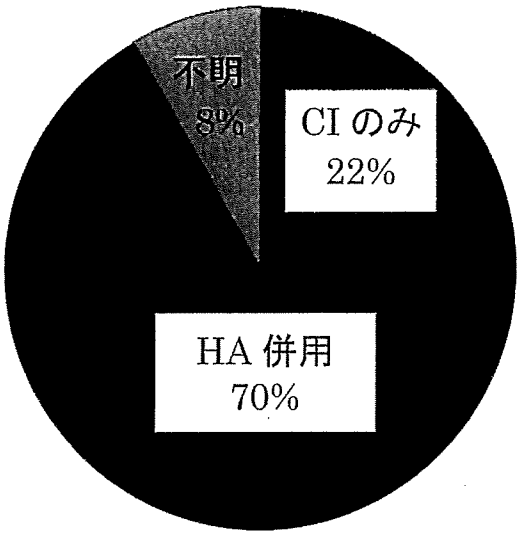


図1　当院での人工内耳装用者における補聴器の装用状況

た小児例108例のうち，補聴器を併用している症例は75例（70%）であった（図1）。人工内耳単独装用は24例（22%），不明は9例（8%）であった。

1．静寂下での聴取能評価

はじめに，静寂下での効果について検討した。対象は2008年までに当院にて人工内耳埋込術を行いかつ対側耳に補聴器を併用している小児例のうち，現在も通院中の症例の中からランダムに選んだ31例（男児15例，女児16例）であり，2006年から2009年にかけて装用効果の評価を行った。対象群の音入れの年齢は2才5ヶ月～7才4ヶ月（平均4才0ヶ月），評価時の年齢は3才5ヶ月～14才1ヶ月（平均7才5ヶ月），装用期間は0年11ヶ月～9年7ヶ月（平均3年5ヶ月）であった。検査は67-S語表を使用し，補聴器単独（HA），人工内耳単独（CI）と，対側に補聴器を併用（CI+HA）した3条件下で検査を行った。3条件の検査順はランダムに行った。検査音は静寂下で，両側外耳道入口を結んだ正中の前方1mに設置したスピーカーより70dB SPLで呈示した。解析はpaired t 検定にて比較を行った。誤差範囲は標準誤差（SE）を呈示した。

HA単独，CI単独，CI+HAの間で67-S語表聴取の正答率を比較した。装用効果は療育期間の長さ・対側耳の聴力レベル，補聴器の装用効果などの要因によって影響を受けている可能性もあるため，他の要素による影響があるかも併せて検討を行った。人工内耳装用開始後の療育期間は0年11ヶ月～9年7ヶ月であり，2群がほぼ同症例数になるように，36ヶ月を境にして，短期療育群（11-36ヶ月，15例）と長期間療育群（37ヶ月以上，16例）の2群にわけ検討した。人工内耳の対側耳の状況により併用効果が異なる可能性も考えられ，人工内耳適応基準の90dBHLに近い残存聴力がある症例の方が補聴器併用効果も高い可能性が存在し，その影響を検討した。対側耳の500Hz，1000Hz，2000Hz各周波数の4分法による平均聴力レベルは，80-120dBHLであり，2群がほぼ同数になるように，105dBHL以内（17例）と，105dBHL超（14例）の2群にわけ比較した。さらに対側耳で，補聴器をより良く使えている状態の方が，補聴器併用効果が高い可能性があるため，補聴器の聴取成績で2群にわけ，検討を行った。補聴器による正答率は0-75%であり，中央値で2群にわけ，0-5%の群（16例）と10%以上の群（15例）で比較を行った。人工内耳単独での正答率が良好で100%に近い場合，天井効果の為に補聴器併用効果が認められにくくなっている可能性も考えられるため，人工内耳単独での正答率によって2群に分けた検討も行った。人工内耳単独の正答率は20-100%であり，検討は2群がほぼ同数になるように80%以上の成績の群（14例）と，80%未満の群の2群（17例）に分けて，比較を行った。

2．騒音下での聴取能評価

次に騒音負荷下での効果について，静寂下の検討を行った症例の中からランダムに選んだ小児6例（男児3例，女児3例，6-9才　平均7.4才）を対象に検討を行った。これらの症例の平均装用期間は4年5ヶ月であった。検査はCI2004学童用日常生活文を使用した。刺激音は70dB SPLとし，CI2004検査実施手引書の双スピーカー法に従い，両側外耳道入口を結んだ正中の前方1mに設置した2台のスピーカーより，上方の1台からは語音を，下方の一台からはノイズを呈示した。測定は，CI，CI+HA両条件下で行った。静寂下での評価の他に，スピーチノイズを50，60，65，70dB SPLと段階的に負荷を行った5条件で行った。条件は，静寂下から開始し，次にノイズを50dB SPLで負荷し，徐々に負荷を増大させて行った。音圧については，何れもスピーカーが呈示する音圧であり，ノイズについてはバ

