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Temporal Changes in Neuronal Activity of the Bilateral Medial Vestibular Nuclei Following Unilateral Labyrinthectomy in Rats

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To investigate the changes in the responses of vestibular neurons with time during vestibular compensation, the resting activity and dynamic responses of type I and II neurons in the medial vestibular nuclei to sinusoidal angular acceleration were recorded following unilateral labyrinthectomy (ULX) in Sprague-Dawley rats. The unitary extracellular neuronal activity was recorded from the bilateral medial vestibular nuclei with stainless steel microelectrodes of 3~5 MΩ before ULX, and 6, 24, 48, 72 hours, and 1 week after ULX under pentobarbital sodium anesthesia (30 mg/kg, i.p.). Gain (spikes/s/deg/s) and phase (in degrees) were determined from the neuronal activity induced by sinusoidal head rotation with 0.05, 0.1, 0.2, and 0.4 Hz. The mean resting activity before ULX was 16.7±8.6 spikes/s in type I neurons (n=67, M±SD) and 14.5±8.4 spikes/s in type II neurons (n=43). The activities of ipsilateral type I and contralateral type II neurons to the lesion side decreased markedly till 24 hr post-op, and a significant difference between ipsilateral and contralateral type I neurons sustained till 24 hr post-op. The gain at 4 different frequencies of sinusoidal rotation was depressed in all neurons till 6 or 24 hr post-op and then increased with time. The rate of decrease in gain was more prominent in ipsilateral type I and contralateral type II neurons immediately after ULX. Although the gain of those neurons increased gradually after 24 hours, it remained below normal levels. The phase was significantly advanced in all neurons following ULX. These results suggest that a depression of activities in ipsilateral type I and contralateral type II neurons is closely related with the occurrence of vestibular symptoms and restoration of activities in those neurons ameliorates the vestibular symptoms.

Key Words: Vestibular compensation, Neuronal activity, MVN, Unilateral labyrinthectomy

INTRODUCTION

The peripheral vestibular receptors in the inner ear transduce acceleration of the head, and initiate the vestibuloocular and vestibulospinal reflexes (Wilson & Melvill Jones, 1979b). Following loss of unilateral vestibular function, the vestibuloocular and vestibulospinal reflexes are severely impaired and vestibular symptoms including nausea, vomiting, dizziness, spontaneous nystagmus and postural disturbance are resulted in. These symptoms can be classified into two categories on the basis of their relationship to head movement: static symptoms, such as deviation of the eyes and head toward the lesion side and spontaneous nystagmus which persists in the absence of head movement; dynamic symptoms, such as a reduced amplitude and abnormal timing (gain and phase) of the vestibuloocular and vestibulospinal reflexes occurring in response to head movement (Fisch, 1973; Curthoys et al, 1988).

Many of these oculomotor and postural symptoms disappear over time in the process of behavioral recovery known as vestibular compensation. This re-

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covery process is particularly striking in the case of static symptoms, which in many species disappear within a few days of unilateral labyrinthectomy (Precht et al, 1966; Schaefer & Meyer, 1974; Precht & Dieringer, 1985; Park et al, 1995, 1997a). Since the peripheral vestibular receptor cells do not regenerate once removed and neurons in Scarpa's ganglion do not undergo any substantial functional recovery (Jensen, 1983; Sirkin et al, 1984), vestibular compensation is assumed to be due to central nervous system (CNS) plasticity and is widely used as a model of lesion-induced CNS plasticity (Lacour et al, 1989).

On the basis of electrophysiological studies, vestibular symptoms result from the loss of vestibular input to the vestibular nuclei ipsilateral to the lesion, causing a large decrease in resting activity in these neurons (Smith & Curthoys, 1989; Curthoys & Halmagyi, 1995). However, over time, resting activity partially recovers in the ipsilateral vestibular nuclei, producing a vestibular compensation (Curthoys & Halmagyi, 1995). Recovery of the resting activity in the ipsilateral vestibular nuclei is considered as resulting from disinhibition of the ipsilateral vestibular nuclei through commissural connections from the contralateral vestibular nuclei (Precht et al, 1966), somatosensory inputs from the neck and other peripheral portion (Petrosini & Troiani, 1979; Park et al, 1995), and intrinsic properties of the vestibular nuclei (Darlington & Smith, 1996). Also, cerebellar efferent signals inhibit the resting activity in contralateral vestibular nuclei (McCabe & Ryu, 1969; McCabe et al, 1972; Kim et al, 1997a, b; Kitahara et al, 1997), number of somal spine and synaptic profile increase in ipsilateral vestibular nuclei (Guyot et al, 1995; Gacek & Schoonmaker, 1997; Gacek et al, 1998), and changes on responses to cholinergic and GABAnergic neurotransmitters are maintained for a long time (Bienhold & Flohr, 1980; Magnusson et al, 1998).

