in bilateral MVN following acute hypotension (Figs. 7, 8).

DISCUSSION

The vestibular system controls posture and movement by

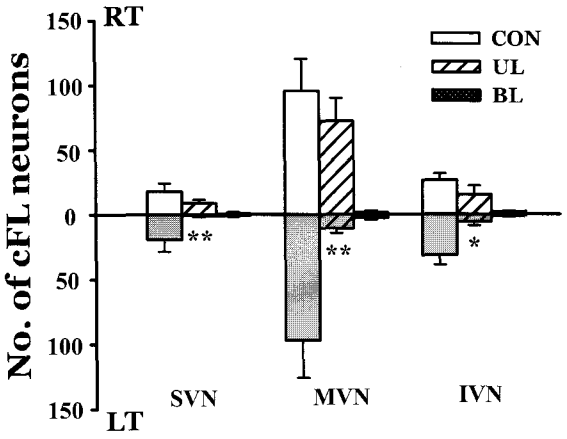

Fig. 8. Bar histographs showing changes in number of cFL protein expression in superior vestibular (SVN), medial vestibular (MVN), and inferior vestibular nuclei (IVN) of control (CON), unilateral labyrinthectomized (UL), and bilateral labyrinthectomized (BL) groups following 30% decrease in blood pressure by sodium nitroprusside. Left (LT) unilateral labyrinthectomy was performed in UL animals. *Denotes significant difference between RT (right, intact) and LT (left, lesion) of UL animals (*$p < 0.05$, **$p < 0.01$). Number of rats in each group is 7.

vestibuloocular and vestibulospinal reflexes as well as controls blood pressure, respiration and gastrointestinal motility by vestibuloautonomic reflex (Yates & Miller, 1998). The vestibuloautonomic reflex has been shown that the lateral and ventrolateral subnucleus of the nucleus tractus solitarius receives direct inputs from the vestibular nuclei. The nucleus tractus solitarius exerts an inhibitory influence on the rostroventrolateral medulla, which regulates sympathetic input to the heart, and therefore changes in the activity of vestibular nuclear neurons have the potential to modulate blood pressure and heart rate (Yates et al, 1995; Balaban, 1998; Biaggioni et al, 1998). Also other evidences indicate that the peripheral vestibular receptors modulate autonomic functions. Motion sickness induced by abnormal stimulation of the vestibular system can not be produced after loss of bilateral vestibular function (Kennedy et al, 1968). Orthostatic hypotension during postural changes persists for a long time following loss of bilateral vestibular function (Doba & Reis, 1974; Lee et al, 1998). Especially, cardiovascular patients resulting in decreased cardiac output complain of vertigo as one of subjective symptoms (Kapoor, 1987; Ohashi et al, 1990; Rea & Thamse, 1993). These results suggest that peripheral vestibular receptors might play an important role, not only to control posture and movement, but also to regulate blood pressure.

Forteen days after UL, electrical activity of type I neurons in ipsilateral MVN to the lesion side at rest decreased, and the activity of contralateral type I neurons increased compared with the activity prior to UL, and the activity of ipsilateral type II neurons increased and contralateral type II neurons decreased compared with the activity before UL (Smith & Curthoys, 1989; Park et al, 1999). But the electrical activity of type I and II neurons after 14 days of UL did not show any significant difference from the activity before UL. And the static vestibular symptoms disappeared 3~4 days after UL in rats (Kim et al, 1997).

Sodium nitroprusside (SNP) decreases blood pressure by

causing the release of nitric oxide (Hamaguchi et al, 1992). The decrease of blood pressure was proportional to the dose of SNP injected. SNP injection elicited excitation of type I neurons and inhibition of type II neurons in the bilateral MVN of intact labyrinthine animals. It was not clear whether the changes in neuronal activity in MVN following acute hypotension were due to the decreased blood flow to the peripheral vestibular receptors or by the direct action of nitric oxide released by SNP on the vestibular nuclear complex. However, acute hypotension induced by hemorrhage also produced a similar response to that induced by SNP injection in type I and II neurons of MVN, suggesting that it is unlikely to direct effect of nitric oxide on changing neuronal activity.

Blood flow in the brain is carefully controlled by autoregulation, even when nearly 50% of blood flow decreases (Bunemann et al, 1991; Hamaguchi et al, 1992). However, blood flow in the cochlea of the inner ear decreases proportionately to a decrease in the arterial blood pressure (Hasegawa et al, 1989; Preckel et al, 1995; Ueda & Matsunaga, 1995), which suggests that 10~30% decrease in arterial blood pressure does not change blood flow in the brain stem, although reduces the blood flow in peripheral vestibular receptors (Angelborg & Larsen, 1985). In this study, the neuronal activities that were evoked in MVN by a 30% decrease in blood pressure were similar to those induced by a 50% decrease.