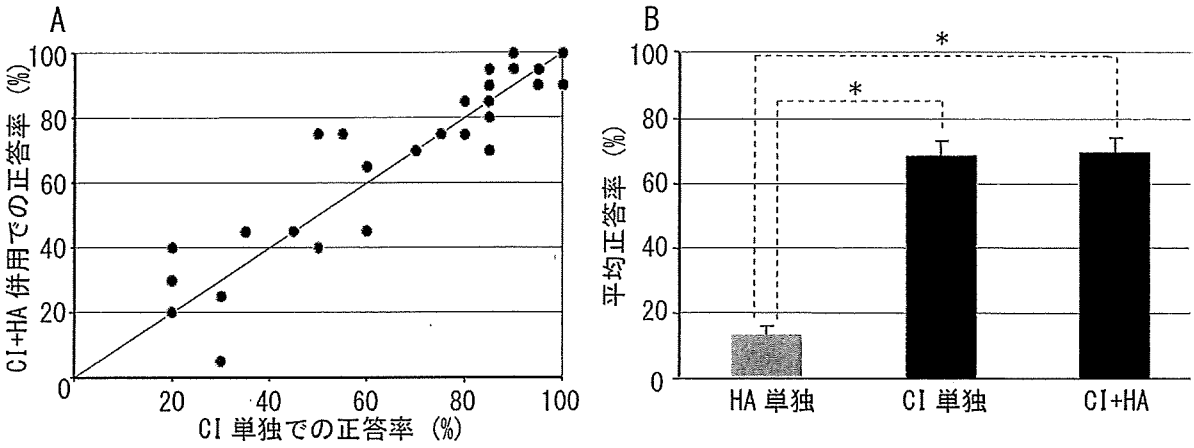


図2　補聴器併用の有無による正答率の比較
A：人工内耳単独と，補聴器併用時の正答率の分布。B：補聴器単独・人工内耳単独・補聴器併用各群の平均正答率。誤差範囲は，標準誤差。＊<0.05

ンドノイズで校正を行った上で使用した。検査の際，被検者が疲労を訴えた場合，または段階的にノイズを負荷して，正答率が50%未満になった場合に中止とした。

結　果

1）静寂下での効果

図2AにCI単独，CI+HA併用の67-S語表の正答率の関係を示した。横軸はCI，縦軸はCI+HAの正答率の分布である。CIとCI+HAはほぼ一致した分布をしている。両条件とHA単独使用時の聴取成績のそれぞれの平均正答率を図2Bに示した。HAでは13.4±3.2%，CIでは68.7±4.7%，CI+HAでは，69.5±13.4%であった。HAと比較して，CI，CI+HAとも，有意に聴取成績は良好であった（p<0.0001）。一方，CIとCI+HAの間には有意差は認められなかった（p=0.56）。

補聴器併用効果を得るには，長期の療育が必要な可能性も考えられるため，36ヶ月を境にして，短期療育群（11-36ヶ月）と長期間療育群（37ヶ月以上）の2群にわけ検討した。短期療育群での，CIの平均正答率は，60.3±7.0%，CI+HAでは65.0±7.0%で，2条件間には有意差は認められなかった（p=0.64）。長期療育群でも，CIでは76.5±5.9%，CI+HAでは74.0±7.0%で，2条件間には有意差は認められなかった（p=0.78）（図3）。

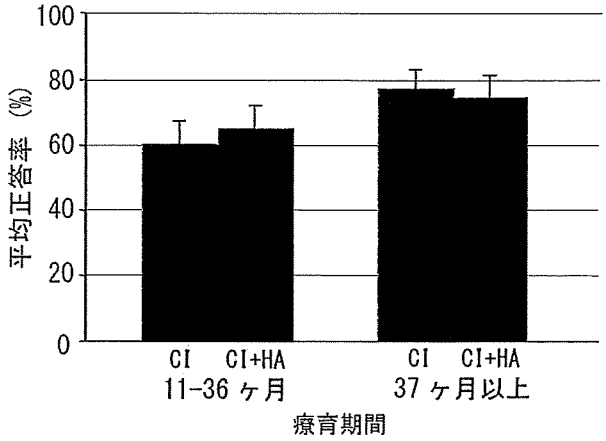


図3　療育期間の長さで分けた2群での比較

人工内耳の対側耳の残存聴力により105dBHL以内と105dBHL超で2群にわけ検討した。その結果，105dBHL以内群（CI：65.0±6.3%，CI+HA：66.6±7.1%）でも，105dBHL超群（CI：73.2±6.9%，CI+HA：72.9±7.3%）でも，CIと，CI+HAでの聴取成績には有意差は認められなかった。つまり，残聴の程度による明らかな差は認められなかった（105dBHL以内群　p=0.87，105dBHL超群　p=0.97）（図4A）。

次に対側耳の補聴器の聴取成績の中央値で2群にわけ，0-5%の群と10%以上の群で検討を行った。0-5%群では，CIの平均正答率は，66.9±6.7%，CI+HAは65.0±7.9%，10%以上の群ではCIは，70.7±6.8%，CI+HAは74.0±7.0%であった。CIとCI+HAの間には，0-5%の群と10%以上の群どちらにおいても，やはり有意差はみられなかった