It is assumed that vestibular compensation is due to the restoration of neuronal activity in the ipsilateral vestibular nuclei to the lesion side, leading to the reestablishment of bilateral symmetry in the resting neuronal activity (Precht et al, 1966; Smith & Curthoys, 1988a, b). Smith & Curthoys (1988a, b) reported that resting activity of type I neurons in contralateral medial vestibular nucleus (MVN) in guinea pigs increased and the activity in ipsilateral MVN decreased compared with normal level immediately after ULX, and the activity in bilateral MVN returned to normal level by 60 hr post-op. However, Newlands & Perachio (1990a, b) reported that recovery of vestibular symptom did not correspond to recovery of neuronal activity. Resting activity of type I neurons in ipsilateral MVN in gerbils decreased significantly immediately after ULX and the activity did not return to normal level by 4~7 months. Also the activity of type II neurons did not change significantly after ULX. In addition to the resting activity, several reports on dynamic activity in MVN by sinusoidal rotation showed different results (Smith & Curthoys, 1988a, b; Newlands & Perachio, 1990a, b). The discrepancies in neuronal activity after ULX may be attributed to the differences in the species of experimental animal and methods.

The present study was designed to provide a more complete picture of the neuronal changes occurred in the bilateral MVN during vestibular compensation. The response of type I and type II neurons in the bilateral MVN of rats to horizontal sinusoidal angular acceleration was quantified over time which coincided with major behavioral changes observed during vestibular compensation which have been quantified in our previous studies of the same species (Kim et al, 1997a, b; Park et al, 1997a, b).

METHODS

Materials

Sixty-seven Sprague-Dawley rats weighing 250~300 g were used in this experiment. The vestibular function was examined by rotatory test to select an intact labyrinthine animal (Park & Park, 1988). They were divided into two groups, control group with intact labyrinth and unilateral labyrinthectomy group.

Labyrinthectomy

Animals were anesthetized with chloral hydrate (100 mg/kg, i.p.) and ossicular bones in the left middle ear cavity were removed to open the oval window through ventral approach under a surgical microscope. Then, a small opening was made around oval window using small dental burr. Through these openings, membranous labyrinth was destroyed surgically with a small right-angled hook and aspirated with suction pump. ULX was confirmed with appearance of spontaneous nystagmus and postural asymmetry after recovery from anesthetic condition. In order to prevent

from post-operative infection, lesioned vestibular portion was applied with an antibiotic ointment, sealed with dental cement, and also ampicillin (20 mg/kg) was injected intramuscularly for 3 days.

Sinusoidal rotation of the vestibular system

The animals were secured with a head holder in a stereotaxic device (David Kopf, U.S.A.), mounted on a servo-controlled turntable. The head was centered over the axis of rotation with nose pitched 30° down to bring the horizontal semicircular canals close to the horizontal plane of rotation. The animal's body was supported by a soft plate. This plate contained a heating element which maintained the animal's body temperature at 37°C. The turntable was driven by DC servo-motor (400 W, LG Co). Rotatory range of the turntable was 180°, and maximum angular velocities were 55°/sec at 0.05 Hz, 110°/sec at 0.1 Hz, 220°/sec at 0.2 Hz, and 440°/sec at 0.4 Hz. Artificial respiration was achieved using a ventilator (Phipps & Bird, U.S.A.).

Electrophysiological recordings

Portions of the occipital bone and dura mater were removed under pentobarbital sodium (30 mg/kg, i.p.) anesthesia. Total number of recorded units was 660. Unitary extracellular neuronal activity was recorded through stainless steel microelectrode (A & M Co, U.S.A.) with impedance of 2~5 MΩ. The electrodes were placed by stereotaxic coordinates (Paxinos & Watson, 1986) and advanced with micromanipulator (Narishige, Japan) through the intact cerebellum into MVN. Attempts were made to sample neurons throughout the entire MVN using multiple penetrations per animal. Signals were amplified and displayed on an oscilloscope (Tektronix 5113, U.S.A.), and idealized spikes identified by real time waveform discriminator (SPS-8701, Australia) were fed into data acquisition system (CED 1401, U.K.) for analysis. At the end of each successful recording, recording site was marked by lesion with DC current (0.3 mA, 30 sec). After finishing recording session, the animal was given an overdose of urethan, the brain was removed, fixed by immersion in a phosphate-buffered 10% formalin solution, sectioned with a freezing microtome into 60~100 μm thick slices and stained with cresyl violet. Recording sites referenced to the dye spots were confirmed by an image analyzer system (Media Cybernetics, U.S.A.).

Data analysis

Resting activity was defined as firing rate (spikes/sec) over a 60-second period in the absence of horizontal rotation. Average firing rate was calculated by Spike 2 (CED Ltd, U.K.). For the measurement of gain and phase of response to horizontal sinusoidal acceleration, the averaged cycle histogram of the response and the stimulus in 5~10 cycles were separately subjected to a non-linear curve fitting routine to compute the least-squares fit of a sinusoid. Gain was computed as peak to peak firing divided by peak to peak velocity and expressed as impulses/s per deg/s. Phase difference between the maximum stimulus input and the maximum response output was

