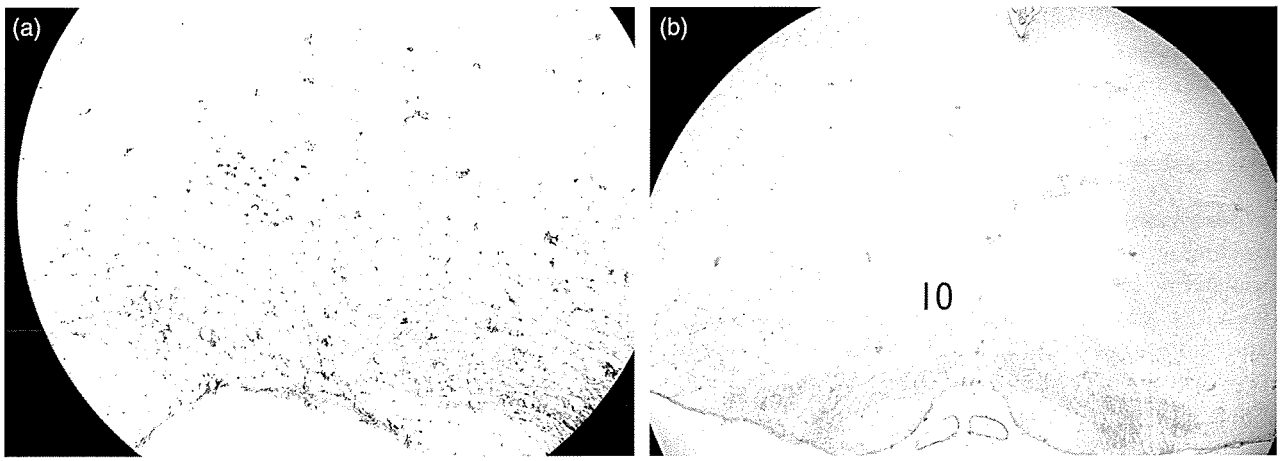

Figure 2. Expression of c-Fos positive cells in the inferior olive nucleus. (a) Positive cells were observed in the inferior olive nucleus (IO) on the intact side. (b) Control.

labyrinthectomy, and 0.79 and 0.78 cells/slice, respectively, in control animals. In PrH, c-Fos positive cells were seen significantly more often only in the intact side of animals with labyrinthectomy than in control animals: 2.60 and 9.58 cells/slice in the operated and intact sides, respectively, of animals with labyrinthectomy, and 1.04 and 1.11 cells/slice, respectively, in control animals. The comparison of the operated and intact sides of animals with labyrinthectomy did not reveal any significant difference, although there were more c-Fos positive cells observed in the intact side in both MVe and PrH but in the operated side in SpVe. In the IO, there were significantly more c- Fos positive cells only in the intact side of animals with labyrinthectomy as compared with control animals:

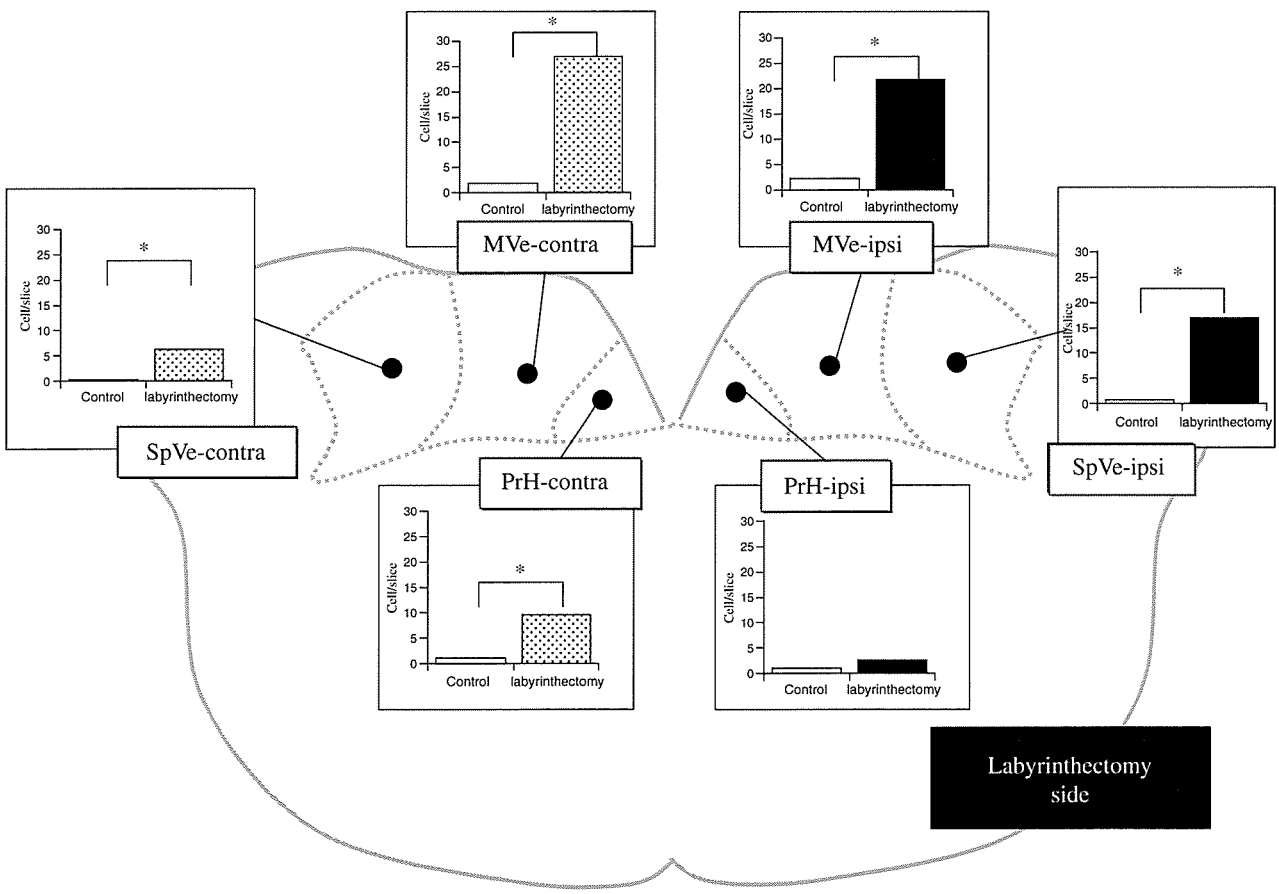

Figure 3. The numbers of c-Fos positive cells were increased in the bilateral medial vestibular nucleus (MVe), bilateral spinal vestibular nucleus (SpVe), and contralateral prepositus hypoglossal nucleus (PrH).

0.6 and 5.6 cells/slice in the operated and intact sides, respectively, of animals with labyrinthectomy, and 0 cell/slice in both sides of control animals.

Discussion

c-Fos positive cells were observed in the vestibular nucleus in the operated and intact sides 24 h after unilateral labyrinthectomy, which almost agreed with the previous results obtained in rats [4,6,7] and guinea pigs [8]. In the present study, positive cells were observed in MVe in both sides, as found for guinea pigs [8], although there was a report that positive cells were observed only in the operated side of rats [7]. However, positive cells were also observed in the intact side of rats 3 h after operation [4], indicating different changes over time among species. The present findings of more positive cells in SpVe in the operated side and in PrH in the intact side agreed with previous reports. Positive cells in the IO were reported to be detectable in rats [7] and to be detectable but disappear early [4], while they were detected in the intact side of mice in the present study. Positive cells were also observed in the PrH in the intact side, which agreed with the previous reports. PrH receives input fibers from bilateral frontal eye fields, optic fascicular nuclei and vestibular nucleus group, and sends projection fibers to all bilateral motor nervous nuclei governing the extraocular muscles, indicating its involvement in the coordination of ocular motility in the stage of vestibular compensation. The present results indicated that the vestibular, prepositus hypoglossal and inferior olive nuclei were activated after unilateral labyrinthectomy in mice like in other species. Recently, gene-deficient mice in which various nervous receptors are knocked out have been supplied, and vestibular function and compensation have been examined in them [9,10]. It is expected that the application of the present procedure to such gene-deficient mice will elucidate the mechanism of the process of vestibular compensation.

