TABLE 2. AMPLITUDES OF CM, SP, AND AP

	CM Amplitude			*SP Amplitude*			*AP Amplitude*		
	Amplitude	*Stat Signif*		*Amplitude*	*Stat Signif*		*Amplitude*	*Stat Signif*	
Group	*(μV)*	*(1)*	*(2)*	*(μV)*	*(1)*	*(2)*	*(μV)*	*(1)*	*(2)*
ALHL (n = 20)	8.1 ± 5.4 (n = 15)	NS		1.8 ± 1.1	NS		5.5 ± 2.9	NS	
MD1 (n = 15)	5.8 ± 3.1 (n = 11)	NS	NS	1.6 ± 0.8	NS	NS	4.4 ± 2.1	$p < .01$	NS
MD2 (n = 11)	5.8 ± 5.3	NS	NS	1.5 ± 0.6	NS	NS	3.3 ± 1.5	$p < .01$	$p < .05$
MD3 (n = 27)	5.7 ± 4.7 (n = 26)	NS	NS	1.7 ± 1.0	NS	NS	3.2 ± 2.0	$p < .01$	$p < .01$
MD4 (n = 5)	8.1 ± 8.4	NS	NS	1.9 ± 2.0 (n = 4)	NS	NS	3.9 ± 4.6 (n = 4)	NS	NS
Controls (n = 29)	5.9 ± 3.1			1.7 ± 0.9			6.7 ± 3.1		

Stimulus intensity was 90 dB normal hearing level. All values are means ± SD.

CM — cochlear microphonics; SP — summating potential; AP — action potential; Stat Signif — statistical significance, (1) — patient groups versus controls; (2) — Meniere's disease groups (MD1, etc) versus group with acute low-tone sensorineural hearing loss (ALHL); NS — no statistical significance.

The bandpass filters were set to be flat from 320 to 1,500 Hz for measuring 1-kHz CM, and from 50 to 3,000 Hz for measuring SP and AP. The CM amplitudes (in microvolts) were measured peak-to-peak; the AP amplitudes were measured from the baseline to the maximum negative deflection of the N1 peak; and the SP amplitudes were measured from the baseline to the notch on the descending limb of the N1. We also used the lowest intensities to determine the CM detection thresholds. A change in potential of 0.2 μV or more was deemed to be a response.

The SP and AP amplitudes were measured at a stimulus intensity of 90 dB nHL in all patients, although AP detection thresholds were assessed in only 18 of the 20 patients with ALHL and 56 of the 58 patients with MD. The CM measurements were carried out in 15 patients with ALHL and 53 patients with MD. The CM input-output curves were divided into 3 types: type 1 had normal slopes, amplitudes, and detection thresholds; type 2 had steep slopes and high detection thresholds; and type 3 had low-amplitude voltage or normal slopes and high detection thresholds. We compared each ECochG parameter in the ALHL and MD groups, as well as in 29 healthy ears that served as controls. All statistical comparisons were made with the Mann-Whitney U test.

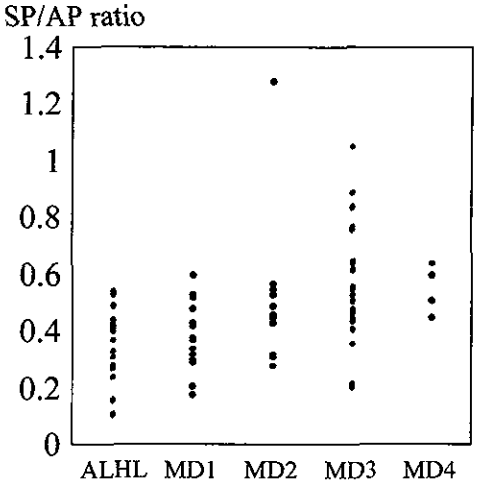

Fig 2. Distribution of summating potential–action potential (SP/AP) ratios. Mean SP/AP ratios of all patient groups were significantly higher than that of control group ($p < .01$). Note similar SP/AP ratios in ALHL and MD1 groups.

RESULTS

CM, SP, and AP Amplitudes. The CM, SP, and AP amplitudes elicited at a stimulus intensity of 90 dB nHL are shown in Table 2. One patient in the MD4 group with no SP or AP was excluded. The CM and SP amplitudes in the ALHL and MD4 groups tended to be larger than those in the control group, but the difference was not significant, nor was there a significant difference between the ALHL and MD groups. The AP amplitudes in all patient groups tended to be smaller than those in the control group, but the difference was only significant for the MD1, MD2, and MD3 groups. In addition, the AP amplitudes in the MD2 and MD3 groups were significantly smaller than those in the ALHL group.

SP/AP Ratios. Figure 2 shows the distribution of SP/AP ratios in each patient group. The mean values ± SD of the SP/AP ratios in the ALHL, MD1, MD2, MD3, and MD4 groups were 0.35 ± 0.13, 0.37 ± 0.13, 0.52 ± 0.27, 0.55 ± 0.19, and 0.55 ± 0.09, respectively, which were all significantly greater than the control value ($p < .01$). The SP/AP ratios in the MD2, MD3, and MD4 groups were also larger than those

TABLE 3. CM AND AP DETECTION THRESHOLDS

	CM Detection Threshold			AP Detection Threshold		
		Stat Signif			Stat Signif	
Group	Threshold (dB HL)	(1)	(2)	Threshold (dB HL)	(1)	(2)
ALHL (n = 20)	32.0 ± 9.4 (n = 15)	p < .01		27.2 ± 10.2 (n = 18)	p < .01	
MD1 (n = 15)	30.9 ± 10.4 (n = 11)	p < .01	NS	27.1 ± 9.1 (n = 14)	p < .01	NS
MD2 (n = 11)	41.8 ± 10.8	p < .01	NS	41.8 ± 16.6	p < .01	p < .01
MD3 (n = 27)	55.4 ± 10.3 (n = 26)	p < .01	p < .01	60.0 ± 13.0 (n = 26)	p < .01	p < .01
MD4 (n = 5)	68.0 ± 14.83	p < .01	p < .01	84.0 ± 11.4 (n = 4)	p < .01	p < .01
Controls (n = 29)	16.2 ± 4.9			11.7 ± 5.4		

All values are means ± SD.

in the ALHL and MD1 groups, which exhibited similar SP/AP ratios, but the difference was only significant for the MD3 ($p < .01$) and MD4 ($p < .05$) groups. When the normal range of SP/AP ratios was defined as being smaller than 0.4 (mean + 2 SD of the control group), 10 of the 20 ALHL patients (50.0%), 6 of the 15 MD1 patients (40.0%), 8 of the 11 MD2 patients (72.7%), 23 of the 27 MD3 patients (85.2%), and all 4 of the MD4 patients (100.0%) showed abnormal SP/AP ratios. Note that among the MD groups, the incidence of abnormal SP/AP ratios increased as the stage was downgraded.

CM and AP Detection Thresholds. Table 3 shows that the CM and AP detection thresholds were significantly higher than the control values in all patient groups and were similar in the ALHL and MD1 groups. Among all patient groups, the CM and AP detection thresholds increased as the stage was downgraded.

CM Input-Output Curves. Figure 3 shows the 1-kHz CM input-output curves for each patient in each group. Of the 15 ALHL patients tested, 8 (53.3%) were classified as type 1, and the other 7 as type 2 or 3. Of the 11 MD1 patients tested, 6 (54.5%) were classified as having type 1 input-output curves, and the other 5 as having type 2 or 3 curves. Note that the percentages of patients categorized as having type 1 curves were similar in the ALHL and MD1 groups, and that the numbers of patients categorized as having type 1 curves declined as the stage was downgraded.

DISCUSSION

A substantial amount of clinical evidence suggests that increases in SP amplitudes and SP/AP ratios reflect specific abnormalities associated with MD and ELH[14,15] and result from displacement of the basilar membrane toward the scala tympani due to the abnormal endolymphatic pressure.[16] Nevertheless, whereas some authors report the usefulness of measuring SP amplitudes,[17] others have found that the SP amplitudes in patients with MD are the same as or smaller than those in healthy ears.[18] This discrepancy likely reflects the large variability in absolute SP amplitudes, which has led to the clinical application of ECochG for monitoring MD and ELH to be focused on the SP/AP ratio.[19,20] In the present study, we found that among patients the SP/AP ratios, but not the absolute SP amplitudes, were significantly larger than control values, and that SP/AP ratios and the incidence of abnormal SP/AP ratios both increased as hearing loss became more profound — findings that are consistent with earlier reports.[8,21,22] Moreover, our finding that SP/AP ratios are elevated in ears with ALHL is consistent with the findings of Yamasoba et al[3,5] and implies that ELH may cause ALHL.

The use of CM amplitude to monitor MD is also controversial. Kumagami et al[8] reported that the CM amplitude is enlarged in patients with early-stage MD, at a time when hearing loss is still reversible. Similarly, Ge and Shea[22] reported that the CM amplitude is larger in patients with MD than in patients without MD, and that the CM amplitude is increased in 69% of ears with MD with hearing loss greater than 40 dB. In contrast, Fetterman[23] reported that the CM amplitudes tended to be smaller in ears with ELH than in those without ELH. In our study, the ALHL and MD4 patients exhibited CM amplitudes that were larger than control values, but no significant change was found among the other patients. It is thus difficult to evaluate MD with only CM amplitude. On the other hand, the AP amplitudes were significantly diminished in many patients, contributing to the significant increase in SP/AP ratios.