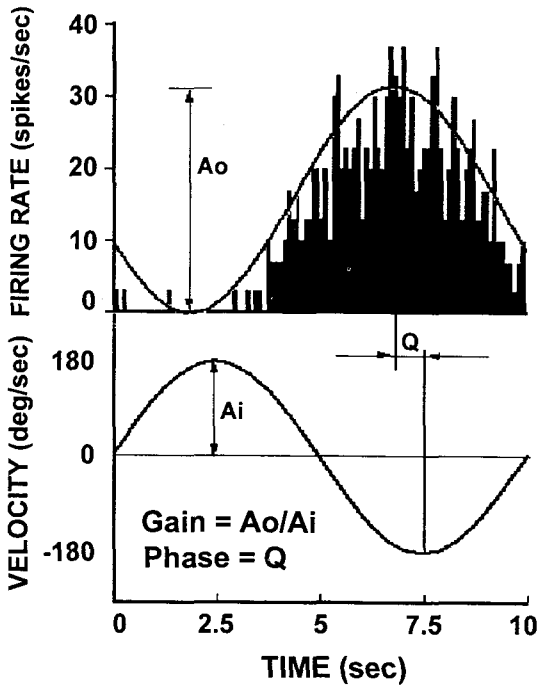

Fig. 1. Analysis of unitary dynamic response in the vestibular neuron to sinusoidal rotation. The unitary response was fitted by least square method (upper pannel) and the velocity of rotation was represented as degree/sec (lower pannel). The gain of the unit response was expressed as the ratio of peak firing rate (Ao) to peak angular velocity (Ai). The phase of the unit response (Q) was defined as the difference in degrees between peak angular velocity and peak firing rate. Positive (+) and negative (−) values of the phase represent phase lead and phase lag, respectively.

determined using a cross-spectral analysis routine and expressed as degree. In phase difference, positive value representing phase lead indicates that the time of maximal response is faster than the time of maximal stimulus, and negative value representing phase lag does faster in the time of maximal stimulus (Fig. 1).

Statistical analysis

All data were represented as mean ± SD. The statistical significance of differences was assessed using Kruskal-Wallis and Mann-Whitney U tests. $p<0.05$ was considered significant.

RESULTS

Resting activity in MVN

In order to classify the type of neurons, the animal on turntable was 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 fashion (Fig. 2). In intact labyrinthine animals (control), the mean resting activity was 16.7±8.6 spikes/sec in type I neurons and the larger number of neurons was recorded in type I neurons than in type II (Table 1). In ULX, mean resting activity of ipsilateral type I neurons was 8.6±6.4 spikes/sec at 6 hr post-op, which showed significant difference from the control ($p<0.05$). Decreased resting activity in ipsilateral type I neurons was persisted to 24 hr post-op and increased gradually to approximately normal levels at 1 wk post-op. The activity of contralateral type I neurons was 13.5±10.0 spikes/sec at 6 hr post-op and decreased activities were maintained till 24 hr post-op. The activity of ipsilateral type I neurons showed significant decrease compared with contralateral type I neurons till 24 hr post-op ($p<0.01$).

In type II neurons, mean resting activity of the animals with an intact labyrinth was 14.5±8.4 spikes/sec. The resting activity was decreased significantly in contralateral ones ($p<0.05$), whereas in ipsilateral ones it did not change significantly after ULX. The pattern of resting activity in bilateral type II neurons was inversely related to that in type I neurons, ipsilateral type II neurons had a higher activity than contralateral ones (Fig. 3).

The number of neurons recorded in MVN increased with time after ULX. The average number of type I neurons recorded was more in contralateral MVN than in ipsilateral one, and type II neurons were more in ipsilateral MVN (Table 1).

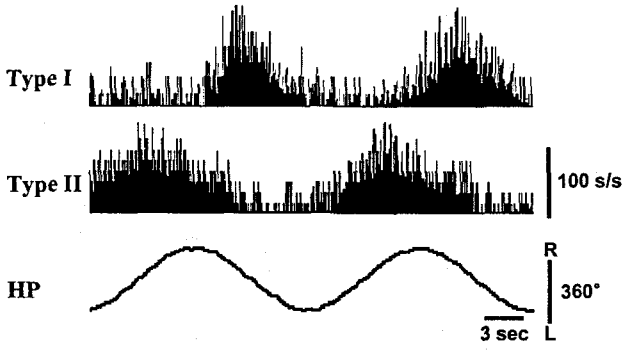

Fig. 2. Typical response of type I and type II neurons in the left medial vestibular nuclei. Type I neuron was activated by rotation toward ipsilateral (left) and inhibited by contralateral (right), while type II neuron was activated by rotation toward contralateral (right) and inhibited by ipsilateral (left). The lowest pannel shows position curve of rotation (HP), in which upward deflection represents rightward rotation (R) and downward represents leftward rotation (L).

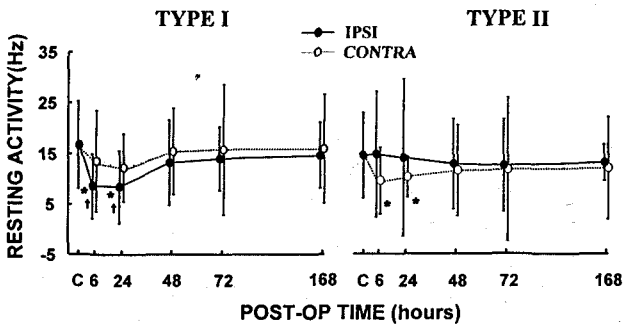

Fig. 3. Changes of resting activity in type I and II neurons of the medial vestibular nuclei following unilateral labyrinthectomy. IPSI, ipsilateral to the lesioned vestibular system; CONTRA, contralateral to the lesioned side; C, resting activity before labyrinthectomy (control group). *denotes significant difference between control and labyrinthectomy groups (*$p<0.05$, **$p<0.01$). †denotes significant difference between ipsilateral and contralateral neurons ($^{\dagger}p<0.05$, $^{\ddagger}p<0.01$). Values are means ± SD.