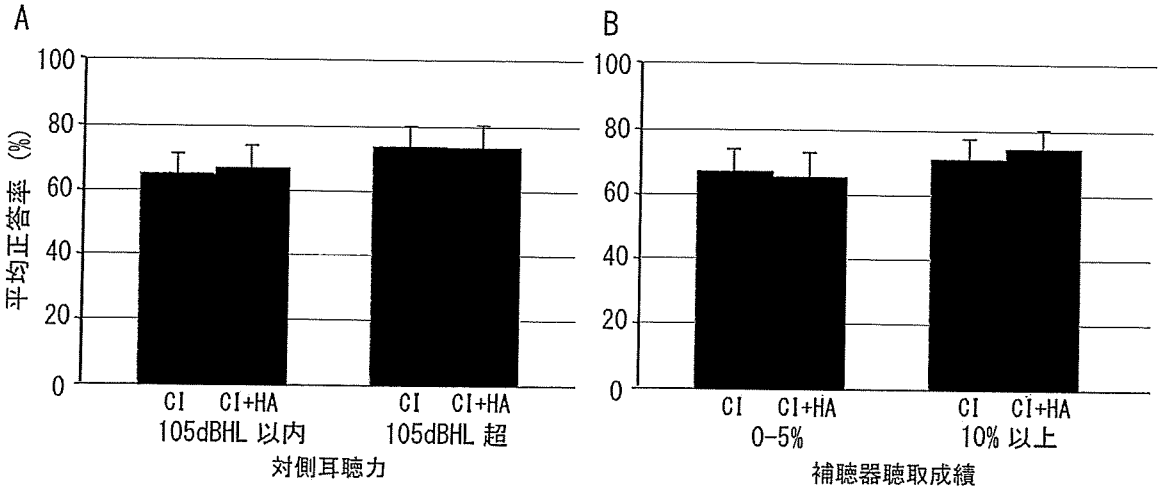


図4　対側耳の成績による比較
A：対側耳の聴力で分けた2群での比較。B：対側耳での補聴器聴取成績で分けた2群での比較。

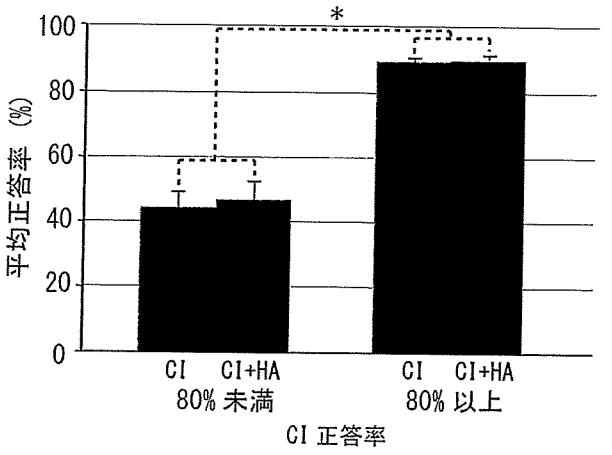


図5　人工内耳単独での聴取成績で分けた2群での比較

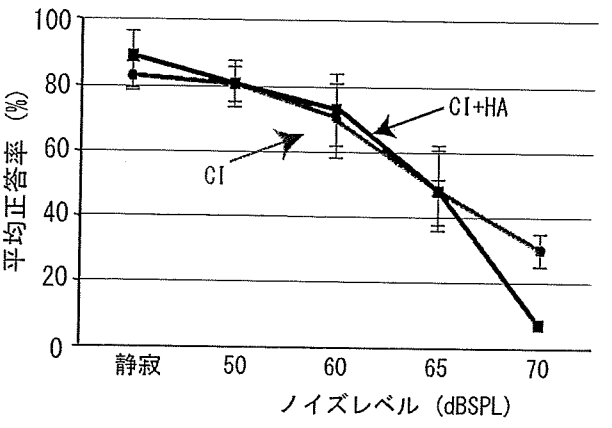


図6　騒音負荷下の人工内耳単独と補聴器併用での聴取成績
黒色は，補聴器併用条件下，灰色は，人工内耳単独条件下での聴取成績。誤差範囲は，標準誤差。

（0－5％群　$p=0.85$，10％以上群　$p=0.72$）（図4B）。

片耳人工内耳下の聴取成績における天井効果を除く為に，人工内耳単独での正答率が80％以上の成績の群と，80％未満の群の2群にわけ，検討を行った。80％以上では，CIの平均正答率は，44.3±5.0％，CI＋HAは46.8±6.0％，80％未満ではCIは，88.8±1.6％，CI＋HAは89.4±2.1％であった。聴取成績は，80％以上の群において，80％未満の群より良好であったが，いずれの群においても，CIとCI＋HAの間では有意差は認められなかった（80％未満群　$p=0.75$，80％以上群　$p=0.84$）（図5）。

静寂下での検討結果をまとめると，CI・CI＋HAとも有意差がみられず，他の要素（療育期間，対側耳の聴力，対側補聴器の聴取成績，人工内耳単独での成績）とあわせた検討でも，聴取成績に対する補聴器の併用効果は確認できなかった。