The CM and AP detection thresholds and input-output curves are more stable and reliable parameters than are absolute amplitudes.[24] The comparatively low CM and AP detection thresholds in the ALHL and MD1 groups implied only slight cochlear impairment. Among the four MD groups, the CM and AP detection thresholds increased as hearing ability diminished, reflecting the increased impairment of the cochlear hair cells. We divided the CM input-output curve into 3 types. Ears with type 1 curves were considered to have nearly normal cochlear hair cells, whereas those with type 2 or 3 curves appeared to

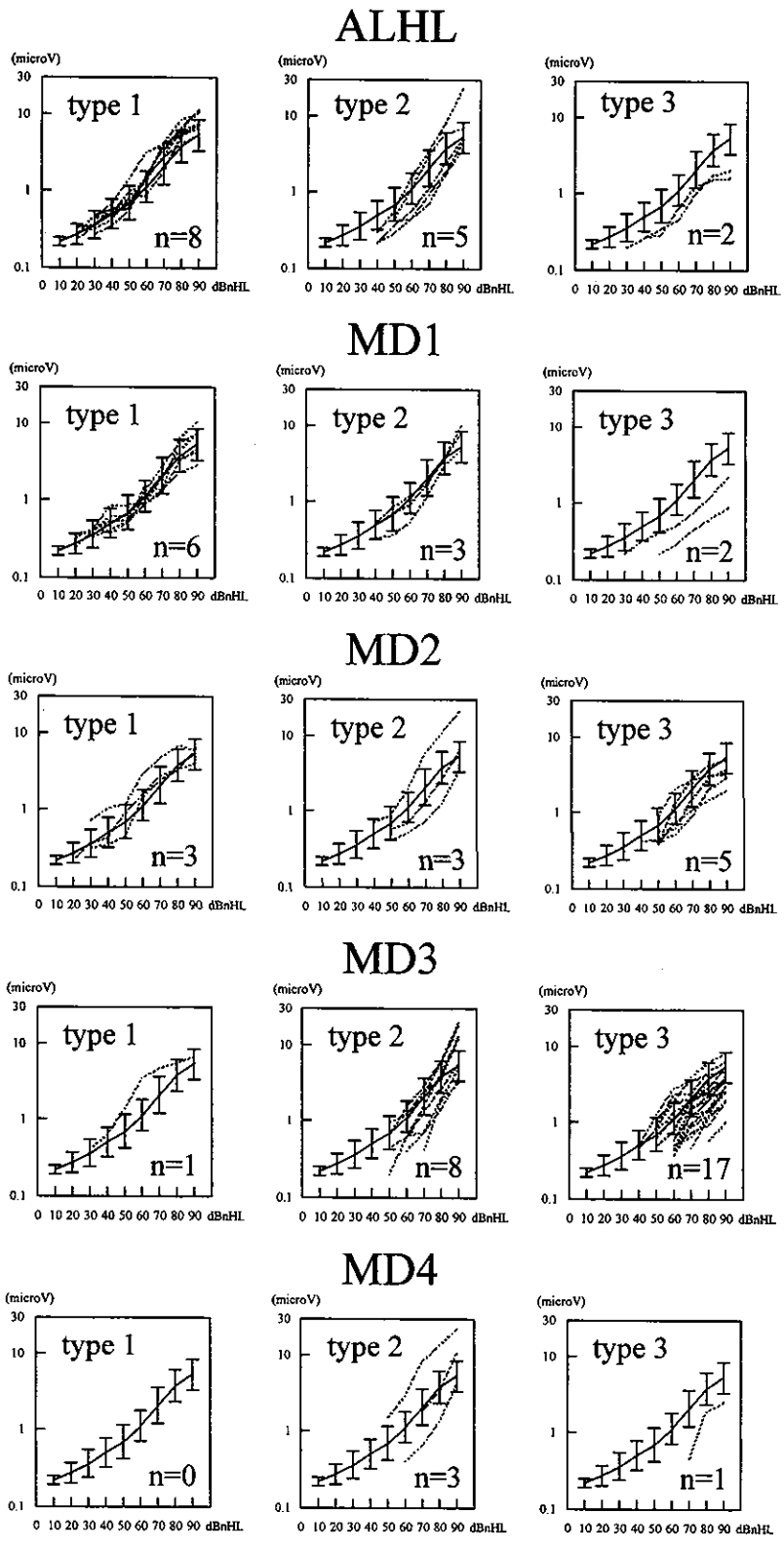

Fig 3. One-kilohertz cochlear microphonic input-output curves (dotted lines) for each patient group. Curves are divided into 3 types as described in text.

have various degrees of cochlear impairment. Furthermore, the steep slope and high detection threshold in the CM input-output curve indicate the existence of the recruitment phenomenon,[11] which corresponds to the H-curve in the AP input-output curve.[25]

In sum, our evaluation of the CM input-output curve indicates that more than half of the patients with ALHL or MD1 had normal cochlear hair cells.

In the present study, ALHL patients exhibited SP/

AP ratios, CM and AP detection thresholds, and CM input-output curves that were similar to those seen in MD1 patients, suggesting a similarity in the pathogenesis of ALHL and early-stage MD. Moreover, the fact that the CM detection threshold and input-output curve showed little or no impairment of the cochlear hair cells of ALHL patients suggests that the source of pathogenesis of ALHL is ELH.

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Acta Otolaryngol 2003; 123: 355–361

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Photochemically Induced Double Lateral Wall Lesions in the Guinea Pig Cochlea

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Takeshita T, Iwasaki S, Nagura M, Watanabe T, Umemura K, Hoshino T. *Photochemically induced double lateral wall lesions in the guinea pig cochlea*. Acta Otolaryngol 2003; 123: 355–361.

Objective—Multiple patches of atrophy have been reported in the stria vascularis (SV) in elderly persons with presbycusis. The aim of this study was to investigate the correlation between sensorineural hearing loss and this strial condition.
Material and Methods—We established a new animal model comprising two small lesions in the SV in the second turn of the cochlea by means of photochemical reaction. Using this model, we investigated morphological and physiological changes in the cochlea at 3, 7 and 14 days after SV damage.
Results—Scanning electron microscopy studies revealed that the strial cells between the two damaged areas of the SV remained intact, although the outer hair cells (OHCs) facing the intact SV area were damaged. Furthermore, damage to the first and second rows of OHCs gradually progressed throughout the 14-day observation period. The endocochlear potential (EP) measured at a point midway between the 2 lesions at 3 and 7 days was found to be significantly lower compared with control values, but had returned to a normal level at 14 days.
Conclusion—The reversible EP change and localized OHC loss seen in the present investigation may help to understand acute idiopathic or progressive sensorineural hearing loss. *Key words: endocochlear potential loss, multiple stria vascularis lesions, scanning electron microscopy, sensorineural hearing loss*

INTRODUCTION

Microcirculation disorders of the cochlea are thought to be one of the causes of sensorineural hearing loss (1). In order to understand the relationship between such circulation disorders and hearing loss, we previously established a model of microvascular disorder induced by photochemical reaction using intravascular Rose Bengal (RB) dye and a 1-mm focused green light in the guinea pig cochlea. Changes resulting from these focal lesions were investigated histologically and physiologically (2–6). In early investigations, illumination perpendicular to the lateral wall of the cochlea resulted in severe damage, not only to the stria vascularis (SV), but also to the inner and outer hair cells 3 days after photochemical reaction. The endocochlear potential (EP) dropped from a preoperative value of 80 mV to 21.7 mV after 3 days. However, after 2 weeks it was found to have returned to pre-illumination levels, although SV and hair cell damage remained (7). In this model, because the illuminating beam struck the lateral wall, organ of Corti and modiolus, both inner and outer hair cells were directly affected by the photochemical reaction. Ocho et al. (8) devised another model in which the illuminating light was directed tangentially to the lateral wall. With this method of illumination, damage was limited to the SV and outer hair cells (OHCs), and did not extend to the inner hair cells (IHCs).

When the temporal bones of elderly persons are examined, strial degeneration usually occurs in multiple patches in persons with flat-type sensorineural hearing loss (9). In order to clarify the relationship between this finding and hearing loss, it is helpful to examine the pathophysiological state of multiple strial lesions.

In the present study, two lesions were induced in the SV at the second turn of the guinea pig cochlea using photochemical reaction, and morphological and concomitant EP changes were examined.

MATERIAL AND METHODS

Animal preparation

Forty-eight healthy male albino guinea pigs weighing 300–400 g with normal Preyer's reflexes were used in this study. Twenty-four animals underwent EP measurements. The animals were anesthetized with an i.p. injection of 35 mg/kg pentobarbital. A catheter was inserted into the left cervical vein in order to administer RB (Wako, Osaka, Japan). Body temperature was maintained at 37.0±0.5°C using a thermostatically controlled heating blanket. The head was fixed in a head-holder, and the tympanic bulla of the left temporal bone was opened using a ventral approach without disturbing the tympanic membrane or ossicles. All animal care and experimental procedures employed in this study were approved by the Animal Welfare Committee of the Hamamatsu University School of Medicine.