Dynamic responses of type I neurons

In animals with an intact labyrinth, gain was 0.42±0.12 at 0.05 Hz, 0.26±0.04 at 0.1 Hz, 0.24±0.05 at 0.2 Hz, and 0.22±0.12 at 0.4 Hz, which represented that neuronal activity was increased by increasing stimulus velocity. Phase difference was 26.4±19.6° at 0.05 Hz, 12.8±8.6° at 0.1 Hz, −9.0±12.7° at 0.2 Hz, and −17.6±7.5° at 0.4 Hz, which indicated that phase lag was increased by increasing stimulus velocity.

Table 1. The number of neurons recorded in the control and unilateral labyrinthectomized rats

	Type I neuron		Type II neuron	
	Ipsi	Contra	Ipsi	Contra
Control (9)	67		43	
6 hr post-op (15)	36	96	44	12
24 hr post-op (13)	42	43	17	12
48 hr post-op (11)	38	22	16	21
72 hr post-op (11)	19	35	30	16
1 wk post-op (8)	17	16	9	9

Number of parentheses represents the number of animals. Ipsi, ipsilateral MVN to labyrinthectomy; Contra, contralateral MVN to labyrinthectomy.

At 6 hr post-op, gain in ipsilateral MVN was 0.19±0.09 at 0.05 Hz, 0.13±0.05 at 0.1 Hz, 0.09±0.02 at 0.2 Hz, and 0.06±0.05 at 0.4 Hz, which was decreased by more than 50% of control. And phase difference in ipsilateral MVN was 32.0±13.4° at 0.05 Hz, 25.3±15.8° at 0.1 Hz, 14.1±10.7° at 0.2 Hz, and 4.8±30.0° at 0.4 Hz, which showed phase lead at all frequencies of stimulus. Gain in contralateral MVN was 0.36±0.09 at 0.05 Hz, 0.24±0.06 at 0.1 Hz, 0.18±0.03 at 0.2 Hz, and 0.13±0.03 at 0.4 Hz, which was significantly decreased compared with the control. In comparison of gain in bilateral MVN, severe asymmetry was resulted from significant decrease in gain of ipsilateral MVN. And phase difference in contralateral MVN was 37.0±17.8° at 0.05 Hz, 26.5±11.0° at 0.1 Hz, 15.1±7.8° at 0.2 Hz, and 8.0±8.9° at 0.4 Hz.

At 24 hr post-op, gain in ipsilateral MVN was decreased significantly compared with the control. Also phase difference showed more phase lead than the control. Contralateral MVN showed the lowest gain at all frequencies of stimulus, however, the gain was significantly higher than ipsilateral MVN, which re-

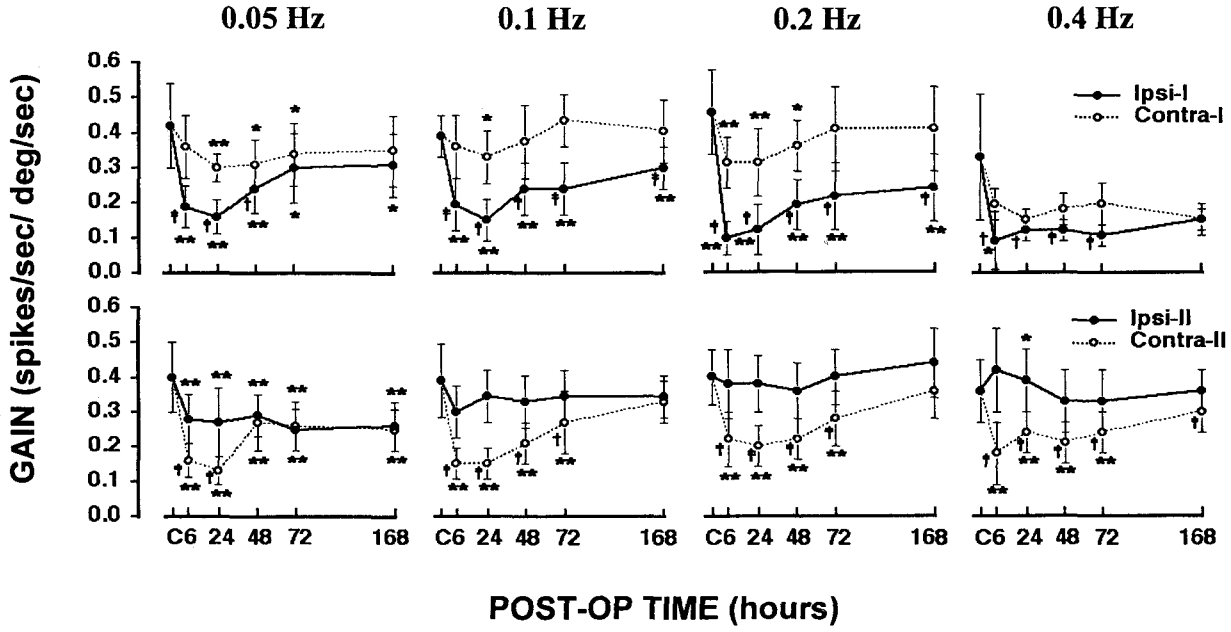

Fig. 4. Dynamic response of gain in type I and II neurons of the medial vestibular nuclei by sinusoidal rotation at 0.05, 0.1, 0.2, and 0.4 Hz following unilateral labyrinthectomy. Upper pannel shows the responses of bilateral type I neurons and lower one shows the responses of bilateral type II neurons. Other notations are as in Fig. 3.