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Vertigo as the sole presenting symptom of cerebellopontine angle meningioma

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Abstract

We report a rare case of cerebellopontine angle (CPA) meningioma whose sole symptom was severe vertigo. A 39-year-old woman with right CPA meningioma was referred for surgery. She experienced severe vertigo for 2 years without any other symptoms. Caloric test indicated right canal paresis of 90%. Her audiogram was normal. After surgery, vertigo symptoms disappeared dramatically. The mechanisms of restoration from vertigo are discussed.

Introduction

Next to acoustic neurinomas, meningiomas are the second most common tumor found in the cerebellopontine angle (CPA), but they comprise only 3–13% of all tumors in that location [1–3]. Since they do not arise from the vestibulocochlear nerve and since they grow slowly, severe vertigo is not a common symptom of these tumors [4,5]. We report a rare case of CPA meningioma whose sole symptom was vertigo. The patient underwent surgery and the symptom disappeared.

Case report

A 39-year-old woman had an increasing sensation that the vision flows for 2 years. She did not have any other symptoms (such as hearing loss, tinnitus, facial palsy or facial pain). She consulted a local neurologist and head MRI revealed a tumor in the CPA. She was referred to the Neurosurgery Department of Kyoto University. The MRI showed that the main portion of the tumor was located in the right CPA and attached to the dura mater of the posterior surface of the petrous bone (Figure 1). Our preoperative diagnosis was meningioma rather than neurinoma because the center of the tumor was out of the eighth nerve, and because the dura mater attached to the base of tumor was enhanced ('dural tail sign') [5]. Before surgery we evaluated her auditory and vestibular functions (Figure 2). Her audiogram was normal. She showed spontaneous nystagmus to the left direction (paretic nystagmus). Caloric test showed right canal paralysis of 90% and left directional preponderance of 19%. Surgery was performed by a suboccipital retrosigmoidal approach. The tumor did not extend into the internal auditory canal. The tumor was extirpated without damage to the seventh and eighth nerves (Figure 3). The histopathological diagnosis was meningioma. The vertigo symptom disappeared on the day after surgery. The nystagmus almost disappeared until postoperative day (POD) 22. The hearing loss due to the surgery was minimal. The right vestibular paralysis was transiently aggravated and returned to the preoperative level at POD 62 (Figure 4). The patient is free of disease 3 years after the surgery.

Discussion

The prevalence of vertigo as the symptom of CPA meningioma is about 22%, and is lower than that of

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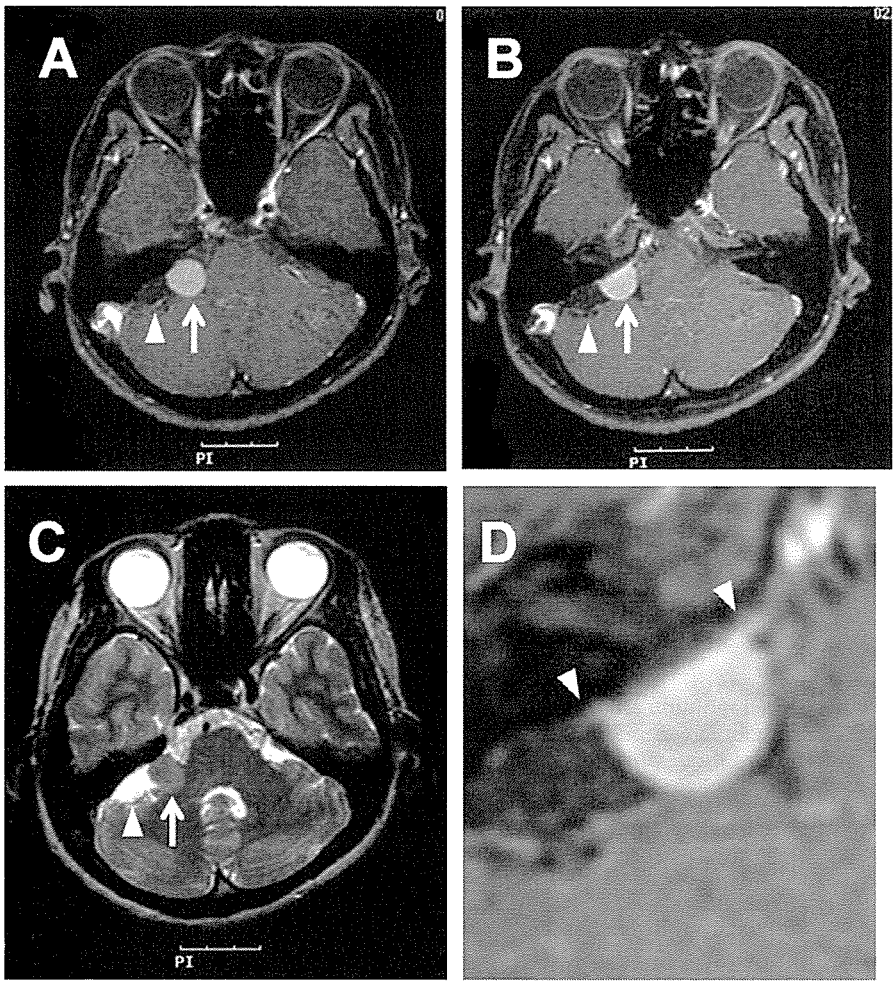

Figure 1. MRI findings of the tumor. (A, B) Gadolinium-enhanced T1-weighted images at different levels. (C) T2-weighted image. Arrows indicate the solid part and arrowheads indicate the cystic part of the tumor. (D) Arrowheads indicate the enhanced dura mater at the attachment to the base of tumor ('dural tail sign').

hearing loss, tinnitus, and facial pain [6]. The present case is rare in the viewpoint of severe vertigo without other symptoms. The present case showed dramatic recovery from severe vertigo by tumor removal. This is probably because the tumor was in a retromeatal location and did not extend into the internal auditory canal [7]. There is a report of dramatic recovery of hearing after removal of CPA meningioma [8]. Recovery from vertigo in our case may be achieved by similar mechanisms. One question is why the vertigo symptom and nystagmus disappeared after surgery although canal paralysis

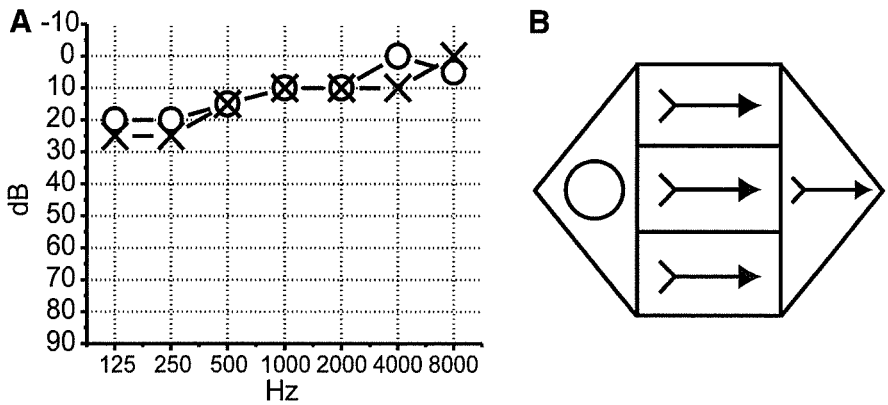

Figure 2. Preoperative neurootological findings of the patient. (A) Normal finding of the audiogram. (B) Spontaneous nystagmus to the left direction.

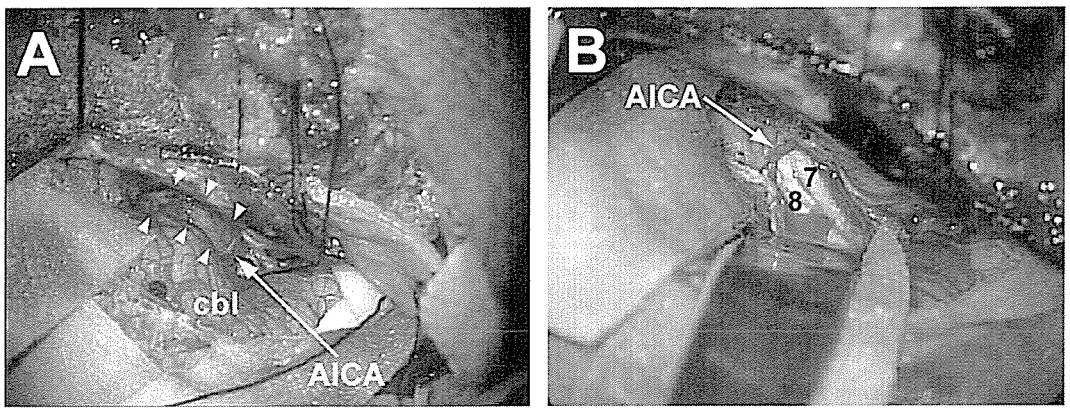

Figure 3. Operative findings before (A) and after (B) the removal of tumor. Arrowheads indicate the tumor. AICA, anterior inferior cerebellar artery; cbl, cerebellum; 7 and 8, facial and vestibulocochlear nerves, respectively.