Photochemical induction of microvascular injury

A 1-mm wide slip of black paper was placed over a portion of the second turn of the exposed cochlea to prevent illumination. RB was dissolved in physiological saline (20 mg/ml) and injected through the catheter over a period of 10 s.

 ISSN 0001-6489

DOI 10.1080.00016480210000028131

The source of illumination was a 75 W xenon lamp (L-3306-01A; Hamamatsu Photonics, Hamamatsu, Japan). After passing through a heat-absorbing green filter, 1-mm focused green light was conducted to the cochlea by means of a 3-mm diameter fiber optic rod, the tip of which was fixed ≈15 mm from the cochlear wall. The green light was a 54-nm wide band centered at 540 nm, and its intensity as it exited the rod was ≈ 8,000 lux.

The light beam was directed perpendicular to the cochlear wall. Illumination of the portion of the cochlea apical to the black paper slip began simultaneously with RB injection and continued for 10 min. Immediately following this, the portion basal to the black paper was also illuminated for 10 min.

Physiological saline injection without RB and subsequent green light illumination were performed in the same manner in control animals ($n = 4$).

EP measurement

In 15 experimental ears, surgical wounds were closed after the completion of illumination and the animals were returned to their cages. Wounds were reopened for EP measurement after 3 ($n = 5$), 7 ($n = 5$) and 14 days ($n = 5$).

Anesthetized guinea pigs were paralyzed with an i.m. injection of succinylcholine chloride (15 mg/kg). A tracheotomy was performed and ventilation was maintained with a respirator (Mass 0253; Medway, USA). Using a fine needle, a small hole (≈50–100 μm) was made in the cochlear bony wall for EP measurement. Measurements were made using a glass microelectrode filled with a 150 mM KCl solution. The tip diameter was ≈2 μm, and the tip resistance was <150 MΩ. The silver chloride wire within the microelectrode was connected to a microelectrode amplifier (MEZ-8300; Nihon Kohden, Japan). The reference electrode was placed in contact with the exposed neck muscle. EP measurements were performed at a point in the unilluminated portion of the cochlea midway between the two illuminated spots on the second turn. Readings were first adjusted to 0 mV with the microelectrode tip placed in contact with the exposed outer surface of the spiral ligament. Next, with the aid of a three-axial micromanipulator, the microelectrode was gently advanced through the hole in the bony wall into the scala media, passing through the spiral ligament and the SV. Potentials at the electrode tip were displayed continuously, as a function of time, on a chart recorder (MEB-5100; Nihon Kohden).

EP measurements were similarly performed in 9 control ears [illumination with saline injection, 3 ($n = 3$), 7 ($n = 3$) and 14 days ($n = 3$)]. During the EP measurement, anoxia was induced by stopping the respirator for 2 min after attaining a constant EP value in order to ascertain the reversibility of a transient decline in EP due to anoxia. EP values of experimental animals were statistically compared with control values using unpaired t-tests.

Morphological study

Scanning electron microscopy. For the scanning electron microscopy (SEM) study, 16 animals were decapitated at 3 ($n = 5$), 7 ($n = 5$), 14 ($n = 5$) and 28 days ($n = 1$) after photochemical treatment, whilst 4 control animals were processed at 14 days after saline injection and illumination. Similarly, all animals that underwent EP measurement were also examined using SEM. Left temporal bones were dissected out and the cochleae were perfused with 2.5% glutaraldehyde in a 0.1 M phosphate buffer (pH 7.4). Cochleae were then immersed in the same fixative overnight. The bony cochlear wall was removed and the membranous labyrinth dissected. Specimens were treated in a 2% tannic acid solution for 2 h and then post-fixed in 1% buffered osmium tetroxide solution for 1 h. They were then dehydrated through a graded ethanol series, immersed in methyl propanol, freeze-dried (JFD-300; JEOL, Tokyo, Japan), coated with gold in a sputter coater (JFC-1100; JEOL) and examined with a scanning electron microscope (Hitachi S-800, Japan).

Diaminobenzidine staining. Four animals were examined using diaminobenzidine (DAB) staining at 14 ($n = 2$) and 28 days ($n = 2$) after photochemical treatment. The left temporal bone was dissected out and perfused with 2.5% glutaraldehyde in a 0.1 M phosphate buffer (pH 7.4). The cochlea was then immersed in the same fixative for 1 h. The fixative was then rinsed from the perilymphatic scalae with phosphate-buffered saline (PBS) and the cochlea immersed in a 3, 3′-diaminobenzidine–peroxidase substrate medium for 1 h. During this time the perilymphatic scalae were perfused several times with the same solution to allow better reaction of endogenous peroxidase in the red blood cells. The cochleae were then rinsed with PBS and microdissected to remove the lateral wall of the second cochlear turn. The specimens were put in glycerol and mounted on glass slides with the endolymphatic surface facing upwards. Mounted specimens were observed using a light microscope.

Sensory cell counts. Sensory cell counts were performed using SEM images of the unilluminated region between the two lesions. The number of hair cells in three OHC rows and one IHC row were counted for each unit of 10 inner pillar cells (IPCs). About 6–8 OHCs and 5 or 6 IHCs per row are usually present in this portion of the second turn of a normal cochlea. Hair cell numbers in experimental animals were

statistically compared with those in control animals using a one-way ANOVA. For the evaluation of significant differences, the Bonferroni/Dunn type of multiple comparison was used. Data are presented as means and standard deviations.

RESULTS

SEM examination of 4 control specimens at 14 days after photochemical treatment revealed no damage to the SV and no decrease in the number of hair cells. In contrast, two damaged spots nearly 1 mm in diameter were observed at the illuminated site of the SV in all treated animals. Marginal cells appeared normal in the unilluminated area between the two lesions (Fig. 1*A* and *B*). No damage was found in either the epithelial cells of the SV or the sensory or supporting cells of the organ of Corti at off-lesion sites apical and basal to the lesions in all animals.

The width of the space between the two illuminated areas of the SV was 840 ± 190, 900 ± 120 and 890 ± 110 μm at Days 3, 7 and 14, respectively and these differences were not statistically significant.

Both OHCs and IHCs showed marked damage in the organ of Corti facing the SV lesions. At Day 3 the area between the lesions showed a slight decrease in the number of OHCs compared to the off-lesion sites. IHCs were intact in this area (Fig. 1*C*). The number of OHCs was not significantly reduced at Day 3. At Days 7, 14 and 28, however, the number of damaged OHCs was markedly increased, especially in the first and second rows. The cuticular plates of the OHCs disappeared and were replaced by the surrounding supporting cell surface. OHC damage was seen to progress slowly (Fig. 2*A*–*D*). The IHCs did not show any changes, in spite of marked damage to the OHCs, for up to 28 days.

DAB staining revealed that the strial vascular supply to the lesion had completely disappeared, whilst the vascular pattern between the two illuminated areas appeared intact (Fig. 3).

In the region between the two lesions, the numbers of OHCs in the first and second rows were significantly decreased compared to control values at Days 7 and 14 ($p < 0.001$) (Table I). Also, the numbers of OHCs in the first and second rows were significantly decreased compared to the number in the third row ($p < 0.001$) at Day 14 (Fig. 4).

EP values are shown in Table II. Average EP values for control animals were 83.0 ± 2.0, 79.7 ± 1.5 and 74.7 ± 5.9 mV at Days 3 ($n = 3$), 7 ($n = 3$) and 14 ($n = 3$), respectively. Average EP values for treated animals were 17.4 ± 7.0, 19.0 ± 6.6 and 80.0 ± 7.1 mV at Days 3