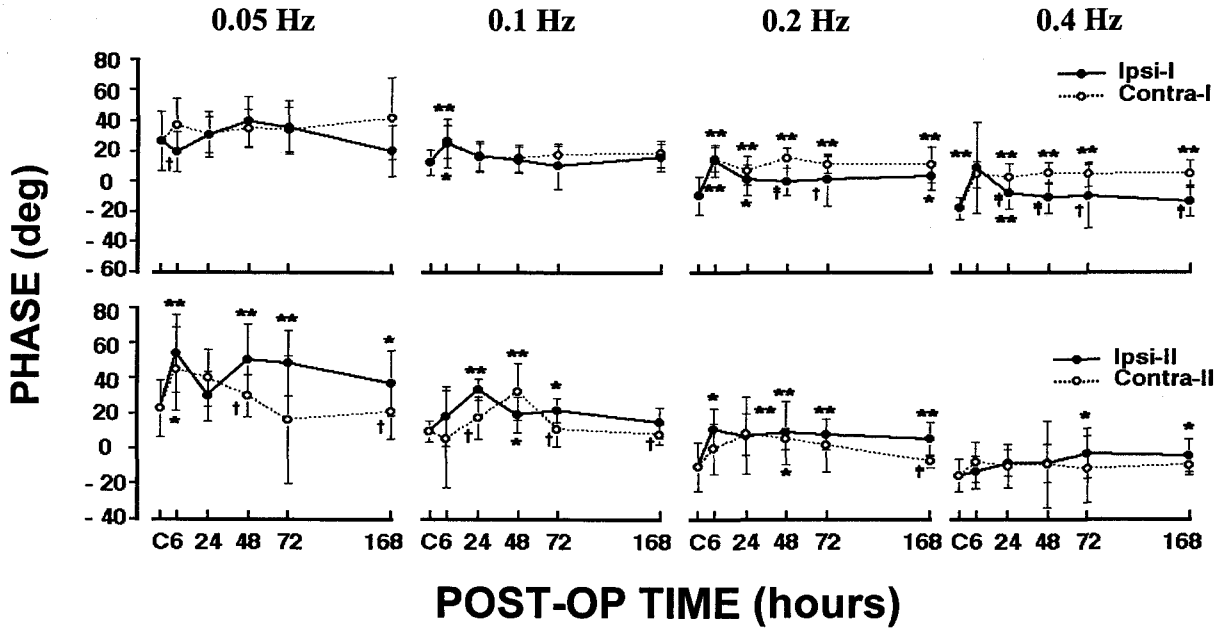

Fig. 5. Dynamic response of phase in type I and II neurons of the medial vestibular nuclei by sinusoidal rotation at 0.05, 0.1, 0.2, and 0.4 Hz following unilateral labyrinthectomy. Upper pannel shows the responses of bilateral type I neurons and lower one shows the responses of bilateral type II neurons. Positive and negative values represent phase lead and phase lag, respectively. Other notations are as in Fig. 3.

sulted in maintenance of asymmetry of gain in bilateral MVN. And phase lead was sustained at all frequencies of stimulus.

After 24 hr of ULX, though the gain in ipsilateral MVN increased gradually with time, asymmetry of gain in bilateral MVN was sustained till 48 hr post-op at all frequencies of stimulus. The asymmetry recovered after 72 hr post-op at all frequencies of stimulus. Phase difference was not recovered till 1 wk post-op and phase lead was continued (Figs. 4, 5).

Dynamic responses of type II neurons

In control, gain was 0.40 ± 0.09 at 0.05 Hz, 0.26 ± 0.07 at 0.1 Hz, 0.20 ± 0.04 at 0.2 Hz, and 0.12 ± 0.03 at 0.4 Hz, which was slightly lower than in type I neurons. And phase difference was $22.8\pm16.2^{\circ}$ at 0.05 Hz, $9.7\pm5.9^{\circ}$ at 0.1 Hz, $-9.8\pm13.8^{\circ}$ at 0.2 Hz, and $-15.3\pm9.4^{\circ}$ at 0.4 Hz, which was similar to type I neurons.

At 6 hr post-op, gain was 0.28 ± 0.07, 0.20 ± 0.05, 0.19 ± 0.05, 0.11 ± 0.04 at 0.05, 0.1, 0.2, 0.4 Hz, respectively, in ipsilateral MVN, and 0.16 ± 0.05, 0.10 ± 0.03, 0.11 ± 0.04, 0.06 ± 0.03 at 0.05, 0.1, 0.2, 0.4 Hz, respectively, in contralateral MVN. Ipsilateral MVN had higher gain than contralateral MVN, which was in inverse manner to type I neurons. And phase difference in ipsilateral MVN was $45.0\pm23.7^{\circ}$, $20.0\pm27.7^{\circ}$, $0.2\pm14.6^{\circ}$, $13.3\pm11.3^{\circ}$ at 0.05, 0.1, 0.2, 0.4 Hz, respectively, and that of contralateral MVN was $53.8\pm22.1^{\circ}$, $18.4\pm16.9^{\circ}$, $11.2\pm11.5^{\circ}$, $7.8\pm9.2^{\circ}$ at 0.05, 0.1, 0.2, 0.4 Hz, respectively. There was no significant difference in phase between bilateral MVN. Asymmetry of gain in bilateral MVN resulting from decreased activity in contralateral MVN was sustained till 48 hr post-op. Gain at 0.05 Hz in contralateral MVN did not recover to normal level till 72 hr post-op (Figs. 4, 5).