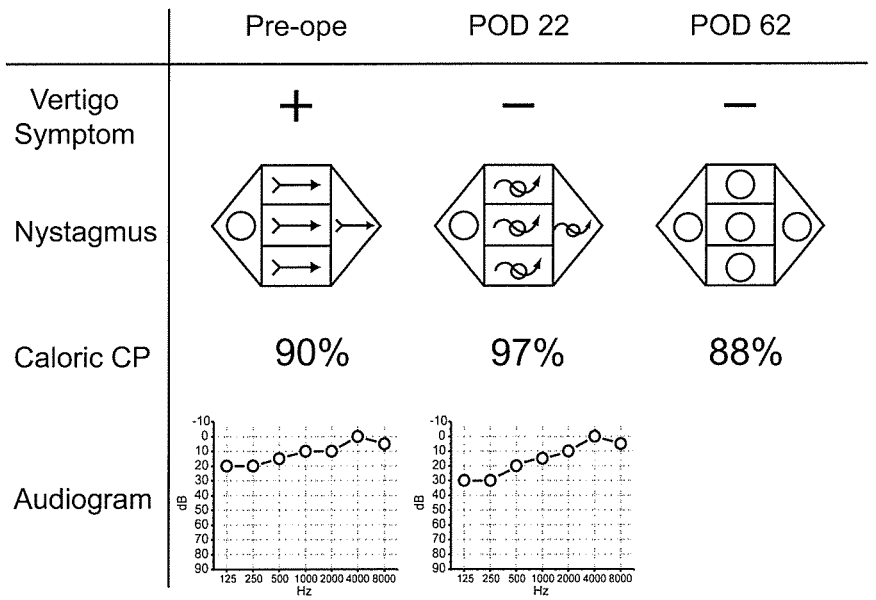

Figure 4. Summary of neurootological findings before and after the surgery. POD, postoperative day.

remains at a high level (Figure 4). One possibility is that the function of visual suppression recovered due to the recovery of the flocculovestibular pathway. Another possibility is that the vestibular compensation function in the cerebellum recovered rapidly after tumor removal.

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A case of cochlear implant with internal mechanical failure

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Abstract
Cochlear implantation has been performed since the 1970s and has been proven to be an effective treatment for profoundly deaf people. In some cases re-implantation has also been reported due to trauma causing implant damage, mechanical failure, extrusion, and wound infections, or device upgrade. We present a case of a 9-year-old boy with a cochlear implant in which mechanical failure occurred after a blow to his temporal region. The clinical presentation and radiographic imaging findings suggested that the cause of mechanical failure was internal failure. We performed cochlear re-implantation to the same ear and it worked well. The explanted device analysis by the manufacturer concluded that the device had failed due to a cracked hybrid integrated circuit.

Keywords: *Mechanical failure, internal failure, re-implantation*

Introduction

Cochlear implantation has been performed since the 1970s and has been proven to be an effective treatment for profoundly deaf people. On the other hand, some cases have been reported to require re-implantation due to trauma causing implant damage, mechanical failure, extrusion, and wound infections, or device upgrade [1,2]. In this report, we present a case of a 9-year-old boy with a cochlear implant in which mechanical failure occurred after a blow to his temporal region.

Case report

A 6-year-old boy who had difficulty in learning language despite the use of hearing aids from the age of 18 months visited our clinic. He was diagnosed as having bilateral profound sensorineural hearing loss. CT scanning demonstrated neither anomaly nor abnormal shadow that suggested ear diseases in the middle and inner ears. Magnetic resonance imaging (MRI) detected the bilateral cochlear nerves clearly. He underwent cochlear implantation to the right ear with a Nucleus® CI24M device (Cochlear Ltd, Austria) at 6 years old. Intraoperative neural response telemetry (NRT) indicated normal evoked compound action potential thresholds. The postoperative course was uneventful. His spoken language progressed well at 12 months after cochlear implantation. However, he received a strong impact on his right temporal region with the head of his friend at 16 months after cochlear implantation. He visited our clinic complaining that he did not hear anything from his right ear after experiencing the impact.

Lateral skull radiograph demonstrated neither a fracture in the skull nor a crack in the device. As compared with the lateral skull radiograph after his first implantation surgery, there was no significant difference. Temporal bone CT scanning also demonstrated neither fracture nor infection, and confirmed the electrode inserting to the second turn of the cochlear. The electrode was found to be normal. Both the electrode impedance test and NRT showed no response. We suspected that internal mechanical

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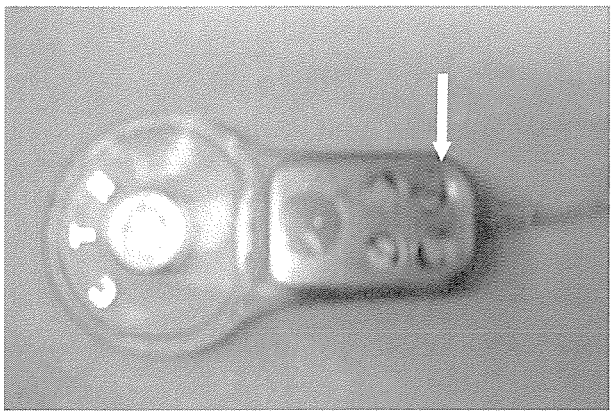

Figure 1. Dents (white arrow) were observed in the titanium casing on the top and bottom of the stimulator.

failure had occurred in the cochlear implant. We performed cochlear re-implantation to the same ear with the Nucleus® CI24M device. Although, intraoperatively, we found neither infection nor fracture in the cochlear and the mastoid cavity, dents were observed in the titanium casing on the top and bottom of the stimulator (Figure 1). An analysis of the explanted device was undertaken by Cochlear Ltd. The device analysis concluded that the device had failed due to a cracked hybrid integrated circuit. The postoperative course to date is good.

Discussion

Cochlear implant has been established as an effective treatment for profoundly deaf people. However, cochlear implant also has the possibility of ceasing to work because of mechanical failures. According to a previous report, there were some main causes of mechanical failure including a fracture of the central pin feed-through for the antenna coil, electrostatic discharges that damaged the internal receiver's integrated circuits, and damage to the electrode [3]. In this case, internal failure of the cochlear implant was most suspected by the radiological findings, the clinical course, and the results of the electrode impedance test and NRT. After re-implantation, the cause of the device failure was confirmed to be a cracked hybrid integrated circuit. This is a rare cause of mechanical failure.

At present, cochlear implant is recognized as a safe and useful treatment for profoundly deaf people all over the world. How long is the survival rate of a cochlear implant? In some papers, the cumulative survival rate of cochlear implants was >90% at 10 years after implant [4,5]. Improvement of the device is increasing the availability of cochlear implant. However, children receiving cochlear implants have a higher possibility of mechanical failure than adult users due to their activity and head growth [3]. In this case, the patient's high level of activity might have caused the internal failure of the cochlear implant, and such a situation is considered to be unavoidable in childhood. In the future, cochlear implants should be made much stronger, because childrens' activity and head growth are factors that cannot be avoided.

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Cochlear implants in post-lingually deafened patients

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Abstract

Conclusion. Post-lingually deafened patients had good speech intelligibility scores with cochlear implantation. The age at the operation, duration of deafness, and the number of electrodes outside the cochlea showed only weak correlation with the postoperative performance, which warrants cochlear implantation in elderly patients and patients with a long history of deafness and leaving dummy electrodes outside the cochlea. Patients with cochlear obstruction showed comparable performance to patients with an open cochlea. *Objective.* To evaluate the background and performance of post-lingually deafened cochlear implantation recipients. *Patients and methods.* Preoperative and intraoperative factors were collected for 109 cochlear implant subjects. Speech intelligibility scores were obtained and the effects of preoperative and intraoperative factors on postoperative performance were evaluated. *Results.* The average speech intelligibility score was 85.1% for vowels, 41.1% for consonant-vowel (CV) syllables, and 80.4% for phrases. The correlation coefficient between the age at the operation, the duration of deafness, and the number of electrodes outside the cochlea and the postoperative performance was between 0.03 and −0.27. Patients with cochlear obstruction and patients with open cochlea did not show significant differences in speech intelligibility tests. The onset of deafness (progressive vs sudden) did not have an effect on the speech intelligibility test.