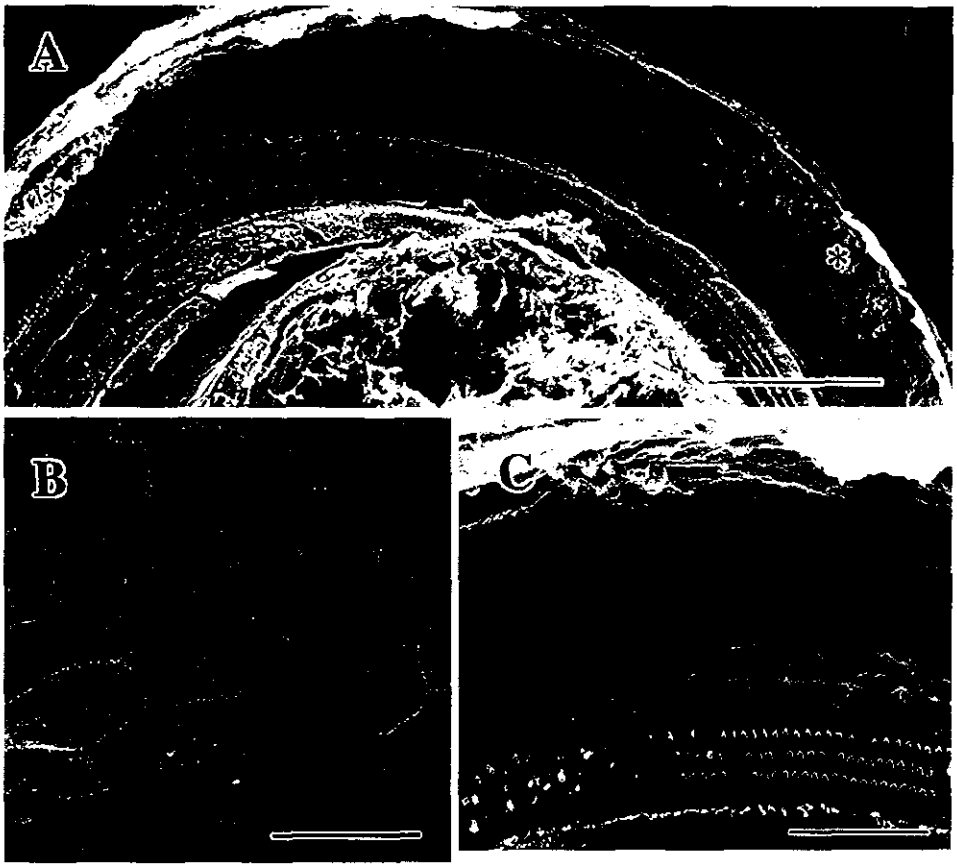

Fig. 1. SEM view of the second turn of the cochlea with two SV lesions at 3 days. (*A*) Two lesions (*asterisks*) are seen ≈1 mm apart. *Bar* = 300 μm. (*B*) Strial marginal cells in the region between the two lesions. *Bar* = 12 μm. (*C*) Magnified view of the left lesion in (*A*). *Bar* = 100 μm.

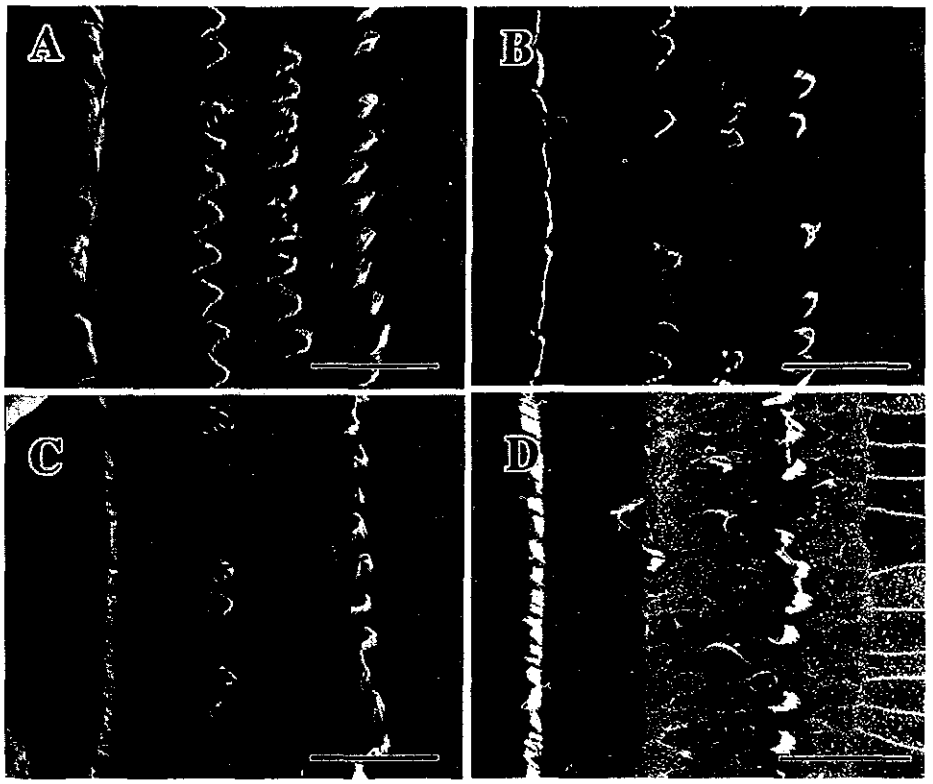

Fig. 2. OHCs and IHCs located between the two SV lesions. OHCs in the first and second rows progressively disappeared between Days 3 (*A*) and 28 (*D*). IHCs remained intact. (*B*) 7-day specimen. (*C*) 14-day specimen. *Bars* = 25 μm.

($n = 5$), 7 ($n = 5$) and 14 ($n = 5$), respectively. There were significant declines compared to control values ($p < 0.001$) at Days 3 and 7; however, there was no significant decline at Day 14. Fig. 5 shows two SV lesions ≈ 1 mm apart with the electrode insertion hole used for EP measurement between them.

DISCUSSION

In the present study two ischemic SV lesions were produced in the same cochlear turn by photochemical reaction without surgical or heat damage. In our previous studies (4, 10), focal lesions produced by photochemical reaction proved to be segmentally avascular. In the present study, double lesions showed similar avascular changes, although the area between the two lesions was normally vascularized, as shown by DAB staining. This segmental vascular distribution of the lateral wall probably results from the unique structure of the radiating arteriole system of the cochlea. In this model, not only the OHCs and IHCs facing the lesions, but also the OHCs facing the region between the two lesions, were damaged. Moreover, disappearance of the OHCs facing the region between the two lesions was more prominent in the first and second rows. OHC loss in this region progressed more slowly than that in the ischemic lesions.

Hakuba et al. (11) reported that a 5-min occlusion of the vertebral artery in gerbils caused hair cell degeneration mainly in the IHCs. In the present study,

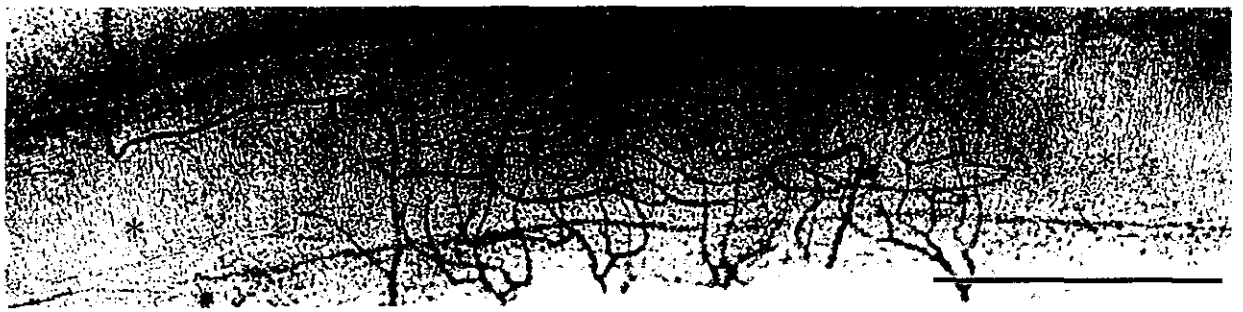

Fig. 3. Capillaries of the cochlear lateral wall stained with DAB in 14-day specimens. The vascular pattern of the SV between the two illuminated areas appears normal, but all vascular supply has disappeared to the illuminated areas (*asterisks*). *Bar* = 500 μm.

Table I. *Numbers of hair cells (mean±SD) per 10 IPCs in controls and experimental animals*

Type of hair cells	Controls	Experimental animals		
		3 days	7 days	14 days
IHCs	5.4±0.1	5.2±0.3	5.2±0.6	5.4±0.3
OHCs				
Third row	6.7±0.3	4.8±1.9	4.8±1.7	5.5±0.5
Second row	6.7±0.2	4.4±1.5	2.0±2.2*	2.3±1.4*
First row	6.8±0.2	4.9±0.6	2.6±1.8*	2.7±1.5*

* $p < 0.001$ vs controls.

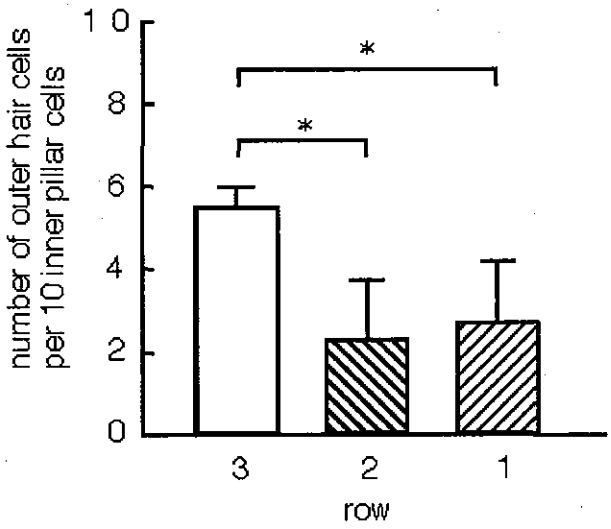

Fig. 4. Average numbers of OHCs facing the area between the two SV lesions at 14 days. The numbers of OHCs in the first and second rows were significantly reduced compared with that in the third row. *$p < 0.001$.

IHCs facing the unilluminated region between the two lesions were almost totally intact, so it would not appear that severe ischemia occurred in the modiolar area of this region. Thus, circulation disorder is probably not the cause of OHC loss. Could it instead be the decline in EP values that caused hair cell damage?