2）騒音負荷における検討

両耳聴取を行うと，カクテルパーティー効果により，騒音下での聴取に有利に働くことが考えられる。今回，片耳に人工内耳を装用した条件（CI）と，対側耳にも補聴器を併用して両耳聴できる条件（CI＋HA）とにおける騒音下の聴取能比較をおこなった（図6）。ノイズ負荷が増大するにつれ，どち

らの条件下においても聴取成績が低下した。2群間の間にも統計上の有意差はみられなかった（静寂下：$p=0.32$，50dBSPL：$p=0.49$，60dBSPL：$p=0.47$，65dBSPL：$p=0.40$）。

考　察

今回，静寂下・騒音下いずれの条件の検討においても，人工内耳の対側耳に補聴器併用による聴取能の向上効果が認められなかった。この結果は海外の先行研究と異なっているが，その理由としていくつかの要因が考えられる。まず，海外に比べて，本邦では人工内耳適応基準が厳しいということが挙げられる。本邦での，人工内耳の適応においては，難聴の程度だけでなく，補聴効果が認められなかった症例を対象とするとされており，もともと補聴効果が期待できない症例が人工内耳の対象となっている。海外では，たとえば米国では，現在成人例では両側70dBHLで，補聴器で静寂下でのThe Hearing and Noise Test（HINT）の正答率が50%のレベルの難聴でも人工内耳の使用はFDAにより認可されているが，本邦では90dBHL以上の難聴者が対象であり，残聴に対する補聴効果が得られにくいと考えられる。二点目として，今回の検討では症例数が少なく，そのため統計的有意差が出にくかった可能性も考えられる。三点目としては，日本語と外国語では，発音，母音の出現頻度，周波数的特徴など，言語的な特徴に違いがあるため，日本語では補聴器併用効果が少ない可能性が考えられる。英語などの外国語では日本語に比べて子音，母音ともに種類が多く，また使われる周波数の幅も外国語の方が大きいと言われている。例えば英語の“r”と“l”のように，わずかなspectrumの違いが聞き分けに重要となってくるものも見られる[7]。チャンネル数の限られる人工内耳と異なり，補聴器ではすべての周波数を伝達することが可能であり，わずかなspectrumの違いの認知が必要な外国語の語音弁別において，より有効に働いているのかもしれない。日本語においても，松代ら[6]による成人6例の検討では，3例で補聴器併用による67-S語表の聴取成績の向上を認めている。この成人の中途失聴症例では失聴前は両耳聴が可能であったことから，両耳聴に関わる脳回路ができあがっていたと考えられる。今回のような小児例では先天的に失聴していたため，脳回路の発達が不十分で，対側耳に補聴器併用しても成人例より両耳聴が困難になっているのかもしれない。なお，今回検討を行わなかった音源定位や音楽聴取などの他の要素に補聴器併用の効果がある可能性は残されている。

人工内耳装用者において補聴器併用による静寂下および騒音下での聴取能の向上が期待されているが，今回の検討ではこれらの効果は認めなかった。現在，我々の施設では人工内耳の適応決定は日本耳鼻咽喉科学会の適応ガイドラインを遵守しており，この基準により選ばれた人工内耳装用者においては補聴器併用の効果が乏しいと言える。この基準では人工内耳の適応とならずに補聴器装用をしている患者に対して人工内耳装用を行った場合には，対側耳補聴器装用による併用効果がみられる可能性はあり，これは今後の検討課題であろう。現在の基準で適応決定を行った場合には聴取成績の向上が補聴器併用では見られなかったことから，この基準を遵守してなおかつ聴取能を更に向上させるためには，人工内耳機器の改良，新たなコード化法の開発などのデバイス機能の改善による聴取能の向上，または補聴器より以上に対側耳を積極的に活用する両側人工内耳装用などが必要と考えられる。

本論文の要旨は，第54回日本聴覚医学会学術講演会（2009年10月，横浜市）の主題に関する演題として口演した。

Benefits of dichotic hearing under silent and noisy conditions in pediatric cochlear implant users wearing a hearing aid for the opposite ear

Takuya Yasui[1)], Akinori Kashio[1)], Erika Ogata[1)], Yusuke Akamatsu[1)], Mitsuya Suzuki[2)], Tatsuya Yamasoba[1)]

[1)]Department of Otolaryngology, Graduate School of Medicine
[2)]Toho University Sakura Medical Center

Auditory localization and the cocktail party effect are examples of the advantages of dichotic hearing. Bilateral cochlear implants have already begun to be used in many countries, and been reported to enable good performances of the patients in speech recognition tasks. In Japan, cochlear implant users generally use a hearing aid for the opposite ear, because the benefits of use of a hearing aid for contralateral ears have been reported by many studies from other countries. We examined the benefits of use of a hearing aid for the contralateral ear in Japanese patients under silent and noisy conditions. Under the silent condition, there was no significant difference in the hearing ability between subjects with unilateral cochlear implants and those with unilateral cochlear implants with a hearing aid for the contralateral ear. According to further analyses taking into consideration other components, such as the period of wearing, hearing ability of the contralateral ear and that of the cochlear implant, no benefits were observed. Under the noisy condition also, no significant difference in the hearing ability was observed between the two groups. Some causes are suggested for the absence of the benefits of contralateral hearing aids in the present study: stringent criteria for the fitting of cochlear implants; the small number of cases in the study; the phonemic features of Japanese. To improve the hearing ability in cochlear implant users, we suggest aggressive use of the contralateral ears, using bilateral cochlear implants if necessary.