Keywords: *Speech perception, performance*

Introduction

About 20 years have passed since the first report of cochlear implantation. With the improvement of the devices and coding strategies, recent studies report fairly good performance [1]. Today, cochlear implantation is widely accepted and regarded as a standard treatment for patients with profound sensorineural hearing loss (SNHL). In Kyoto University Hospital Department of Otolaryngology-Head and Neck Surgery, the first cochlear implantation was performed in 1987. In 1994, Nucleus 22 (Cochlear, Australia) was covered by public insurance, and cochlear implantation became a popular treatment. In 2000, Nucleus 24 (Cochlear, Australia) and Clarion S (Advanced Bionics, USA) were approved by the Japanese Ministry of Health and Welfare, and now these are the two most popular devices in Japan. In this paper, we report the background and performance of post-lingually deafened patients who underwent cochlear implantation with these devices. Additionally, we examined how the preoperative and intraoperative factors affected the postoperative speech intelligibility score.

Patients and methods

Between April 1987 and August 2005, 184 cochlear implantations were performed at the Kyoto University Hospital Department of Otolaryngology-Head and Neck Surgery. Among these patients, we investigated the background and performance of post-lingually deafened patients. In total, 109 patients were included in this study (52 males, 57 females). We analyzed patient demographics, implant devices, intraoperative findings, and postoperative performance of cochlear implants.

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Patient demographics

Patient demographics include the age at operation, etiology of the deafness, duration of profound deafness, and the presence of prior cochlear implantation. In most cases, the etiology of the deafness was unknown and the patients were divided into two groups – idiopathic progressive SNHL and idiopathic sudden SNHL. The duration of profound deafness was defined by determining the time when patients became unable to communicate with speech, even with hearing aids.

Implant devices and coding strategies

All the implant devices were multi-channel devices. Between 1987 and 1999, all the recipients received Nucleus 22. After 2000, Nucleus 24 was the first-choice device. Clarion S was implanted in patients who desired to receive Clarion S. With the introduction of new coding strategies, patients were given the opportunity to choose the best strategy.

Intraoperative findings

Intraoperative factors considered in this study were surgical approach, obstruction of the cochlea, and the number of electrodes outside the cochlea (in patients with Nucleus 22 and Nucleus 24). These data were obtained from the operation records.

Speech intelligibility test

The performance was evaluated with the speech intelligibility test. Vowels, consonant-vowel (CV) syllables, and short sentences were phonated by a male professional announcer and digitized at the sampling rate of 44 100 Hz. These speech samples were presented through speakers at 70 dB SPL using a computer (PowerMac PM-7300/166, Apple, USA) in random order, and the percentage of correct answers was obtained. In the vowel intelligibility test, 5 Japanese vowels were presented twice (total 10 vowels). In the CV syllable intelligibility test, 13 CV syllables, composed of 13 Japanese consonants and the vowel /a/, were presented twice (total 26 CV syllables). In the phrase intelligibility test, 10 short sentences were arranged to contain 40 phrases. The vowel and CV syllable intelligibility test were closed set, and the phrase intelligibility test was open set. These tests were performed at least 6 months after the operation.

Statistical analysis

Tests for statistical significance of correlations between patient demographics and intraoperative numerical parameters and speech intelligibility scores were performed using Spearman's correlation coefficient. For categorical parameters, the speech intelligibility scores were compared between different categories using the Mann-Whitney U test.

Results

Patient demographics

The etiologies of deafness were as follows: idiopathic progressive SNHL (51 patients); idiopathic sudden SNHL (13); chronic otitis media (12); drug-induced (6); head trauma (6); endolymph hydrops (5); otosclerosis (4); meningitis (4); large vestibular aquaduct (2); MELAS (1); radiation-induced (1); mucopolysaccharidosis (1); steroid-dependent hearing loss (1); hemosiderosis (1); Usher syndrome (1). Seventy-four patients reported that their hearing ability deteriorated gradually, and in the other 35 patients the onset of deafness was abrupt. Six patients had received cochlear implantation before, and were re-implanted because of mechanical trouble (five patients) or local infection (one patient). The age at the operation ranged from 10.4 to 81.5 years, and the average was 52.8 years (Figure 1). The duration of deafness was ranged from 1 month to 40 years, and the average was 7.6 years (Figure 2). Table I shows the demographic data for these parameters.

Implant devices and coding strategies

Fifty-four patients were implanted with Nucleus 22, 47 patients with Nucleus 24, and the other 8 patients with Clarion S. Coding strategies were SPEAK in 76 patients, ACE in 25, CIS in 3, SAS in 3, and PPS in 2.

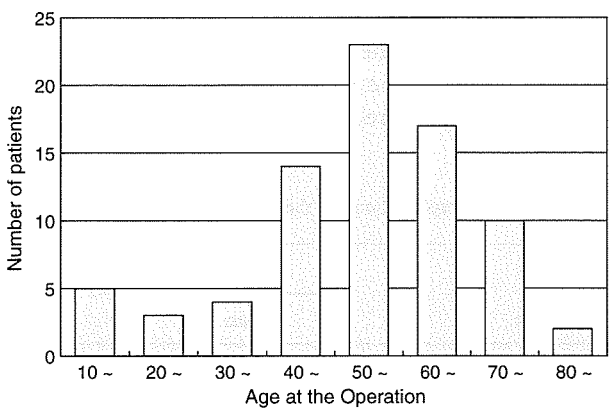

Figure 1. Age at the operation. The age at implantation ranged from 10.4 to 81.5 years, and the average was 52.8 years.

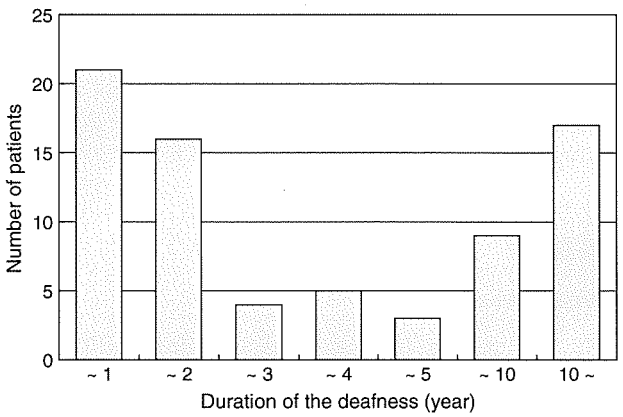

Figure 2. Duration of the deafness. The duration of deafness ranged from 1 month to 40 years. The age distribution did not follow the standard deviation with a first peak at <1 year and a second peak at >10 years.

Intraoperative findings

In 101 patients, posterior tympanotomy was performed and the electrodes were inserted by a transmastoid approach. In eight patients, canal wall down procedure and blind sac surgery were performed because of an earlier operation (four patients) or chronic otitis media (four patients). In nine patients, cochlear obstruction was identified during the operation. In four patients, the basal turn was filled with granulation tissue (re-implantation in two patients, head trauma in one, and idiopathic progressive SNHL in one). In the other five patients, partial ossification was identified (drug-induced, steroid-dependent, endolymph hydrops, idiopathic progressive SNHL, and head trauma, respectively). In three patients, ossification around the cochleostomy was removed and the electrodes were inserted as deep as possible. In one patient, the scala tympani was totally ossified and the electrodes were inserted into the scala vestibuli. In one patient deafened by head trauma, the X-ray revealed that the electrodes were straight and insertion into cochlea was uncertain. In this case, the number of electrodes outside the cochlea and the postoperative speech intelligibility test score were unobtainable.

In patients with Nucleus 22 and Nucleus 24, 0–16 electrodes including the dummy electrodes were left outside the cochlea. The average number of electrodes outside the cochlea was 5.0. The numbers of electrodes outside the cochlea are shown in Figure 3.

Speech intelligibility test

In 78 patients, a speech intelligibility test was performed >6 months after the operation. The average speech intelligibility score was 85.1% for vowels, 41.1% for CV syllables, and 80.4% for sentences (Figure 4).

Statistical analysis

The correlation coefficients estimated between the age at the operation, duration of deafness, and the number of electrodes outside the cochlea and the speech intelligibility score are shown in Table II. The correlation coefficients were below zero but the absolute value of correlation coefficient was no larger than 0.27, which means that these factors have only weak deteriorative effects on the result of postoperative speech intelligibility tests.