DISCUSSION

Vestibular compensation is known to be the restoration of neuronal activity in bilateral vestibular nuclear complex following unilateral loss of vestibular function (Precht et al, 1966; Smith & Curthoys, 1988a, b; Newlands & Perachio, 1990a, b). A number of studies have demonstrated that electrical activity of type I neurons in ipsilateral MVN to ULX is almost absent due to loss of primary afferent input from peripheral receptors and increased commissural inhibition (Precht et al, 1966; Ried et al, 1984). In the

contralateral MVN, type I neurons exhibit an increased activity because they are released from commissural inhibition (Smith & Curthoys, 1988a). With compensation, resting activity of type I neurons in bilateral MVN has been shown to return towards the control level in some studies (Smith & Curthoys, 1988a, b). Restoration of the resting activity in ipsilateral MVN is attributed to either extravestibular afferent signals (Pukonen et al, 1977; Park et al, 1995), intrinsic properties of ipsilateral MVN (Darlington & Smith, 1996), or a reduction in commissural inhibition (Fetter & Zee, 1988). In contralateral type I neurons, some reports suggested that the resting activity is reduced by commissural inhibition resulting from the recovery of ipsilateral type I neuronal activity (Yagi & Markham, 1984; Smith & Curthoys, 1988b). The net result is the restoration of symmetry in bilateral resting activity, which is believed to account for the recovery of static vestibular symptoms (Schaefer & Meyer, 1973; Yagi & Markham, 1984).

Our results support the assertion that ULX reduces the activity in ipsilateral type I neurons, while the activity in contralateral type I neurons is not affected significantly (Precht, 1986; Newlands & Perachio, 1990a). In the present data, the resting activity of contralateral type I neurons as well as ipsilateral type I neurons was decreased following ULX, which is assumed to be the effect of extravestibular afferent inputs or intrinsic properties of the vestibular nuclei. This assumption is based on the immunohistochemical studies. c-Fos protein is more expressed in the contralateral MVN than in the ipsilateral MVN immediately after ULX, but the pattern of c-Fos protein expression is reversed after 6 hs of ULX (Kim et al, 1997b; Park et al, 1997b).

The resting activity of type II neurons was slightly increased in ipsilateral MVN and significantly decreased in contralateral MVN at early stage of compensation, which corresponded to other studies (Smith & Curthoys, 1988a, b; Newlands & Perachio, 1990b). The number of type II neurons recorded was two-thirds of type I neurons, which was similar to reports from Melvill Jones & Millsum (1971) and Newlands & Perachio (1990a, b). The number of contralateral type I and ipsilateral type II neurons increased with time after ULX. Increase in the number of neurons recorded may also closely related with recovery of vestibular symptoms.

However, the number of resting activity in labyrinthine intact animal showed some difference in several reports. Ried et al (1984) reported that resting activity was 22.4 ± 14.0 spikes/sec in type I neurons and 27.5 ± 14.6 spikes/sec in type II neurons in ketamine anesthetized cats. Smith & Curthoys (1988a, b) observed 10.9 ± 16.5 spikes/sec in type I neurons and 5.9 ± 8.7 spikes/sec in type II neurons in pentobarbital sodium anesthetized guinea pigs. Newlands & Perachio (1990a, b) reported 39.0 ± 28.3 spikes/ sec in type I neurons and 32.3 ± 31.5 spikes/sec in type II neurons in decerebrated gerbils. And the present study in pentobarbital sodium anesthetized rats showed 16.7 ± 8.6 spikes/s in type I neurons and 14.5 ± 8.4 spikes/sec in type II neurons. These different findings are probably due to different animal species, methods, and anesthetics. Especially, the activity of type I neurons is strongly affected by anesthesia, since ipsilateral type I neurons receive afferent inputs via polysynapse following ULX (Precht & Shimazu, 1965; Shimazu & Precht, 1966). Considering the above results, it is not so easy to obtain a constant result by electrophysiological technique.

In labyrinthine intact animal, excitation of unilateral type I neurons by ipsilateral rotation excites contralateral type II neurons and inhibits ipsilateral type II neurons by commissural connection. This commissural effect causes summation of excitation in ipsilateral type I neurons to the side of rotation. But rotation directed toward lesion side following ULX causes inhibition of contralateral type I neurons and excitation of ipsilateral type II neurons since ipsilateral peripheral receptors can not respond to rotation and only contralateral receptors can respond. And rotation directed toward intact side can not summate excitation in contralateral type I neurons because of absence of commissural inhibition. Considering the above assumption, it is reasonable that gain of both type I and II neurons in bilateral vestibular nuclei decreased till 48 hr post-op, and contralateral type I neuron and ipsilateral type II neurons showed higher gain than ipsilateral type I neuron and contralateral type II neurons, respectively, in this study. These results correspond with reduction of spontaneous nystagmus by rotation toward lesion side and enhancement of the nystagmus by rotation toward intact side (Park et al, 1995), reduction of sensitivity of bilateral type I neurons in unilateral 3-canal plugging (Abend, 1978), and decreased resting activity in ipsilateral vestibular neurons by making a small hole on ampullary portion of horizontal canal in cats (Ezure et al, 1983).