参考文献

1) Broadbent DE: Perception and communication. Pergamon Press, New York, 1958

2) Nabelek AK, Pickett JM: Monaural and binaural speech perception through hearing aids under noise and reverberation with normal and hearing-impaired listeners. J Speech Lang Hear Res **17**: 724-739, 1974

3) Papsin BC, Gordon KA: Bilateral cochlear implants should be the standard for children with bilateral sensorineural deafness. Curr Opin Otolaryngol Head Neck Surg **16**: 69-74, 2008

4) Litovsky RY, Johnstone PM, Godar S, et al: Bilateral cochlear implants in children: localization acuity measured with minimum audible angle. Ear Hear **27**: 43-59, 2006

5) Mok M, Galvin KL, Dowell RC, et al: Speech perception benefit for children with a cochlear implant and a hearing aid in opposite ears and children with bilateral cochlear implants. Audiol Neurootol **15**: 44-56, 2010

6) 松代直樹，佐藤崇，井脇貴子，他：人工内耳と補聴器の両耳装用における両耳聴効果について。日耳鼻会報 **106**: 211-219, 2003

7) Flege JM, Takagi N, Mann V: Lexical familiarity and English-language experience affect Japanese adults' perception of /r/ and /l/. J. Acoust. Soc. Am **99**: 1161-1173, 1996

(原稿受付 平成22. 3. 25)

別冊請求先：〒113-8655
東京都文京区本郷7-3-1
東京大学医学部耳鼻咽喉科
安井 拓也

Reprint request:
Takuya Yasui
Department of Otolaryngology, Graduate School of Medicine, The University of Tokyo, 7-3-1 Hongo, Bunkyo-ku, Tokyo 113-8655, Japan

Activation of the Auditory Cortex in a Child with a Cochlear Implant: an Optical Topography Study

Y. Osaki, K. Doi, C. Masumura, K. Suwa, M. Hanamoto, H. Inohara.
Department of Otorhinolaryngology, Head and Neck Surgery,
Osaka University Graduate School of Medicine, Suita, Osaka 565-0871, Japan.

Summary

We measured neural activation of the central auditory system in a prelingually deaf cochlear implant (CI) patient on the day of first fitting. Optical topography was used to assess cortical activity non-invasively while auditory stimuli were presented through the CI. Deoxyhemoglobin (deoxy-Hb) as well as sum of oxyhemoglobin (oxy-Hb) and deoxy-Hb increased in the temporal region during the auditory stimuli, reflecting activation of the temporal cortex. Examination of the central auditory system would benefit the rehabilitation process of the CI.

Introduction

Cochlear implantation (CI) is a well-established treatment for prelingually deaf children. These days CI operation tends to be performed earlier in the patient's life, making the postoperative fitting more difficult. Although neural responses of the peripheral auditory system can be recorded by most of modern CIs, it is still difficult to evaluate the activity of the central auditory system, because functional MRI (fMRI) cannot be used for CI patients and because the parents hesitate to participate in PET studies due to irradiation. Optical topography, or Near-Infrared Optical Spectroscopy (NIRS), is a neuroimaging method which measures brain activations non-invasively. Near infrared light penetrates the tissue to a certain depth and undergoes partial absorption by blood hemoglobin (Hb) along the light path. By continuously measuring the reflected light on the skull, relative changes of the concentration of oxyhemoglobin (oxy-Hb),

deoxyhemoglobin (deoxy-Hb), and total hemoglobin (total-Hb) in specific brain region can be monitored, reflecting local brain responses. In this study we used an optical topography system to study activation of the auditory cortex in an infant CI user.

Materials and Methods

A two-year-old prelingually deaf girl participated in this study. She was diagnosed as severe hearing loss at the age of 12 months, and continued to use hearing aids on both sides. Auditory brainstem response was absent at 105 dBnHL at all times. She had implanted with a Nucleus® 24 system on the left ear at the age of 24 months. This optical topography study was done 13 days after the operation, on the day of first fitting. Before the study, two speech therapists obtained neural response telemetry (NRT) and set T and C levels by evaluating the patient's behavioral responses. A portable CD player was connected to the external input of the speech processor to present auditory stimuli.