The administration of loop diuretics such as ethacrynic acid is known to decrease the potassium concentration of the endolymph, resulting in a decrease in the EP. Acute ototoxicity induced by ethacrynic acid has been reported to cause the collapse and splaying of OHC stereocilia (12) and the loss of cross-links between stereocilia (13); however, no investigators have observed the disappearance of the OHCs seen in the present study. Pratt and Comis (14) observed the effects of chronic administration of loop diuretics to guinea pig cochlea. They reported that changes occurred mainly in the organ of Corti, as opposed to the SV, without mentioning the details of such changes. Matz et al. (15) reported extensive OHC loss in the basal turn of the cochlea in a patient treated with a loop diuretic. However, this patient was concomitantly administered an aminoglycoside antibiotic, so in this case OHC damage might have been caused by a synergistic effect.

Why does degeneration of OHCs occur between the lesions? One possibility is the effect of excessive glutamic acid in the perilymph, as reported in a transient cochlear ischemic experiment (11). Glutamic acid may have a cytotoxic effect on the OHCs, such as that found in ischemic brain tissue (16). The problem, however, is that glutamic acid receptors have not been found to date in the OHCs of the guinea pig cochlea. Another possibility is the participation of free radicals. Disappearance of OHCs, predominantly in the first and second rows, has been reported as a result of ototoxic drug administration (17) and in lateral wall damage produced by photochemical reaction using a tangentially irradiating beam (8). In such cases free radicals might be suspected of playing a role. At present it is not possible to decide whether free radicals or glutamic acid are causative factors in hair cell loss confined to the OHCs. However, considering

Table II. *Sequential changes in EP (mean±SD) in controls and experimental animals*

Group	Time (days)			*n*
	3	7	14	
Controls	83.0±2.0	79.7±1.5	74.7±5.9	3
Experimental animals	17.4±7.0*	19.0±6.6*	80.0±7.1	5

* $p < 0.001$ vs controls.

Fig. 5. SEM image of a 3-day specimen showing two SV lesions (*asterisks*) and the hole (*arrowhead*) for EP measurement. *Bar* = 150 μm.

these morphological changes, we strongly suspect that free radicals participated in the change in OHCs in the area between the lesions. An experiment is ongoing to examine the alleviating effect of free radical scavengers on damage in this area using the same animal model.

The normal EP value for the scala media of guinea pigs is generally accepted as being ≈ +80 mV. SV changes are thought to greatly influence the EP values. For instance, low EP values were reported in Ws rats and Wv mice with congenital strial agenesis (18). However, Wu and Hoshino (19) reported that small photochemically induced strial lesions caused a decrease in EP that recovered 1–2 weeks later. In the present study, the EP in the region between the two SV lesions showed a recovery similar to that observed by Wu and Hoshino. These findings suggest that if acute strial damage occurs and the damaged area is relatively small compared with the total area of the SV, the EP value may be restored after a transient decline.

As the marginal cells and vascular net appeared normal in the region between the two lesions, the reason why EP in that region should decrease is not clear. Wu and Hoshino (19, 20) reported that EP values recorded apically to a photochemically induced small lateral wall lesion showed a decrease at 3 days and a recovery to pre-illumination levels at 14 days in the absence of any structural changes. This apicalwards suppression of EP in the SV was first reported by Okumura (21). He tried to attribute this phenomenon to a disorder of the electrical circuit of the cochlea. No proof, however, has so far been obtained to explain the apicalwards suppression of EP from a localized strial lesion. A basalwards flow of the endolymph and a subsequent change in the endolymph ion content are also unlikely to explain the decrease in EP. Endolymph circulation is supposed to mostly occur radially (22) and the longitudinal flow of the endolymph is very slow in the cochlear duct (23). The mechanism responsible for the decrease in EP found in the present study would seem to be the same as that found in a localized single lesion (7), but a clear explanation of this mechanism has not yet been found.

A decrease in EP causes sensorineural hearing loss. Namely, a decrease in EP occurs in parallel with reductions in cochlear microphonics, summating potential and compound action potential. Every millivolt loss of EP results in ≈ 1 dB of threshold elevation (24). The decrease in and recovery of EP after 2 weeks in a localized area of the second turn of the cochlea found in the present study would presumably cause a transient elevation in hearing threshold for limited frequencies. Even though EP recovers after 2 weeks, some distortion of tone perception might possibly remain due to OHC loss in that region. Careful investigation using methods for examining OHC function, such as distortion product otoacoustic emissions, may detect subtle changes due to localized OHC loss.

In conclusion, the double lesions in the SV caused a reversible decrease in EP and irreversible OHC loss in the region between the lesions. It is speculated that multiple small skipped lesions in the SV produced widespread cochlear dysfunction.

ACKNOWLEDGEMENTS

This study was supported by the Acute Profound Deafness Research Committee of the Ministry of Health and Welfare, Japan.

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Submitted May 6, 2002; accepted December 12, 2002

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HHIA(Hearing Handicap Inventory for Adults) 日本語版を用いた聴覚障害の評価法に関する検討

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日本耳鼻咽喉科学会会報〔Nippon Jibiinkoka Gakkai Kaiho (Tokyo)〕107：489～493，2004（平成16年）.

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難聴の臨床における心理的評価には，社会面および感情面からのアプローチが必要である．本研究では，欧米においてその有用性が評価されているアンケート調査，HHIAを翻訳して，HHIA日本語版を作成し，聴力，精神状態が安定している感音難聴症例に施行した．

HHIA日本語版の標準化を試みたところ，心理検査としての信頼性(カッパ値)は全問およびスクリーニング版において各々0.912，0.842と非常に良好であったが，社会面の質問に関しては，全問0.785，スクリーニング版0.690であった．

全問のスコアは一側性感音難聴の方が両側性感音難聴より低く，両側性難聴では罹患後2-10年で高くなりその後は低下していた．また，施行した聴覚検査のうち，両耳の全周波数平均聴力レベルとの相関が高かった．社会面の質問や，一側性感音難聴症例の検討など再考の余地を残すが，HHIA日本語版の活用により，難聴患者の心理的評価が可能であり，難聴の臨床において有用であると考えられた．

キーワード：HHIA，心理的評価，アンケート調査，聴覚障害

はじめに

聴覚障害の社会的・心理的評価を各種聴覚検査によって行うことは困難であると考えられる．これらの評価のためには，アンケート調査が適切であるという考えから，1960年代のHHS（Hearing Handicap Scale）以降[1]多くの評価法が作られてきた．65歳以上の高齢者を対象とした評価法には，HHIE（Hearing Handicap Inventory for the Elderly)[2][3]やそのスクリーニング版のHHIE-S[4]が知られているが，今回検討したHHIA（Hearing Handicap Inventory for Adults)[5][6]は，1990年，米国のNewmanらによって提唱された，65歳未満，成人向けの評価法である．HHIEのうちの3問がより職業を意識した質問に改変されたものである．難聴患者の感情面，および社会面における心理状態を把握するための25の質問からなり，そのうちの10問をスクリーニング用としている．

本研究では，これを日本語に翻訳したHHIA日本語版を作成し，その信頼性および有用性について検討した．

対象と方法

対象は，顕著な聴力の変化または変動を認めない一側性または両側性感音難聴の64歳以下の成人で，難聴や耳鳴りに対し，向精神薬等を投薬されていない症例とした．著者らが原著[5][6]を翻訳し，HHIA日本語版として，「聞こえが悪い患者さんのためのアンケート」を作成した（表1）．HHIA日本語版は25問からなり，様々な状況において聞こえなくて困るか，いらいらするかといった感情面の質問13問（2，4，5，8，10，12，14，17，18，20，22，24，25）と，人間関係，公共の場において難聴が影響しているかといった社会面の質問12問（1，3，6，7，9，11，13，15，16，19，21，23）で構成されている．このうち，2，5，7，8，9，11，14，15，20，21の10問がスクリーニング用である．スコアは，当てはまる場合を4点，時々を2点，当てはまらない場合を0点とし，合計点を算出した．全問では0-100点，スクリーニングでは0-40点にスコアが分布する．

第1回目検査より4-5週の期間をおいて同様のアンケートを郵送した．2回分の回答を得た症例のスコアを比較し，Spearmanの順位相関におけるカッパ値を求めた．この値が0.8を超えた場合を心理検査として信頼性ありと判定した[7]．