Patients with or without cochlear obstruction did not show significant differences in the speech intelligibility test ($p=0.09$ for vowels, $p=0.55$ for CV syllables, and $p=0.82$ for phrases, using the Mann-Whitney U-test). The onset of deafness (progressive vs sudden) did not have an effect on the speech intelligibility test ($p=0.43$ for vowels, $p=0.37$ for CV syllables, and $p=0.67$ for phrases, using the Mann-Whitney U-test) (Table III).

Discussion

Cochlear implantation is the only surgical treatment for profound SNHL. Our results revealed that patients with cochlear implants showed good performance in the speech intelligibility test, which reconfirmed the previous reports [1–3]. However, the inter-subject variability was prominent. As predictive factors, we examined the effects of the age at

Table I. Demographic data for the cochlear implantation recipients.

	Total ($n=109$)		Nucleus 22 ($n=54$)		Nucleus 24 ($n=47$)		Clarion S ($n=8$)	
Parameter	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Male:female ratio	52:57		25:29		22:25		5:3	
Age at operation (years)	52.8	17.1	52.9	17.4	51.9	17.9	57.8	9.5
Duration of deafness (years)	7.6	10.6	7.6	9.9	6.4	10.3	14.5	15.7

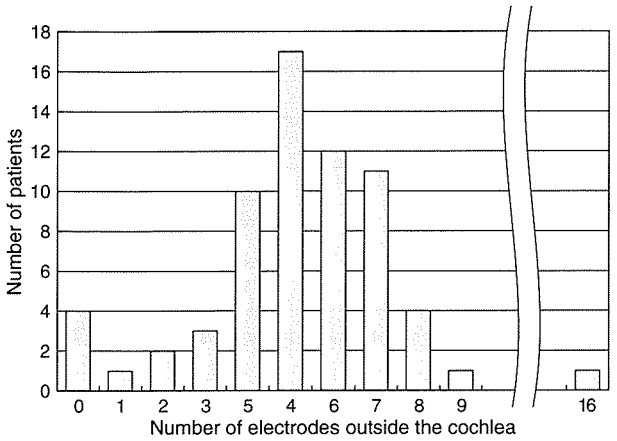

Figure 3. Number of electrodes outside the cochlea. In all but one case, all the active electrodes were inserted into the cochlea. The average number of electrodes outside the cochlea was 5.0.

the operation, duration of the deafness, number of electrodes outside the cochlea, cochlear obstruction, and the onset of deafness on the performance in the speech intelligibility test. The effects of these factors on the postoperative performance are still controversial. Good performance is reported in elderly cochlear implantation recipients [4–6]. Shin et al. [4] reported that there are no significant differences between young and old patients. In other studies, poorer performance in elderly patients was reported compared with younger patients [5,6]. The longer duration of deafness has been believed to have negative effects on the outcome [5,7]. However, some authors think that the effect is small [8]. Geier et al. [9] reported that patients with longer duration of deafness demonstrated a slower rate of speech recognition improvement than those with shorter durations of deafness, but still continued to improve

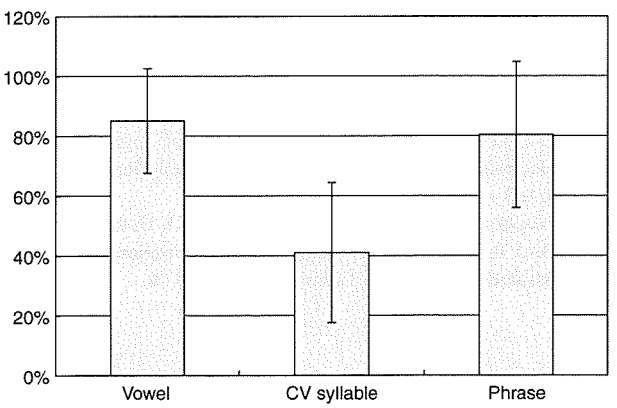

Figure 4. The results of postoperative speech intelligibility tests are shown. The mean speech intelligibility scores and standard deviation for three tests are shown. The average score was 85.1% for vowels, 41.1% for CV syllables, and 80.4% for sentences.

Table II. Correlation coefficient between the background and the performance (Spearman's correlation coefficient test).

	Vowels	CV syllables	Phrases
Age at operation (years)	−0.15	−0.25*	−0.27*
Duration of deafness (years)	−0.26*	−0.08	−0.26*
Number of electrodes outside the cochlea	−0.19	−0.25*	0.03

The absolute value of correlation coefficients is no larger than 0.27, which means that these factors have only weak effects on the results of postoperative speech intelligibility tests.
*$p < 0.05$.

with increased implant experience. Hamzavi et al. [10] reported that the duration of deafness had no effect on the postoperative performance 1 year after the implantation. These inconsistent results may be attributed to different methods of analysis. Some studies divide patients into two groups and compare the postoperative performance between groups. This analysis may be influenced by how the patient groups are defined and the size of effects is rarely mentioned. Some studies use parametric analysis. The duration of deafness is usually obtained according to self-report and may not follow the normal distribution, as show in Figure 2. In the present study, we obtained the correlation coefficient by a non-parametric method and showed that these factors have only weak correlation with speech intelligibility score. Waltzman et al. [8] used the same method as us and reported that the correlation coefficients for the age at implantation and the length of profound deafness were −0.29 and −0.29 each, very close to the values in our study. Our results proved that the age at operation and the duration of deafness have only weak deteriorative effects on postoperative performance. These results warrant cochlear implantation in elderly patients and patients with long duration of deafness.

The electrode insertion depth represented by the number of electrodes outside the cochlea showed only weak correlation to the performance. Khan et al. [11] reported that there was no significant correlation between the depth of insertion of the electrode array and postoperative word intelligibility score, and concluded that there are other clinical variables not yet identified that play an important role in determining success with cochlear implantation. Yukawa et al. [12] reported that deeper electrode insertion evaluated by postoperative imaging improved speech perception, but electrode insertion depth calculated from the number of electrode bands outside the cochlea was not related to performance. In the present study, too, the number of electrodes outside the cochlea was not a

Table III. The mean speech intelligibility scores in patients with or without cochlear obstruction and in patients whose onset of hearing loss was progressive or sudden.

	Vowel (%)		CV syllable (%)		Phrase (%)	
Condition	Mean	SD	Mean	SD	Mean	SD
Obstruction (−)	85.9	17.6	41.7	23.6	80.5	24.3
Obstruction (+)	77.1	15.0	35.1	21.6	79.0	27.2
Progressive	84.6	15.7	42.9	23.1	79.0	24.5
Sudden onset	86.5	21.4	37.0	23.9	83.9	24.5

Neither the cochlear obstruction nor the types of onset of deafness showed significant effects on the postoperative speech intelligibility scores.

decisive factor. In our study, the number of electrodes outside the cochlea ranged between two and seven in most cases. This may mean that insertion depth is not an influential factor if adequate numbers of electrodes are inserted into the cochlea.

The effect of etiology on performance is unknown because most of the causes of profound hearing loss are idiopathic. In this study, we divided hearing loss into two groups: sudden onset and progressive. These two groups did not show differences in the speech intelligibility test. The effect of etiology on postoperative performance should be investigated further. The speech intelligibility scores in patients with cochlear obstruction and patients with open cochlea did not show statistically significant difference. Hodges et al. [13] reported that speech recognition results of patients with ossified cochlea are essentially equal to those of patients with open cochlea, which is consistent with our results. However, in our study the number of patients was small, similar to the study by Hodges et al. Further investigation is necessary to determine the significance of cochlear obstruction.

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Clinical characteristics of delayed endolymphatic hydrops: long-term results of hearing and efficacy of hyperbaric oxygenation therapy

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Abstract

Conclusion. Diuretics significantly improved hearing in patients with contralateral-type DEH, whereas they did not inpatients with ipsilateral-type DEH. *Objective.* We report a review of 26 cases of DEH treated in recent 6 years. *Patients and methods.* The study group comprised 22 contralateral and 4 ipsilateral types of DEH. The efficacy of diuretics on the improvement in hearing was examined quantitatively. The efficacy of hyperbaric oxygenation therapy (HBO) on hearing was examined in six patients. *Results.* The general properties of these cases were similar to those reported previously, except for the high proportion of patients with contralateral-type DEH. Diuretics significantly improved the hearing of patients with contralateral-type DEH. In contrast, no significant improvement by diuretics was noted in ipsilateral-type DEH.