Three light emitting and three light receiving probes of an optical topography system (ETG-100, Hitachi, Japan) were attached to the temporal region of the head opposite to the CI (Figure 1). Each probe was kept 3 cm apart by a probe holder. Quantitative changes of oxy-Hb, deoxy-Hb, and total-Hb were recorded at seven different recording sites (channels), which were expected to cover the perisylvian region (Figure 1). Auditory stimuli, which were consisted of spoken words of four syllables, were presented for twenty seconds, and then turned off for twenty seconds. This was repeated for ten times, making the total measurement time for about seven minutes. The patient was tested while seated in a chair playing with toys. Written informed consent was obtained from the parents. The protocol was in compliance with the ethical committee of the institute.

Results

No obvious behavioral change was observed between the stimulated and

silent periods. In channel 13, which was located in the anterior-inferior part of the measurement site, oxy-Hb and total-Hb decreased during the auditory stimuli (Figure 2). In channel 15 and 18, located in the anterior portion, deoxy-Hb and total-Hb increased while oxy-Hb decreased during the stimuli (Figure 2). Hb concentration did not change significantly in other channels.

Neural activation typically induces an increase of regional cerebral blood flow (CBF) as well as cerebral blood volume (CBV), which are reflected by increase of oxy-Hb and total-Hb[1]. However, increase of deoxy-Hb during task stimuli is also reported in normal neonates[2]. Increase in oxygen consumption is thought to exceed increase in oxygen delivery during neural activation, presumably due to immature neurovascular coupling[2]. Our findings, that deoxy-Hb and total-Hb increased in channels 15 and 18 during the stimuli, might reflect neural activation of the temporal auditory cortex.

Conclusions

Our optical topography study demonstrated that the auditory cortex of an infant CI patient was activated on the day of the first fitting. In some cases it is difficult to evaluate the behavioral response of infant CI patients to sound stimuli. Examination of the central auditory system might help the rehabilitation process of the CI.

References

1 Y. Hoshi, N. Kobayashi, and M. Tamura. Interpretation of near-infrared spectroscopy signals: a study with a newly developed perfused rat brain model. J. Appl. Physiol. 90: 1657-1662, 2001.

2 K. Sakatani, S. Chen, W. Lichty, H. Zuo, and Y.P. Wang. Cerebral blood oxygenation changes induced by auditory stimulation in newborn infants measured by near infrared spectroscopy. Early. Hum. Dev. 55: 229-236, 1999.

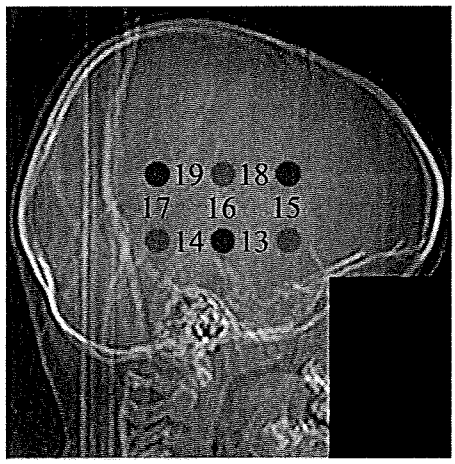
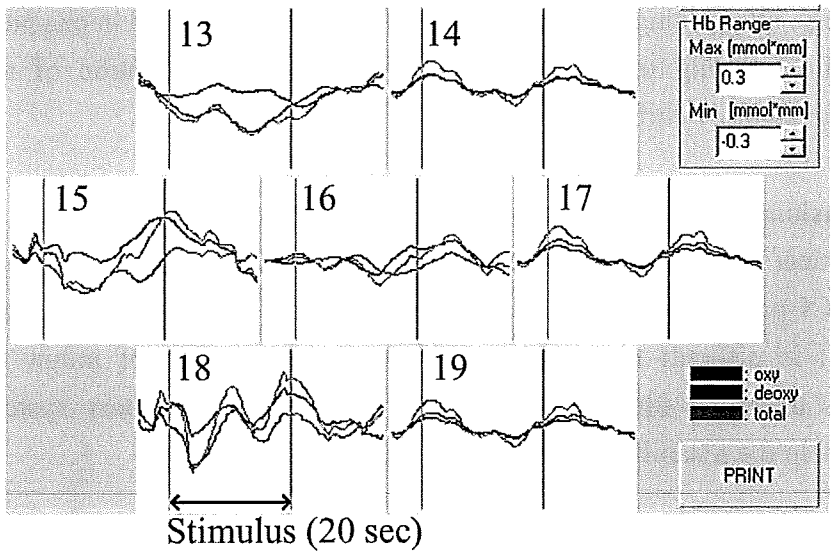


Figure 1.

Schematic diagram of the three light emitting (red) and three light receiving (blue) probes on the right temporal region. Numbers indicate the layout of the seven recording sites, called channels.

Figure 2



Changes of oxy-Hb (red), deoxy-Hb (blue) and total-Hb (green) concentrations during the experiment. Cyan and green vertical lines represent start and stop of the sound stimuli. Waveforms were obtained by averaging the data of ten measurement cycles. Note that the channel locations are rotated 180 degrees from Figure 1. During the auditory stimuli, oxy-Hb and total-Hb decreased in channel 13 (upper left), while deoxy-Hb and total-Hb increased in channels 15 and 18 (left and lower left).