The three different types of response patterns of electrical activity in MVN following acute hypotension might be due to the various characteristics of vestibular nuclear neurons (Wilson & Melvill Jones, 1979). In UL, the decreased neuronal activity in type I neurons of ipsilateral MVN to the lesion side following acute hypotension resulted from deprivation of afferent signals from ipsilateral peripheral vestibular receptors as well as inhibitory commissural connections from contralateral type I neurons. However, intact peripheral vestibular receptors produce excitatory signals by acute hypotension and excite ipsilateral type I neurons to the intact side, and subsequently, contralateral type II neurons and inhibitory interneurons to the intact side are excited through the commissural connections, which inhibit contralateral type I neurons to the intact side. Therefore, type I neurons are excited and type II neurons are inhibited following acute hypotension in intact labyrinthine animals, but ipsilateral type I and contralateral type II neurons to the lesion side are inhibited and contralateral type I and ipsilateral type II neurons are excited following acute hypotension in UL animals.

It is still not clear whether the peripheral vestibular receptors or the vestibular nuclear complex in the brain stem produces the changes in neuronal activity in MVN following acute hypotension. Inhibition of type I neurons ipsilateral to the lesion side and excitation of contralateral type I neurons following acute hypotension in UL animals indicate that the decreased blood flow activates the intact peripheral vestibular receptors but can not influence peripheral receptors in the injured vestibular system. These results suggest that the changes in neuronal activity in the vestibular nuclei following acute hypotension are caused by activation of the peripheral vestibular receptors rather than the vestibular nuclear complex in the brain stem.

Expression of cFL protein which is a neural marker (Morgan & Curran, 1991) increased proportionately to the decrease of blood pressure. Considering that expression of cFL protein is related to excitation of vestibular neurons (Kaufman et al, 1992), increased expression of cFL protein following acute hypotension represents excitation of vestibular neurons. Our previous study (Park et al, 1997) represented that expression of cFL protein just after UL showed asymmetry in bilateral MVN and the expression disappeared 3 days after UL. SNP-induced hypotension in intact labyrinthine rats produced marked expression of cFL protein in bilateral MVN. In UL animals, an increased expression of cFL protein in contralateral MVN to the lesion side was closely related to neuronal activity. Moreover, in bilateral labyrinthectomized animals, SNP- induced hypotension did not produce cFL protein expression in bilateral MVN. These results strongly suggest that peripheral vestibular receptors might be the main target organs responding to changes in blood pressure.

However, it is not clear how a decrease in blood flow causes activation of the peripheral vestibular receptors. One possible explanation is that the decreased blood flow to the inner ear produces an ischemic environment for the hair cells. The neurotransmitter glutamate has been implicated in acute excitotoxicity of the synapses between inner hair cells and radial auditory dendrites following cochlear ischemia (Pujol et al, 1993). It is tempting to speculate that expression of cFL protein in the vestibular nuclei would result partly from ischemic activation of the hair cells by reduction of blood flow in the inner ear following acute hypotension. However, functional changes in the central vestibular nuclei caused by the acute hypotension cannot be excluded, since the vestibular nuclei are in a region vulnerable to ischemia (Yamamoto et al, 1985).

Physiological significance of the peripheral vestibular receptors on blood pressure regulation might be a subsidiary organ to baroreceptors in the carotid sinus and aortic arch. The baroreceptors respond to minimal changes in blood pressure and their reaction time is very short (Guyton & Hill, 2000). However, the peripheral vestibular receptors may modulate blood pressure when blood flow is decreased in the vestibular system, although the receptors only respond to changes of more than 30% of blood pressure, and have a delayed response time because of complicated neural circuits. This assumption is based on that the blood flow to the vestibular system is easily affected by changes in systemic blood pressure (Preckel et al, 1995; Ueda & Matsunaga, 1995), and neural circuits from the vestibular nuclei to the rostroventrolateral medulla which controls sympathetic center were identified (Balaban, 1998; Biaggioni et al, 1998). Also, recovery of orthostatic hypotension is delayed following bilateral labyrinthectomy (Doba & Reis, 1974; Lee et al, 1998), and the expression of cFL protein in MVN following acute hypotension increases in intact labyrinthine animals. However, cFL is not expressed in bilateral labyrinthectomized animals. In summary, the peripheral vestibular receptors most likely control not only posture and movement by feedforward system, but also blood pressure by feedback system.

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