Introduction

Delayed endolymphatic hydrops (DEH) is an entity characterized by the endolymphatic hydrops that develops decades after the onset of unilateral profound hearing loss of the ipsilateral or contralateral side. After several reports on delayed onset episodic vertigo [1–3], Schuknecht [4] established the concept of this entity. DEH is usually treated in the same way as Meniere's disease, but is often intractable and hearing loss often progresses despite the pharmacotherapy. In this paper, we review 26 cases of DEH treated over a period of 6 years. We describe the characteristics of these cases, focusing on the efficacy of diuretics and long-term results of hearing. In addition, we report the efficacy of hyperbaric oxygenation therapy (HBO), which was performed in six cases.

Patients and methods

General characteristics of 26 cases

Cases were primarily retrieved from the patient database of Kyoto University Hospital between 2000 and 2006. Then the cases that met the following criteria were selected: (1) preceding profound hearing loss, and (2) fluctuating low-tone hearing loss and/or episodic vertigo. The general characteristics of these 26 cases are summarized in Table I. There were 9 males and 17 females; 22 cases were contralateral type and 4 cases were ipsilateral type. The average age at the onset of hydrops was about 48 years in both groups. The level of preceding hearing loss was significantly more profound in the patients with contralateral DEH. The average interval between the onset of hydrops and the onset of preceding hearing loss was longer in contralateral DEH than ipsilateral DEH, but there was no significant statistical difference between the two groups (unpaired t test).

Results

Efficacy of diuretics and long-term results of hearing

The mean follow-up periods of patients in each group were 3.85 (contralateral) and 5.15 (ipsilateral) years (range 0.34–7.28). None of the patients received surgery. Most of the patients (23/26) were treated with diuretics. The follow-up results of hearing in relation to the duration of diuretic

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Table I. General characteristics of 26 DEH cases.

Case no.	Age at onset of hydrops	Sex	Side of hydrops	Cause of preceding hearing loss	Level of preceding hearing loss[a] (dB)	Interval between hearing loss and hydrops (years)	Symptoms of hydrops: Hearing loss	Symptoms of hydrops: Vertigo
Contralateral type								
1	10.2	M	R	Unknown	95	10.2	+	−
2	20.5	M	L	Sudden deafness	90.8	10.5	−	+
3	23.0	F	R	Sudden deafness	>105.8	12.0	+	−
4	25.0	F	R	Unknown	>115	25.0	+	+
5	26.0	F	R	Unknown	>111.7	20.0	+	−
6	26.8	M	R	Unknown	>115	26.8	+	+
7	27.3	M	R	Unknown	>106	27.3	+	−
8	32.0	F	L	Unknown	>115	32.0	+	−
9	36.1	M	R	Otitis media	86.7	16.1	+	−
10	42.5	F	L	Mumps	>115	2.5	+	+
11	57.9	F	R	Sudden deafness	>109.2	9.9	+	+
12	59.3	F	L	Unknown	>115	59.3	+	+
13	61.8	M	L	Acoustic trauma	72.5	56.8	+	−
14	62.1	F	L	Sudden deafness	>90.8	7.1	+	−
15	64.3	F	R	Otitis media	92.5	64.3	+	−
16	65.0	F	R	Sudden deafness	72.5	38.0	+	−
17	65.7	F	L	Sudden deafness	78.3	6.7	+	+
18	67.7	M	R	Otitis media	95	57.7	+	+
19	68.3	F	L	Otitis media	67.5	58.3	+	−
20	69.0	F	L	Unknown	>115	69.0	+	−
21	72.7	M	L	Otitis media	>115	39.7	+	+
22	77.0	F	L	Otitis media	>115	67.0	+	+
Mean±SD	48.2±21.0 (NS)				83.4±10.8[b]*	32.6±22.8 (NS)		
Ipsilateral type								
23	36.0	F	L	Head injury	57.5	11.0	+	+
24	48.0	F	L	Sudden deafness	83.3	18.5	+	+
25	54.0	F	R	Otitis media	68.5	23.1	+	−
26	54.0	M	L	Head injury	62.5	8.3	+	+
Mean±SD	48.0±8.5 (NS)				68.0±11.2*	15.2±6.8 (NS)		

[a]PTA threshold is calculated as (A+2B+2C+D)/6 (A, 0.5 kHz; B, 1 kHz; C, 2 kHz; D, 4 kHz). [b]Values such as >105.8 were calculated as 105.8. *Significant difference ($p < 0.05$) between values in contralateral and ipsilateral DEH examined by unpaired t test. NS, no significant difference ($p \geq 0.05$) between values in contralateral and ipsilateral DEH examined by unpaired t test; F, female; M, male; L, left; R, right.

therapy are summarized in Table II. Isosorbide was administered to all 23 patients as the first choice of diuretics. In some patients, acetazolamide and/or furosemide were also used. For simplicity, we did not sort the patients by the kind or the dose of diuretics administered. Most patients took the diuretics for only part of the follow-up period. Hearing results were quantified by calculating the difference in the threshold of pure tone audiogram (PTA) (dB; average of lower three frequencies, i.e. 0.125, 0.25, and 0.5 kHz) divided by the duration of follow-up period (years)). This index was calculated for: (1) the overall follow-up period, (2) the period in which diuretics were administered, and (3) the period without diuretics. A positive value indicates improvement and a negative value indicates aggravation.

In most patients with the contralateral DEH, the PTA threshold evidently improved during the administration of diuretics whereas it slightly worsened in the period without diuretics. There was a highly significant difference between these two periods ($p < 0.01$; paired t test). In contrast, there was no significant difference between periods with and without diuretics in patients with ipsilateral DEH (paired t test). There was no significant difference in hearing improvement between patients with contralateral and ipsilateral DEH in either period with or without administration of diuretics (unpaired t test).

Table II. Long-term results of hearing in relation to the efficacy of diuretics.

Case no.	Follow-up period (years)	Period in which diuretics were administered (years)	PTA threshold[a] (dB) First	PTA threshold[a] (dB) Last	PTA difference (dB)/year (overall)	PTA difference (dB)/year (with diuretics)	PTA difference (dB)/year (without diuretics)
Contralateral type							
1	4.69	0.44	50.00	45.00	1.07	22.81	−1.18
2	6.75	1.50	5.00	5.00	0.00	3.34	−0.95
3	4.30	0.35	20.00	20.00	0.00	9.51	−0.84
4	4.29	1.78	40.00	36.67	0.78	2.81	−0.66
5	4.14	0.60	33.33	20.00	3.22	27.65	−0.94
6	4.00	0.26	90.00	85.00	1.25	57.63	−2.67
7	3.88	0.00	30.00	30.00	0.00	0.00	0.00
8	5.25	0.00	13.33	8.33	0.95	0.00	0.95
9	4.25	1.48	38.33	38.33	0.00	1.13	−0.60
10	2.42	0.96	15.00	26.67	−4.81	−3.48	−5.69
11	2.35	0.46	63.33	38.33	10.65	61.56	−1.77
12	3.41	0.41	33.33	35.00	−0.49	4.06	−1.11
13	6.49	2.33	30.00	15.00	2.31	5.73	0.40
14	7.28	3.32	28.33	33.33	−0.69	0.80	−1.93
15	1.21	0.15	10.00	5.00	4.14	21.73	1.42
16	3.67	2.01	70.00	28.33	11.37	16.55	5.04
17	3.82	1.45	53.33	56.67	−0.87	−1.15	−0.70
18	3.96	1.82	35.00	15.00	5.05	5.51	4.66
19	0.47	0.25	70.00	61.67	17.68	27.04	7.42
20	3.75	0.16	53.33	31.67	5.78	60.83	3.26
21	0.34	0.00	26.67	30.00	−9.89	0.00	−9.89
22	4.08	0.62	43.33	48.33	−1.22	2.70	−1.92
Mean±SD	3.85±1.77	0.92±0.90			2.10±5.68 (NS)	17.20±21.30 (NS)	0.35±3.57 (NS)
							**
Ipsilateral type							
23	5.30	0.62	60.00	76.60	−3.13	−5.41	−2.83
24	4.40	0.66	81.60	90.00	−1.91	2.53	−1.80
25	7.10	4.25	66.60	75.00	−1.18	−0.39	−2.36
26	3.80	0.21	65.00	66.60	−0.42	0.00	−0.45
Mean±SD	5.15±1.44	1.43±1.89			−1.66±1.15 (NS)	−0.82±3.32 (NS)	−1.86±1.03 (NS)
							(NS)

[a]PTA threshold is calculated as (A+B+C)/3 (A, 0.125 kHz; B, 0.25 kHz; C, 0.5 kHz). NS, no significant difference ($p \geq 0.05$) between values in contralateral and ipsilateral DEH examined by unpaired t test. **Highly significant difference ($p < 0.01$) between values linked by bridge by paired t test. NS, no significant difference ($p \geq 0.05$) between values linked by bridge by paired t test.