Benefits of Cochlear Implantation in Elderly Patients

S Hio, K. Doi, Y. Osaki, K. Ohata, K. Suwa, M. Hanamoto, H. Inohara, T. Hasegawa
Department of Otorhinolaryngology, Head and Neck Surgery,
Osaka University Graduate School of Medicine, Yamadaoka2-2, Suita, Osaka 565-0871, Japan.

INTRODUCTION

Due to improvements in preventative healthcare, the number of elderly patients in our community has risen dramatically. Hearing impairment is one of the most common disabilities in the elderly. It was previously thought that cochlear implantation (CI) in the elderly may not be beneficial because of age-related generation of both central and peripheral auditory system, surgical risk, and overall cost to benefit ratio. However, recent studies have shown that this procedure improves auditory performance, enhances self-confidence, and well tolerated in the elderly[1-2].

In this study we quantified and compared the listening performances of our CI patients. Especially we questioned whether listening performances of CI users who had implanted after becoming 65 years old were different from those who had operated before becoming 65 years old.

MATERIALS AND METHODS

Totally 263 adult patients had CI in Osaka University Medical Hospital between 1991 and 2008. Those who elected to participate completed a standard history and physical examination. This included documentation of their sex, age at implantation, side implanted, the cause of deafness, and device of CI.

Patients were divided into two groups according to the patient's age at implantation (older than 65 yo or younger than 65 yo). We assessed their performances of listening by means of intelligibility scores of consonants, words, and short sentences at different times after the implantation; 6 months, 1 year, 2 years, 3 years, 4 years, and more than 5 years after operation. Scores of the two patient groups were compared by means of t-test, with a statistical threshold of $p<0.05$.

RESULT

Demographic characteristics

The median age of the study group at the time of implantation was 57 years. The male to female ratio was about 1:2. The side of implantation is about the same. In 69.4% of our subjects, we could not identify the precise cause of sensorineural hearing

loss. The commonest identifiable causes were otitis interna and chronic otitis media. Other important causes were meningitis, streptomycin ototoxicity and Meniere's disease (Fig.1).

All the patients received a multi-channel implant. The most commonly used type was the Nucleus CI22M (n=99) followed by the Nucleus CI24M (n=44), the Nucleus CI24RCS. Nine patients received HiRis CI and one received a HiRis 90K. Medel Combi40+ devices were used in three patients.

Audiological outcomes

Generally, intelligibility scores tended to be low in the patient group of 65 or older in all of the consonant, word and sentence conditions. However, a significant difference of the scores was seen only in the short sentence condition three years after the operation (Fig.2).

We examined influence of visual information in the language intelligibility. There was no significant difference between the two groups in the visual influence on intelligibility scores, indicating that auditory-visual association cortex might be still active even in the elderly patients.

DISCUSSION

CI in the elderly poses special considerations because of age-related degeneration of the spiral ganglion cells and the deficits central auditory pathways. However, the results of this study show that patients greater than 65 years old experience a significant improvement in auditory performance. Additionally, the listening performances between elderly patients and those less than 65 have shown no significant difference between the two groups in most term. These results are similar to those observed in previous studies[1-2].

CONCLUSION

There were little differences of intelligibility scores between the two patient groups, indicating that the patient's age at the time of operation does not influence much on the listening performances of elderly CI users. The results suggest that the elderly population with profound hearing loss obtain significant benefits from CI despite possible age-related auditory processing problems.

REFERENCES

1. AA. Eshraghi, M. Rodriguez, TJ. Balkany, FF. Telischi, S. Angeli, AV. Hodges, E. Adil. Cochlear implant surgery in patients more than seventy-nine years old.

Laryngoscope 119: 1180-1180, 2009.
2. K. Vermeire, JP. Brokx, FJ. Wuyts, E. Cochet, A. Hofkens, PH. van de Heyning. Quality-of-life benefit from cochlear implantation in the elderly. Otol. Neurotol. 26: 188-195, 2005.

FIGURE LEGENDS

Fig. 1.