Gain representing degree of response in vestibular neurons is calculated from maximum neuronal activity divided by maximum velocity of rotation (Wilson & Melvill Jones, 1979a). Newlands & Perachio (1990a, b) demonstrated that gain increased by increasing frequency of rotation in labyrinthine intact animals, but increasing frequency of rotation induced reduction of gain in this study. The difference in gain is explained by different method of rotation. We modulated frequency of rotation at constant range of rotation, while other studies modulated frequency at constant maximum velocity of rotation. Severe asymmetry of gain in bilateral type I and II neurons decreased after 48 hr post-op, which was corresponded to the time of disappearance of spontaneous nystagmus following ULX (Park et al, 1997a). Incomplete restoration of gain may support that the dynamic vestibular symptoms sustained after 1 week post-op.

Phase representing the temporal difference between transmitting time from peripheral receptors to vestibular nuclei and stimulation time by rotation depends on time needed for signal transduction in peripheral receptors and synaptic transmission in vestibular nuclei (Wilson & Melvill Jones, 1979b). Phase lag increased by increasing rotatory velocity, which means that phase mainly relates with stimulus velocity in labyrinthine intact animals. Increased phase lead immediately after ULX resulted from the response of only contralateral peripheral receptors to the lesion side because of interruption of afferent signals from ipsilateral receptors. Decreasing phase lead with time after ULX may relate with recovery of neuronal activities by increased synaptic formation in contralateral vestibular nuclei. However, phase difference did not show any consistent response compared with gain in this study. These results corresponded with other studies (Smith & Curthoys, 1988a, b; Newlands & Perachio, 1990a, b). Slower recovery of phase than gain is related with that regeneration of peripheral cilia is more important than CNS plasticity during vestibular compensation in chicken (Carey et al, 1996).

Considering the results obtained in this study, restoration of resting activity in bilateral MVN corresponds to disappearance of spontaneous nystagmus following ULX. Recovery of static vestibular symptoms does not simply depend on resting activity, but other components may be involved. Incomplete restoration of resting activity as well as gain and phase by sinusoidal rotation till 1 wk post-op represents that dynamic vestibular symptoms sustain for long period.

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REFERENCES

Abend WK. Response to constant angular acceleration of neurons in the monkey superior vestibular nucleus. *Exp Brain Res* 31: 459−473, 1978

Bienhold H, Flohr H. Role of cholinergic synapses in vestibular compensation. *Brain Res* 195: 476−478, 1980

Carey JP, Fuchs AF, Rubel EW. Hair cell regeneration and recovery of the vestibuloocular reflex in the avian vestibular system. *J Neurophysiol* 76: 3301−3312, 1996

Curthoys IS, Halmagyi GM. Vestibular compensation: a review of the oculomotor, neural and clinical consequences of unilateral vestibular loss. *J Ves Res* 5: 67−107, 1995

Curthoys IS, Smith PF, Darlington CL. Postural compensation in the guinea pig following unilateral labyrinthectomy. *Prog Brain Res* 76: 375−384, 1988

Darlington CL, Smith PF. The recovery of static vestibular function following vestibular lesions in mammals: The intrinsic mechanism hypothesis. *J Vest Res* 6: 185−201, 1996

Ezure E, Cohen MS, Wilson VJ. Response of cat semicircular canal afferents to sinusoidal polarizing currents: Implications for input-output properties of second-order neurons. *J Neurophysiol* 49: 639−648, 1983

Fetter MTC, Zee DS. Recovery from unilateral labyrinthectomy in rhesus monkey. *J Neurophysiol* 59: 370−393, 1988

Fisch U. The vestibular response following unilateral vestibular neurectomy. *Acta Otolaryngol* 76: 229−238, 1973

Gacek RR, Khetarpal U, Schoonmaker JE. Morphological and neurochemical correlates of vestibular compensation. *Auris Nasus Larynx* 25: 193−201, 1998

Gacek RR, Schoonmaker JE. Transneuronal down regulation of vestibulo-ocular neurons following vestibular ablation. *Acta Otolaryngol (Stockh)* 117: 810−814, 1997

Guyot JP, Lyon MJ, Gacek RR, Magnin C. Ultrastructural changes in superior vestibular commissural neurons following vestibular neurectomy in the cat. *Ann Otol Rhinol Laryngol* 104: 381−387, 1995

Jensen DW. Survival of function in the deafferented vestibular nerve. *Brain Res* 273: 175−178, 1983

Kim MS, Jin BK, Chun SW, Lee MY, Lee SH, Kim JH, Park BR. Role of vestibulocerebellar N-methyl-D aspartate receptors for behavioral recovery following unilateral labyrinthectomy in rats. *Neurosci Lett* 222: 171−174, 1997a

Kim MS, Jin BK, Chun SW, Lee MY, Lee SH, Kim JH, Park BR. Effect of MK801 on c-Fos like protein expression in the medial vestibular nucleus at early stage of vestibular compensation in uvulonodullectomized rats. *Neurosci Lett* 231: 147−150, 1997b

Kitahara T, Takeda N, Kubo T, Kiyama H. Role of the flocculus in the development of vestibular compensation: immunohistochemical studies with retrograde tracing and flocculectomy using Fos expression as a marker in the rat brainstem. *Neuroscience* 76: 571−580, 1997