Efficacy of HBO

HBO was performed in six patients (nos 1, 5, 13, 16, 17, and 25). HBO was administered 15 times over a period of 21 days (on every weekday for 3 weeks). The HBO was provided as inhalation of 100% O_2 under 2 atm for 70 min. Because HBO was performed when diuretic therapy was not effective, no diuretics were administered during HBO in any of the patients. The effects of HBO on hearing are summarized in Table III. PTA thresholds (average of lower three frequencies) at the start and end of HBO are shown. In four patients, the hearing improved, and the hearing worsened in the other two patients. The degree of hearing improvement during HBO was calculated by the same method as described before, and compared with the improvement through the overall follow-up period. Although significant improvement was observed in four patients, there was no significant improvement of hearing following HBO in the average of all six patients who underwent this therapy (paired t test).

Discussion

The general characteristics of DEH of the patients in this report are basically similar to those in previous reports [5–7]. The most obvious difference from

Table III. Efficacy of HBO on hearing in patients with DEH.

Case no.	HBO term (days)	PTA[a] (dB) Start of HBO	PTA[a] (dB) End of HBO	PTA difference (dB)	PTA difference (dB)/year (during HBO)	PTA difference (dB)/year (overall)
Contralateral type						
1	21	63.33	53.33	10.00	173.81	1.07
5	21	40.00	33.33	6.67	115.87	3.22
13	21	35.00	40.00	−5.00	−86.90	2.31
16	21	75.00	63.33	11.67	202.78	11.37
17	21	56.67	53.33	3.33	57.94	−0.87
Mean±SD				5.33±6.60	92.70±114.78	3.42±4.70
Ipsilateral type						
25	21	66.67	68.33	−1.67	−28.97	−0.40
Mean				−1.67	−28.97	−0.40

[a]PTA threshold is calculated as (A+B+C)/3 (A, 0.125 kHz; B, 0.25 kHz; C, 0.5 kHz).

previous reports is the high proportion of patients with contralateral-type DEH compared with those with ipsilateral-type DEH. In the past reports the ipsilateral type was more frequent or both types had almost the same frequency.

There have been no reports on quantitative analysis for the efficacy of diuretics on DEH. The present report proved the efficacy of diuretics at least for hearing loss in contralateral DEH. At the same time, our report showed that the hearing worsened without therapy in most cases. The reason why diuretics did not act well in the ipsilateral type is unclear. Perhaps the number of cases with ipsilateral DEH was insufficient for the statistical analyses.

There have been several reports on the efficacy of HBO in Meniere's disease [8–10]. The supposed mechanisms of HBO for the treatment of hydrops are: (1) rescue of inner ear hair cells from hypoxia and recovery of normal metabolism, and (2) recovery of communication in the narrowed or obstructed endolymphatic pathway by pressure effect. In our cases, no significant improvement was obtained in average of all six patients, although significant improvement was observed in four patients. Further trial might prove the better effectiveness of HBO in patients with DEH.

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Severe acoustic trauma in adult rats induced by short duration high intensity sound

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Abstract

Conclusion. Short duration high intensity sound (SDHIS) induced severe functional damage in adult rats. *Objective:* Previous reports showed that SDHIS induced severe histological changes in the cochleae of guinea pigs. This study examined the hearing functions of rats exposed to SDHIS. *Materials and methods.* Animals were exposed for 1 min to a 137 dB sound pressure level (SPL) broadband noise. Auditory functions of the experimental animals were assessed using an auditory brainstem response (ABR) measurement system at frequencies of 8, 16, and 32 kHz before and 14 days after exposure to SDHIS. *Results.* After SDHIS, none of the experimental animals showed any response when stimulated by maximum SPLs at all frequencies of our ABR system.

Keywords: *Short duration high intensity sound, auditory brainstem response, acoustic trauma model*

Introduction

A previous study showed that high intensity sound (sound pressure level (SPL), 140 dB; exposure time, 5 min) induced severe histological damage in the guinea pig [1]. However, the details of functional damage caused by short duration and high intensity sound (SDHIS) have not been examined. In this study, we measured hearing levels of Sprague-Dawley (SD) rats at frequencies of 8, 16, and 32 kHz before and 14 days after exposure to SDHIS (137 dB SPL broadband noise).

At 14 days after SDHIS, all the experimental animals showed severe hearing disorders for all frequencies, suggesting permanent threshold shifts. This acoustic trauma model in rats may contribute to studies on the protection and functional regeneration of the inner ear.

Materials and methods

The experiments in this study were approved by the Animal Research Committee, Graduate School of Medicine, Kyoto University. Animal care was under the supervision of the Institute of Laboratory Animals, Graduate School of Medicine, Kyoto University.

Sound exposure

Six adult male SD rats were used for this sound exposure experiment. Both sides of the ears of three animals were exposed to SDHIS (experimental animals). The other three were used as a control. The animals were anesthetized by an intramuscular injection of ketamine (87 mg/kg) and xylazine (13 mg/kg). Under deep anesthesia, the experimental animals were fixed by clamping their incisors and tails to a handmade apparatus and were then exposed to sound (Figure 1). Broadband noise was generated by a combination of a noise generator (NP-203, JR Sound, Tokyo, Japan) as a source of white noise, an amplifier (SRP-P150, Sony, Tokyo, Japan), and speakers (horn super tweeter T925A, Fostex, Tokyo, Japan) with a frequency response from 5 kHz to 40 kHz. The three experimental rats were exposed to 137 dB broadband noise for 1 min in a soundproof room used for the measurement of human hearing function. Sound levels

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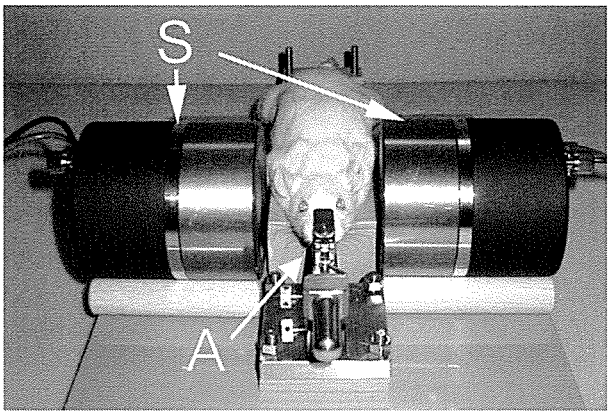

Figure 1. Under deep anesthesia, an experimental animal was fixed to a handmade apparatus by clamping its incisors (A). High-intensity broadband noise was generated from two speakers (S).

were monitored and calibrated using a sound level meter (LA2560, Onosokki, Yokohama, Japan).

Auditory brainstem response

To assess the auditory function of the animals, their auditory brainstem responses (ABRs) were measured 1 day before and 14 days after the acoustic exposure. The ABR threshold was measured at 8, 16, and 32 kHz. Generation of acoustic stimuli and subsequent recording of evoked potentials were performed using a PowerLab/4 sp (AD Instruments, Castle Hill, Australia). Acoustic stimuli, consisting of tone burst stimuli (0.1 ms cos2 rise/fall and 1 ms plateau), were delivered manually through a speaker connected to a funnel fitted into the external auditory meatus. To record bioelectrical potentials, subdermal stainless steel needle electrodes were inserted at the vertex (ground), ventrolateral to the measured ear (active), and contralateral to the measured ear (reference). Stimuli were calibrated against a ¼ inch free-field microphone (ACO-7016, ACO Pacific Inc., Belmont, CA, USA) connected to an oscilloscope (DS-8812 DS-538, Iwatsu Electric, Tokyo, Japan) or a sound level meter (LA-5111, Ono Sokki, Yokohama, Japan). The responses between the vertex and mastoid subcutaneous electrodes were amplified with a digital amplifier (MA2, Tucker-Davis Technologies, Alachua, FL, USA). Thresholds were determined from a set of responses at varying intensities with 5 dB SPL intervals and electrical signals were averaged over 1024 repetitions. Thresholds at each frequency were verified at least twice. An overall effect on the threshold shift was examined by two-way factorial ANOVA.