表1　聞こえが悪い患者さんへのアンケート

記入日 ＿＿年＿＿月＿＿日

聞こえが悪い患者さんへのアンケート

お名前　　歳　　診察券番号 □□-□□□□□

この検査は、聞こえにくいために、あなたがどのように困っているか調べるものです。
当てはまる数字に丸をお付け下さい。

各質問について、あてはまる番号に○をつけてください。		はい	時々ある	いいえ
1	聞こえにくいために電話をかけたくないと思いますか？	4	2	0
2	初対面の人と会うときに聞こえなくて困ることがありますか？	4	2	0
3	聞こえにくいために人とつきあうのを避けてしまうことがありますか？	4	2	0
4	聞こえなくて、いらいらしますか？	4	2	0
5	家族と話をする時、聞こえにくくていらいらすることがありますか？	4	2	0
6	パーティーや会合で、聞こえにくくて困ることがありますか？	4	2	0
7	職場の人や顧客のはなしを聞いたり理解する時、聞こえにくくて困ることがありますか？	4	2	0
8	聞こえが悪いと障害者だと感じますか？	4	2	0
9	友人、親戚、近所の人と話をする時、聞こえにくくて困ることがありますか？	4	2	0
10	職場の人や顧客のはなしを聞いたり理解する時、聞こえにくくていらいらすることがありますか？	4	2	0
11	映画館や劇場で聞こえが悪くて困ることがありますか？	4	2	0
12	聞こえにくくて神経質になっていますか？	4	2	0
13	聞こえにくくて、友人、親戚、近所の人と会いたくなくなりますか？	4	2	0
14	聞こえにくくて、家族の人と口論になることがありますか？	4	2	0
15	テレビやラジオを聴く時、聞こえにくくて困ることがありますか？	4	2	0
16	聞こえにくいために買い物に行きたくなくなりますか？	4	2	0
17	聞こえが悪かったり聞こえにくいために体調が悪いですか？	4	2	0
18	聞こえにくいためにひとりでいたいと思うことがありますか？？	4	2	0
19	聞こえにくいために家族との会話が減りますか？	4	2	0
20	聞こえにくいことで、あなたの私生活や社会活動が制限されていると思いますか？	4	2	0
21	親戚や友人とレストランにいる時に、聞こえにくくて困ることがありますか？	4	2	0
22	聞こえにくいために気分が落ち込んでいますか？	4	2	0
23	聞こえが悪いためにテレビを見たりラジオを聴かなくなりますか？	4	2	0
24	友人とおしゃべりをする時に聞こえにくいことを不愉快に感じますか？	4	2	0
25	仲間といるとき聞こえにくいために取り残されているように感じますか？	4	2	0

表2　2回分の回答が得られた18症例のスコアの比較

		第1回目全問	第2回目全問	1回目スクリーニング	2回目スクリーニング
合計点	分布	14～80	16～84	6～38	8～36
	平均	50.0	50.3	24.0	23.9
	SD	21.4	22.7	9.6	9.3
感情面	分布	2～42	4～46	0～20	2～18
	平均	25.0	24.8	9.6	10.0
	SD	12.9	13.5	5.9	5.0
社会面	分布	8～38	6～42	6～20	4～20
	平均	25.0	25.6	14.4	13.9
	SD	9.5	10.1	4.7	5.0

次に，全例について検査から得られたスコアと，罹患期間・疾患・聴覚検査結果の相関を Pearson の相関係数を用いて検討した[8]．聴覚検査としては全例に純音聴力検査，28例中17例に67式語音聴力検査を施行した．純音聴力検査結果については，両耳の4分法，5周波数（250-4000Hz）平均，7周波数（125-8000Hz）平均聴力レベルを算出し，その平均を適用，語音聴力検査も両耳の最高語音明瞭度の平均を用いた．

結　果

第1回目検査は，18歳から63歳の28例（男性18例，女性10例，平均年齢±標準偏差（以下 SD）＝42.4±15.3歳）に施行した．全問のスコアは0～82点（平均47.7，SD22.5），スクリーニング版のスコアは0～38点（平均22.9，SD10.0）に分布した．このうち18例（64.3%）より2回分の回答を得た．2回目検査のスコアは全問16～84点（平均50.3，SD22.7）に分布し，スクリーニング版のスコアは8～36点（平均23.9，SD9.3）に分布した．表2に，2回分の回答が得られた18例のスコアの

比較を示した．カッパ値は，全問においては0.912（感情面＝0.945，社会面＝0.785），スクリーニングでは0.842（感情面＝0.894，社会面＝0.690）であった．

対象症例のうち，一側性難聴を除いた両側性感音難聴症例の罹患期間とスコアの関係を比較すると（表3），スコアは罹患後2年から10年が62.0点と最も高く，10年以上になると低下する傾向が見られた．これは感情面，社会面，ともに同様の傾向であった．

疾患別の症例数とスコアを表4に示した．両側性感音難聴17例は，進行性またはその疑い，および5周波数平均100dB以上のろうまたはろう型感音難聴症例を除外した，原因不明の両側性感音難聴症例である．一側性感音難聴3例はすべて発症後2年以内の陳旧性突発性難聴である．疾患別のスコアは，一側性感音難聴では29.3点と低く，これに対して進行性感音難聴は60.3点，ろうは，63.0点，両側性難聴は44.7点であった．また，一側性すなわち陳旧性突発性難聴では感情面と社会面の点数の差が，他疾患に比べ大きく，社会面のスコアが高い傾向がみられた．

聴覚検査結果とスコアの散布図を図1に示した．相関係数を比較すると，最高語音明瞭度よりも聴力レベルとの相関が高く，4分法よりも5周波数平均，さらに全7周波数の平均聴力レベルの方が高い相関を示した（表5）．

考　察

第1回目と第2回目検査のスコアのカッパ値は全問で

表3　両側性感音難聴例の罹患期間別平均スコアの比較

	例数	全問	感情面	社会面
0～2年（一側性感音難聴を除く）	5	42.0 (31.3)	28.8 (20.0)	24.8 (13.9)
2～10年	7	62.0 (18.1)	32.9 (10.0)	29.1 (12.0)
10～20年	8	48.5 (16.6)	21.8 (10.9)	26.8 (7.9)
20年以上	5	43.2 (20.2)	21.2 (11.7)	22.0 (9.6)

（　）内は標準偏差

表4　疾患別の平均スコアの比較

	例数	全問	感情面	社会面
両側性感音難聴	17	44.7 (23.2)	22.5 (10.9)	22.2 (13.7)
進行性難聴またはその疑い	2	60.3 (13.3)	30.7 (8.9)	29.7 (9.8)
ろうまたはろう型	6	63.0 (15.6)	31.0 (4.2)	32.0 (11.3)
一側性感音難聴（陳旧性突発性難聴）	3	29.3 (25.7)	12.7 (11.0)	16.7 (14.7)

（　）内は標準偏差

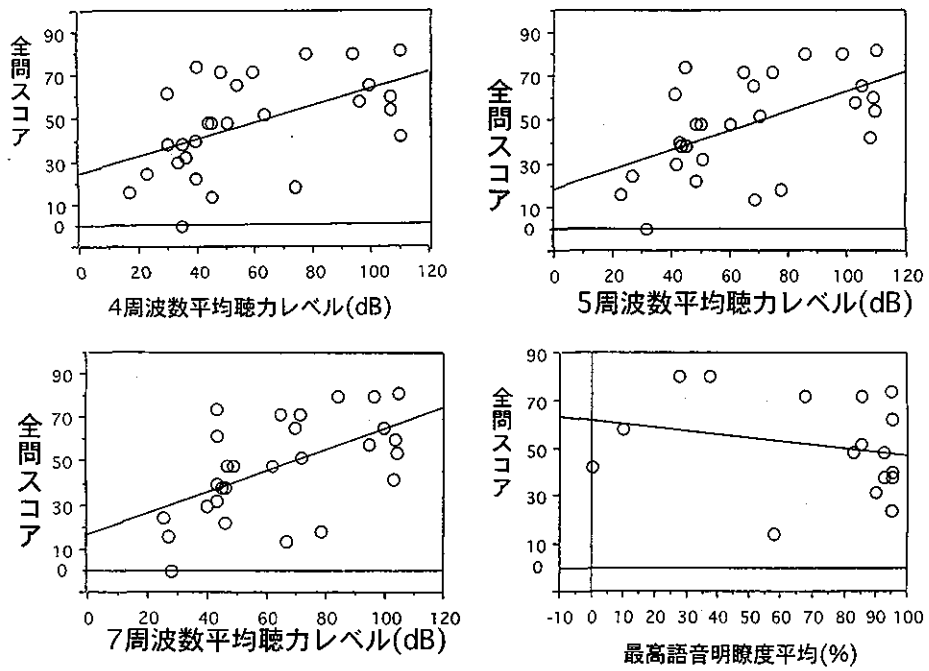

図1　HHIA全問のスコアと聴覚検査結果の比較および回帰直線

表5　聴覚検査結果とスコアの相関係数

	全問	感情面	社会面
4分法平均	0.518	0.463	0.347
5周波数平均	0.555	0.484	0.557
7周波数平均	0.569	0.471	0.737
語音明瞭度平均	−0.238	−0.183	−0.005

0.912，スクリーニングで0.842で共に0.8を超えており，全問施行した場合の心理検査としての信頼性は，“excellent”[7]であった．また感情面の質問に関しても，全問，スクリーニングとも0.8を超えており，心理検査の信頼性は全く問題ないと考えられる．しかし，社会面の質問に関するカッパ値は，全問0.785，スクリーニング0.690で，信頼性は，“fair”[7]にとどまった．社会面の質問，たとえば，パーティーや会合へ行く，映画館，劇場へ行く，などの質問に1回目と2回目の回答のばらつきが大きくみられ，欧米と日本の慣習の違いが影響しているのではないかと推測された．これらの質問に関しては，冠婚葬祭，町内会など，日本人の生活環境を反映した言語に置換すべきではないかと考えられた．海外では，原著英語版と翻訳されたスペイン語版の2種のHHIE-Sを各症例に施行し，翻訳版の信頼性を検討した報告もあるが[9]，本邦においてはバイリンガルといえる人口は僅少であり，そのような試行は困難であると考えられる．