Lacour M, Toupet M, Denise P, Christen Y. Vestibular compensation: Facts, theories, and clinical perspectives. Elsevier, Paris, 1989

Magnusson AK, Eriksson B, Tham R. Effects of the GABA agonists baclofen and THIP on long-term compensation in hemilabyrinthectomised rats. *Brain Res* 795: 307−311, 1998

McCabe BF, Ryu JH. Experiments of vestibular compensation. *Laryngoscope* 79: 1728−36, 1969

McCabe BF, Ryu JH, Sekitani T. Further experiments on vestibular compensation. *Laryngoscope* 82: 381−396, 1972

Melvill Jones G, Milsum JH. Frequency response analysis of central vestibular unit activity resulting from rotational stimulation of the semicircular canals. *J Physiol* 219: 191−215, 1971

Newlands SD, Perachio AA. Compensation of horizontal canal related activity in the medial vestibular nucleus following unilateral labyrinth ablation in the decerebrate gerbil. Type I neurons. *Exp Brain Res* 82: 359−372, 1990a

Newlands SD, Perachio AA. Compensation of horizontal canal related activity in the medial vestibular nucleus following unilateral labyrinth ablation in the decerebrate gerbil. Type II neurons. *Exp Brain Res* 82: 373−383, 1990b

Park BR, Doh NY, Kim MS, Chun SW, Lee MY, Lee SH. Correlation between electrical activity of type I neuron and c-Fos expression in the medial vestibular nuclei follwoing unilateral labyrinthectomy in rats. *Korean J Physiol Pharmacol* 1: 505−513, 1997a

Park BR, Hwang HR, Lee MY, Kim MS. Effect of electrical stimulation of the vestibular system on vestibuloocular reflex and c-Fos expression in the medial vestibular nuclei of unilateral labyrinthectomized rats. *Korean J Physiol Pharmacol* 1: 275−284, 1997b

Park BR, Park HA. A study of the sinusoidal head rotator. *Chonnam Med J* 25: 25−30, 1988

Park BR, Suh JS, Kim MS, Jeong JY, Chun SW, Lee JH. Effect of sensory deprivation or electrical stimulation on acute vestibular symptoms following unilateral labyrinthectomy in rabbits. *Acta Otolaryngol Suppl* 519: 162−167, 1995

Paxinos G, Watson C. The rat brain in stereotaxic coordinates. Academic Press, London, 1986

Petrosini L, Troiani D. Vestibular compensation after hemilabyrinthectomy: effects of trigeminal neurotomy. *Physiol Behav* 22: 133−137, 1979

Precht W. Recovery of some vestibuloocular and vestibulospinal functions following unilateral labyrinthectomy. *Progr Brain Res* 64: 381−389, 1986

Precht W, Dieringer N. Neuronal events paralleling functional recovery (compensation) following vestibular lesions. In: Berthoz A, Melvill Jones G ed, Adaptive mechanisms in gaze control. Elsevier, Amsterdam, p 251−268, 1985

Precht W, Shimazu H, Markham CH. A mechanism of central compensation of vestibular function following hemilabyrinthectomy. *J Neurophysiol* 29: 996−1009, 1966

Precht W, Shimazu H. Functional connections of tonic and kinetic vestibular neurons with primary vestibular afferents. *J Neurophysiol* 28: 1014−1028, 1965

Pukonen PT, Courjon JH, Jeannerod M. Compensation of postural effects of hemilabyrinthectomy in the cat. A sensory substitution process? *Exp Brain Res* 28: 249−257, 1977

Ried S, Maioli C, Precht W. Vestibular nuclear neuron activity in chronically labyrinthectomized cats. *Acta Otolaryngol* 98: 1−13, 1984

Schaefer KP, Meyer DL. Compensation of vestibular lesions. In: Handbook of sensory physiology, edited by HH Kornhuber. Springer, Berlin, p 463−490, 1974

Schaefer KP, Meyer DL. Compensation mechanisms following labyrinthine lesions in the guinea pig: a simple model of learning. In: Memory and transfer of information, edited by H Zippel. Plenum Press: New York, London, p 203−232, 1973

Shimazu H, Precht W. Inhibition of central vestibular neurons from the contralateral labyrinth and its mediating pathway. *J Neurophysiol* 29: 467−492, 1966

Sirkin DW, Precht W, Courjon JH. Initial, rapid phase of recovery from unilateral vestibular lesion in rat not dependent on survival of central portion of vestibular nerve. *Brain Res* 302: 245−256, 1984

Smith PF, Curthoys IS. Neuronal activity in the contralateral medial vestibular nucleus of the guinea pig following unilateral labyrinthectomy. *Brain Res* 444: 295−307, 1988a

Smith PF, Curthoys IS. Neuronal activity in the ipsilateral

medial vestibular nucleus of the guinea pig following unilateral labyrinthectomy. *Brain Res* 444: 308−319, 1988b

Smith PF, Curthoys IS. Mechanisms of recovery following unilateral labyrinthectomy: a review. *Brain Res Rev* 14: 155−180, 1989

Wilson VJ, Melvill Jones G. Mammalian vestibular physiology. Plenum Press, New York, p 15, 1979a

Wilson VJ, Melvill Jones G. Mammalian Vestibular physiology. New York: Prenum Press, p 77−123, 1979b

Yagi T, Markham CH. Neural correlates of compensation after hemilabyrinthectomy. *Exp Neurol* 84: 98−108, 1984