Results

ABR threshold data are shown in Table I. Before acoustic stimulation, the hearing levels of the experimental and intact animals were measured by ABR. The average hearing levels were −3.6 dB (SD = 5.5) SPL at 8 kHz, −4.5 dB (SD = 2.7) at 16 kHz, and 8.6 dB (SD = 6.7) at 32 kHz. The average right-side hearing thresholds were −3 (SD = 7.6), −4 (SD = 2.2), and 4 (SD = 2.2) dB, respectively. The average left-side thresholds were −4.2 (SD = 3.8), −4.2 (SD = 2.2), and 12.5 (SD = 6.9) dB, respectively. There was no significant difference between the right and left ears. The averages of the experimental group were −6.7 dB (SD = 2.6) SPL at 8 kHz, −5.8 dB (SD = 2.0) at 16 kHz, and 5.8 dB (SD = 3.8) at 32 kHz. The averages of the controls were −6.7 dB (SD = 2.6) at 8 kHz, −5.8 dB (SD = 2.0) at 16 kHz and 5.8 dB (SD = 3.8) at 32 kHz. There were no significant differences between the hearing thresholds of experimental animals and controls before the acoustic exposure. Two weeks after the acoustic stimulation, the ABR thresholds of the experimental and control animals were measured again. No response was observed in any of the experimental animals (Figure 2A), while the control animals showed no significant differences compared to the thresholds measured before SDHIS. The averages of threshold shifts in the experimental animals were 101.7 dB (SD = 2.6) at 8 kHz, 95.8 dB (SD = 2.0) at 16 kHz, and 99.2 dB (SD = 3.8) at 32 kHz (Figure 2C).

Discussion

In this study, a severe acoustic trauma model in rats was established by SDHIS. The thresholds of the hearing levels of all experimental animals were over the limits of our ABR measurement system. Previous reports showed that SDHIS (5 min, 140 dB white noise) exposure in guinea pigs caused disintegration or distortion of the organ of Corti (e.g. missing organ of Corti, outer hair cells swallowed, and pillar cell heads ruptured) [1]. Severe hearing disorders may be caused by these histological changes. The extent of the cochlear lesion depends on the exposure time of the sound, suggesting that the damage caused by the SDHIS in this experiment was restricted. ABR data showed SDHIS-induced severe auditory disorder. This irreversible hearing disorder may involve not only local damage to the organ of Corti but also disorders of vascular permeability, and/or potassium motility [2–6].

Acoustic trauma induces acute and chronic histological changes in the damaged inner ear. Acute phase alteration is suggested to affect the later phase sensory cell death caused by metabolic decompensation that induces cell death via the necrotic or apoptotic pathway. It is important to understand

Table I. ABR threshold data.

Group	No.	Side	8 kHz		16 kHz		32 kHz	
			Pre-SDHIS (dB SPL)	14 days SDHIS (dB SPL)	Pre-SDHIS (dB SPL)	14 day SDHIS (dB SPL)	Pre-SDHIS (dB SPL)	14 day SDHIS (dB SPL)
	1	Right	−10	s.o.	−10	s.o.	5	s.o.
		Left	−10	s.o.	−5	s.o.	5	s.o.
AOS	2	Right	−5	s.o.	−5	s.o.	0	s.o.
		Left	−5	s.o.	−5	s.o.	10	s.o.
	3	Right	−5	s.o.	−5	s.o.	5	s.o.
		Left	−5	s.o.	−5	s.o.	10	s.o.
	4	Right	−10	−10	−5	−5	10	10
		Left	−10	−5	0	5	0	10
Control	5	Right	10	0	−5	10	5	10
		Left	0	10	−5	0	15	20
	6	Right	0	0	−5	10	5	10
		Left	−5	5	−5	10	10	35

s.o., scale out; pre-SDHIS, ABR threshold 1 day before SDHIS; 14 day SDHIS, ABR threshold 14 days after SDHIS.

the mechanisms of fate determination of the damaged cells after acoustic trauma to protect inner ear sensory cells from cell death. Immediate early genes (IEGs) encode transcription factors that regulate downstream genes involved in cell proliferation, differentiation, and death of these cells. The genes expressed in several tissues within a few minutes after damage are candidates for those that decide the fate of damaged cells in the inner ear after acoustic trauma (i.e. apoptotic, necrotic cell death, or survival). It is known that several genes are expressed immediately after damage [7,8]. IEGs are up-regulated by stimuli from optimal ambient conditions, generally within a few minutes; their

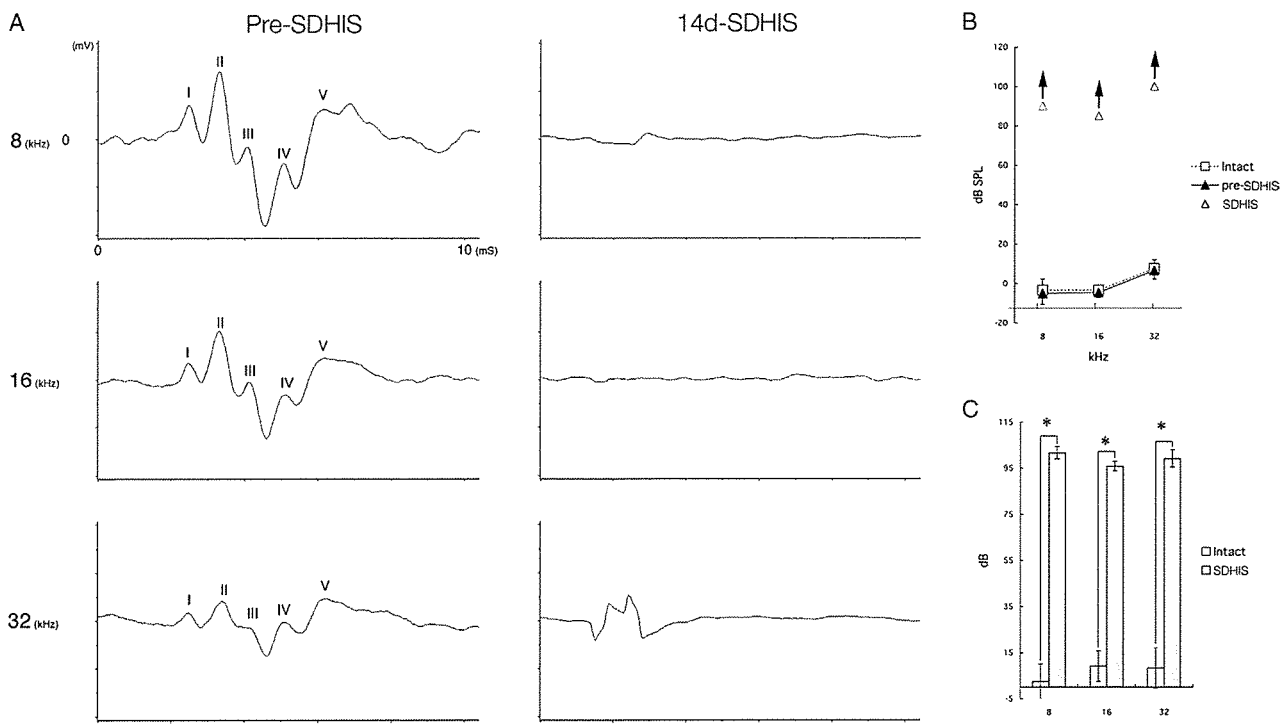

Figure 2. ABR results showed that the threshold of experimental animals exposed to the SDHIS increased. (A) When the ABR of the experimental animal (no. 4) was measured before the acoustic stimulation, wave peaks I, II, III, IV, and V were observed at frequencies of 8, 16, and 32 kHz. Two weeks after the acoustic stimulation, no wave peaks were observed at any frequency. Pre-SDHIS, ABR 1 day before SDHIS; 14d SDHIS, ABR 14 days after acoustic stimulation. (B) The ABR thresholds of the experimental animals were markedly increased. Two weeks after SDHIS, thresholds at all frequencies in the experimental animals were above the range of our ABR system, while there was no significant difference in the ABR thresholds at each frequency between the control and experimental animals before SDHIS. (C) ABR measurement showed significant differences in threshold shift at all frequencies between experimental and intact animals ($p < 0.0001$).

expression then decreases within a few hours. In this study, we established a rat acoustic trauma model by 1 min exposure to SDHIS. This acoustic trauma model may contribute to the analysis of gene expression profiles within a few minutes after SDHIS.

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