疾患別には，一側性感音難聴より両側性感音難聴の方がスコアは高く，また両側性感音難聴の中では，進行性またはろうといった，聴力が悪いあるいは，今後の聴力悪化が予想される症例のスコアが高かった．予想されたことではあるが，これらの症例では，聴覚障害の心理的影響，社会的ストレスが大きいと考えられた．一方，両側性感音難聴症例のみで罹患期間との関係を見ると，発症より2年までのスコアは2-10年までよりも低く，難聴発症当初より，難聴が固定してから数年が最も心理的に辛い時期であると推測された．また，発症後10年以上経過している症例のスコアが逆に低くなったことは，聴覚障害を許容し，それなりの解決策や思考回路を獲得し，ストレスを解消する，といった，病気の受け入れができてくるのではないかと考えられた．感情面の質問がすべて当てはまる場合は52点，社会面の質問では48点で感情面のスコアが高くなるが，10年以上経過した症例における両者のスコアは，感情面よりむしろ社会面のスコアの方が高かったことも，これを裏付ける結果ではないかと考えられる．

疾患別で感情面と社会面とのスコアの差が最も大きかった一側性感音難聴はすべて罹患後2年以内の陳旧性突発性難聴であった．突発性難聴の罹患期間とスコアは相関しないという報告もあるが[10]，今回の突発性難聴症例はすべて罹患後2年以内であること，また症例数が少ないため，さらに症例を加えて検討する必要がある．

今回試みたHHIA日本語版は，難聴患者の心理的評価が可能であり，薬剤や心理治療の効果の判定や，高得点のものに対して，補聴器適応も検討するなど，難聴の診療場面に有用であると考えられた．

ま と め

1. HHIAを翻訳して，HHIA日本語版を作成した．
2. 聴力，精神状態が安定している感音難聴症例を対象として，HHIA日本語版の検査を施行し，その有用性を検討した．
3. HHIA日本語版の標準化においては全問およびスクリーニング版双方ともカッパ値0.8以上の値が得られた．感情面の質問に関するカッパ値も0.8以上であったが，社会面の質問に関しては0.6—0.8の値であった．
4. 検査のスコアは一側性感音難聴の方が両側性感音難聴より低かった．両側性感音難聴では，罹患後2-10年で高くなりその後は低下していた．
5. 聴力検査との関係は最高語音明瞭度より，両耳平均の聴力レベル，特に全7周波数の平均聴力レベルとの相関が認められた．
6. 検査の活用により，難聴患者の心理的評価が可能であり，難聴の臨床において有用であると考えられた．

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(2003年11月1日受稿　2004年1月9日受理)

別刷請求先　〒160-8582 東京都新宿区信濃町35
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Adaptation of Japanese Version of the Hearing Handicap Inventory for Adults (HHIA)

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We used social and emotional approaches to psychologically evaluate hearing disorders, translating the Hearing Handicap Inventory for Adults (HHIA) into Japanese and using it to evaluate Japanese adults with sensorineural hearing loss. The HHIA is a 25-item self-assessment scale composed of 2 subscales, emotional and social/situational, which has been used to evaluate adult patients with hearing disorders in Europe and North America.

The test-retest reliability of the Japanese version and its screening version (HHIA-S) were excellent (kappa coefficients were 0.912 and 0.842). Due to the limitation of social/situational items, test-retest reliability was only good (0.6 $<$kappa coefficient$<$0.8), possively because of problems in translating these items.

We discovered that the average of scores of the HHIA Japanese version was higher in bilateral hearing disorder patients than in those with unilateral hearing disorder. This score peaked in 2 to 10 years after onset and decreased thereafter in bilateral hearing disorder patients. The correlation coefficient between the average hearing level of 7 frequencies and scores of the test was highest among the 4 audiological evaluations.

The HHIA Japanese version is thus useful for following up patients with hearing disorders.

Keywords: hearing disorder, HHIA, psychological evaluation, coefficient

Nippon Jibiinkoka Gakkai Kaiho (Tokyo) 107: 489-493, 2004

REPRINTED FROM *ANNALS OF OTOLOGY, RHINOLOGY & LARYNGOLOGY*
June 2004 Volume 113 Number 6

BLOOD FLOW IN THE EARS OF PATIENTS RECEIVING COCHLEAR IMPLANTS

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We measured cochlear blood flow (CBF) in 55 patients who received cochlear implants, using a laser-Doppler probe placed over the site of drilling in the cochlear bony wall. The subjects included 29 patients with congenital deafness of unknown cause, 8 with idiopathic progressive sensorineural hearing loss, 4 with postmeningitic deafness, 3 with Waardenburg's syndrome, 3 with congenital cytomegalovirus infection, and 8 whose deafness had other causes. There was a wide range of CBF values in patients with congenital deafness of unknown cause. In the patients with idiopathic progressive sensorineural hearing loss, the CBF was significantly lower in patients more than 40 years old. Intracochlear calcification following meningitis appears to be associated with a reduced CBF.

KEY WORDS — cochlear blood flow, cryopreserved embryo, intrauterine aminoglycoside ototoxicity, laser-Doppler flowmetry, mitochondrial point mutation, profound hearing loss.

There have been many reports of hearing loss supposedly caused by blood flow disturbance in the cochlea. However, direct evidence of this is still lacking in most cases.[1] This is because the cochlea is surrounded by bone that prevents direct observation of blood vessels, unlike the ocular fundus. The cochlea is not large enough for angiography, as can be used in the brain.

Laser-Doppler flowmetry has been used to evaluate cochlear blood flow (CBF) experimentally and clinically. We showed that CBF could be measured during cochlear implantation surgery by placing a laser-Doppler probe to the site in which the cochlea has been opened.[2] It is also possible to evaluate CBF more directly by inserting the tip of the probe into the scala tympani to avoid measuring the blood flow of the bone surrounding the cochlea. Using this method, we have measured CBF in 55 patients who received cochlear implants, and here present the results according to the cause of deafness and the age of the patients.

MATERIALS AND METHODS

Procedure. All parents of the children and all adult patients received an explanation of the method and purpose of the study and provided their informed consent. The methods for blood flow measurement have been described previously in detail.[2] Briefly, CBF was measured with a laser-Doppler flowmeter (model ALF 21, Advance, Tokyo, Japan) with the patient under general anesthesia with sevoflurane and nitrous oxide. The outer diameter of the probe was 0.8 mm, and the fiber separation between the exciting and receiving optic fibers was 0.3 mm. The tip of the probe was attached manually to the site of drilling for cochlear implantation. We measured blood flow before, during, and after the cochlear bony wall had been opened, placing the tip of the probe as follows: 1) on the mucous membrane of the promontory; 2) on the bone after the mucous membrane of the promontory had been removed; 3) when the bony wall had been drilled halfway through; 4) when the bony wall had been drilled down to the mucous membrane surrounding the perilymph; and 5) inside the perilymph.

The measurements could not be done at some positions if it was considered that the drilling had proceeded too deep for safe measurement, but final CBF measurements were performed in all 55 patients with the tip of the probe inside the perilymph.

Patients. We studied 55 patients who were receiving cochlear implants. There were 32 who were male and 23 who were female, and their ages ranged from 1 to 66 years. Table 1 shows the patients according to the cause of deafness and the number of patients in each group.

In group A, there were 3 who were 1 year of age, 13 who were 2 years of age, 10 who were 3 years of age, 2 who were 4 years of age, and 1 girl who was 16 years of age. For these patients, it was estimated

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TABLE 1. PATIENTS RECEIVING COCHLEAR IMPLANTS

Group	Category	No. of Patients (Sex)
A	Congenital deafness of unknown cause	29 (19M, 10F)
B	Idiopathic progressive sensorineural hearing loss	8 (2M, 6F)
C	Postmeningitic deafness	4 (all M)
D	Waardenburg's syndrome	3 (all F)
E	Congenital cytomegalovirus infection	3 (all M)
F	Other causes	8 (4M, 4F)

that at least 2 patients (a 3-year-old boy and the 16-year-old girl) had hereditary deafness because 1 of their siblings was deaf, but the cause was unknown. A 2-year-old boy with congenital deafness of unknown cause was born from a cryopreserved and thawed embryo after in vitro fertilization.

In group B, the ages ranged from 4 to 55 years, and the average age was 30.8 years. In group C, there were 3 children and 1 adult. Cochlear ossification and narrow perilymphatic spaces were demonstrated by magnetic resonance imaging (MRI) and computed tomography (CT) in the group C patients. A narrow perilymphatic space of the cochlear basal turn was found bilaterally in 2 of these patients and unilaterally in the other 2. In the 2 patients with bilateral changes, cochlear implantation was performed on the less affected side. In 2 patients with unilateral changes, cochlear implantation was performed on the side in which no abnormal findings were recognized by MRI and CT.

In groups D and E, the patients were 2 or 3 years old. In group F, there was a 17-year-old boy with the CHARGE association (coloboma of eye, heart anomaly, choanal atresia, retardation, and genital and ear anomalies), a 46-year-old woman with a mitochondrial DNA point mutation, a 3-year-old girl with large vestibular aqueduct (LVA) syndrome, a 3-year-old boy with narrow internal auditory canals, a 4-year-old girl whose hearing had decreased after she had measles, a 6-year-old boy whose hearing had decreased after typhoid fever, a 53-year-old man with sudden deafness, and a 66-year-old woman with Meniere's disease.

The patient with the CHARGE association had microphthalmia. He had hypoplastic cochleas and no semicircular canals on either side. Because his hearing level deteriorated gradually and conversation became difficult in spite of hearing aids, he received cochlear implants when he was 17 years old. One patient with a mitochondrial DNA point mutation suffered fetal streptomycin ototoxicity when her mother had tuberculosis during pregnancy. Because her mother subsequently developed profound deafness, the patient had never received streptomycin after birth. However, her hearing level deteriorated gradually and she became profoundly deaf when she was about 42 years old. She received cochlear implants when she was 46 years old. Mitochondrial DNA analysis revealed a point mutation at nucleotide position 1555, but she had no symptoms other than those of her auditory system.

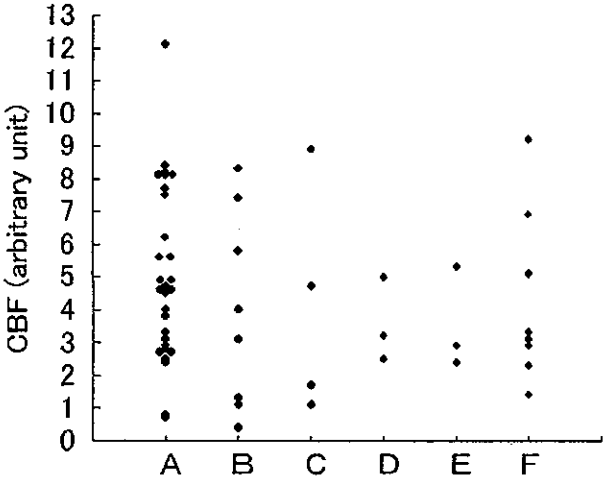

Fig 1. Cochlear blood flow (CBF) in each patient in 6 groups. Group A — congenital deafness of unknown cause; group B — idiopathic progressive sensorineural hearing loss; group C — postmeningitic deafness; group D — Waardenburg's syndrome; group E — congenital cytomegalovirus infection; group F — other causes.

Statistical Analysis. Data concerning age, gender, laser-Doppler CBF output measured at the 5 positions listed above, and causes of deafness were entered into a computer and analyzed with STATA. Distributions of numerical data are reported as mean ± SD.

RESULTS

Figure 1 demonstrates the values of the laser-Doppler output with the tip of the probe inside the perilymph in each group of patients. The overall CBF was 4.5 ± 2.6 (arbitrary units). The CBF was less than one third of the average in 2 patients with congenital deafness of unknown cause, in 3 patients with idiopathic progressive sensorineural hearing loss (IPSNHL), in 1 patient with postmeningitic deafness and cochlear calcification, and in 1 patient with narrow internal auditory canals.

In 29 patients with congenital deafness of unknown cause (group A), the CBF measured when the tip of the probe was inside the perilymph was 5.0 ± 2.6. The CBFs in the 3-year-old boy and the 16-year-old girl whose siblings were deaf were 7.5 and 2.7, respectively. In the patient born from a cryopreserved and thawed embryo, the CBF was 4.7.

In 8 patients with IPSNHL (group B), the mean

TABLE 2. COCHLEAR BLOOD FLOW OF PATIENTS WHO RECEIVED COCHLEAR IMPLANTS AFTER MENINGITIS

Pt	Age at Cochlear Implantation	Sex	Interval Between Meningitis and Cochlear Implantation	Narrowing of Basal Turn on Side of Operation	Cochlear Blood Flow (arbitrary units)
1	59 y 10 mo	M	1 y 9 mo	Yes	1.1
2	3 y 8 mo	M	11 mo	No	4.7
3	1 y 10 mo	M	4 mo	Yes	1.7
4	3 y 5 mo	M	2 y 8 mo	No	8.9

CBF was 3.9 ± 3.0. The CBF volume was significantly smaller in the patients more than 40 years of age (0.9 ± 0.5, n = 3) than in those less than 40 years of age (5.7 ± 2.2, n = 5). In a 53-year-old patient with IPSNHL, the perilymphatic space of the basal turn was partially occluded by fibrous tissue.

Table 2 shows the CBFs in 4 patients with postmeningitic deafness (group C). A narrow perilymphatic space was recognized bilaterally in patients 1 and 3. In patients 2 and 4, a narrow perilymphatic space was recognized unilaterally by MRI and CT, and cochlear implantation was performed on the side in which no abnormalities were found. The CBF was low in the cochleas with a narrow perilymphatic space.

The CBF was 3.6 ± 1.3 in the patients with Waardenburg's syndrome (group D) and 3.5 ± 1.6 in patients with congenital cytomegalovirus infection (group E). The CBFs were 2.9 in the patient with the CHARGE association, 3.1 in the patient with intrauterine streptomycin ototoxicity, 3.3 in the patient with LVA syndrome, 1.4 in the patient with narrow internal auditory canals, 9.2 in the patient whose hearing decreased after measles, 6.9 in the patient whose hearing deteriorated after typhoid fever, 2.3 in the patient with sudden deafness, and 5.1 in the patient with Meniere's disease. In the patient whose hearing decreased after typhoid fever, the perilymphatic space of the basal turn was partially occluded by fibrous tissue.

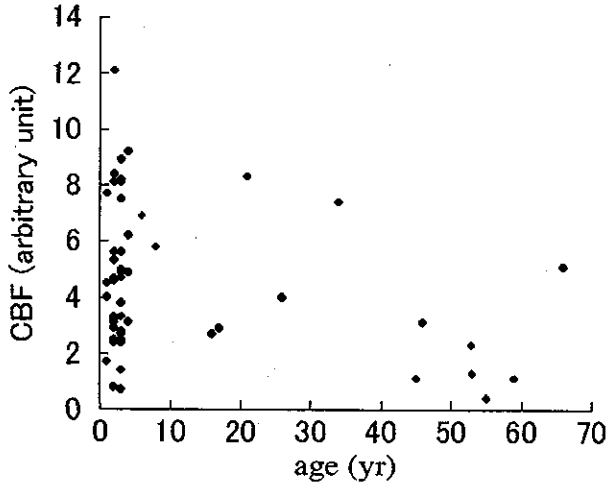

Fig 2. Relationship between age and CBF in all patients. CBF was measured when tip of probe was inside perilymph.

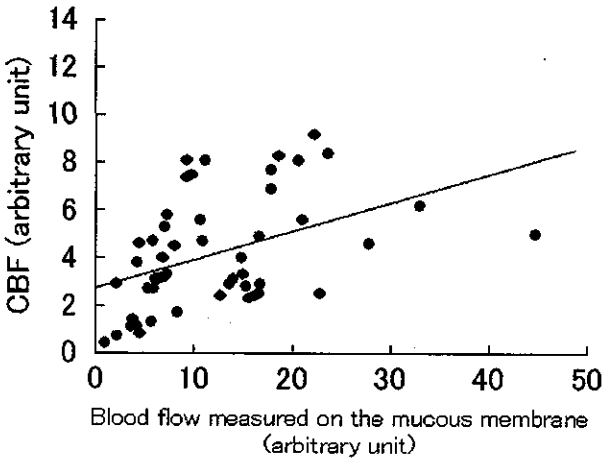

Fig 3. Relationship between blood flow measured on promontory mucous membrane and CBF.

Figure 2 shows the overall relationship between the CBF and the age of the patients as a whole. The percentage of patients with a low CBF tended to be greater in adults; however, this difference was not statistically significant.

The laser-Doppler output measured when the tip of the probe was placed on the mucous membrane of the promontory before drilling was 12.3 ± 8.6 (n = 50). In 3 patients, this measurement was not made because epinephrine (0.05%) was applied to the mucous membrane to stop bleeding. In 2 patients with otitis media with effusion, the measurement on the mucous membrane was omitted for the present study. Figure 3 shows a positive correlation between the values of the laser-Doppler output measured when the tip of the probe was attached to the mucous membrane and those measured when the tip of the probe was inserted into the perilymph ($p < .001$).

When the tip of the probe was put on the bone surface after removal of the mucous membrane, the laser-Doppler output decreased significantly (4.9 ± 3.3, n = 41). Figure 4 also shows a positive correlation between the laser-Doppler outputs measured when the tip of the probe was attached on the bone surface and those measured when the tip of the probe was inserted into the perilymph ($p < .001$).

The mean output measured when one half of the bone had been drilled was 3.7 ± 2.1 (n = 50), and the mean output measured when the tip of the probe was put on the membrane surrounding the perilymph was 3.8 ± 3.2 (n = 26). There were also significant correlations between the values measured when the tip of