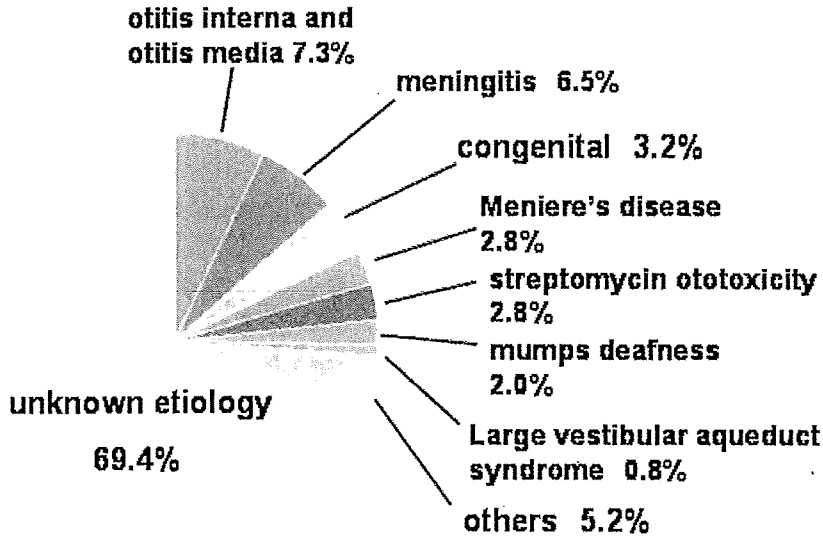
Indications for cochlear implantation

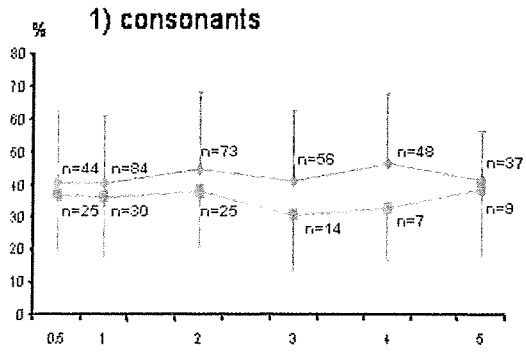
In 69.4% of our subjects, we could not identify the cause of sensorineural hearing loss. The commonest identifiable causes were otitis interna and chronic otitis media.

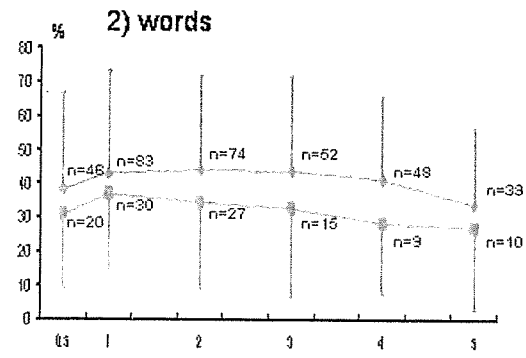
Fig.2

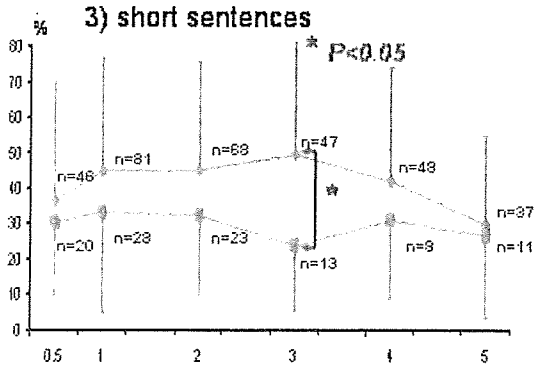
Language intelligibility score

A significant difference of the scores was seen only in the short sentence condition three years after the operation









younger than 65 yo

older than 65 yo

Incidence of Revision Cochlear Implantation in Both Children and Adults

K. Doi, Y. Osaki, T. Kawashima, K. Ohata, T. Yoshinami, K. Suwa, Inohara H, S. Hio, T. Sato, H. Nishimura.
Department of Otorhinolaryngology, Head and Neck Surgery,
Osaka University Graduate School of Medicine, Yamadaoka 2-2, Suita, Osaka 565-0871, Japan.

SUMMARY

To identify the incidence of and common causes for cochlear implant (CI) revision, operative records were reviewed for all CI cases from 1991 to 2008. The causes were classified as hard device failure, soft device failure, CI exposure/infection, CI/electrode migration.

Four hundred and fifty CI surgeries were performed during the study period including 23 (5.4%) revision procedures. The revision rate was 7.8% for children and 4.2% for adults but did not reached statistical significant difference. While the mean interval to revision surgery was 37.6 months for children and 93.8 months for adults and reached statistical significant difference (P=0.003). The most common causes were device failures (74%; 44% hard failure, 30% soft failure) followed by CI exposure/infection (22%), and CI/electrode migration (4%).

While the need for revision CI surgery is uncommon, its incidence appears to be higher in children than in adults and the interval to revision surgery is shorter in children than in adults. There exists the potential for improvement in speech perception and both children and adults benefit from revision CI surgery.

INTRODUCTION

Revision surgery for cochlear implantation is an unusual but not uncommon occurrence (3-8%). A number of etiologies exist for revision CI surgery including hard device failure, soft device failure, CI exposure/infection, CI/electrode migration. Previous studies have demonstrated a higher revision rate in children, presumably due to an increased incidence of head trauma, increased risk of otitis media causing implant infection, and a potential increased risk of electrode migration associated with normal growth of the skull [1-3]. Both the feasibility and successful results of revision CI surgery have been identified; the majority of re-implanted patients have results that are as good or better than their best results with their first CI.

The purpose of this study was to identify the incidence of and common causes for revision CI surgery in both children and adults.

MATERIALS AND METHODS

The operative records for all cases of CI performed at the Osaka University Hospital from 1991 to 2008 were systematically reviewed. A total of 450 cases were identified. From these cases, 23 patients were identified that required revision CI surgery. Patient characteristics (overall and for the individual groups of children or adults) were identified including the reason for revision surgery, and the time interval between initial and revision surgery. The reasons necessitating revision surgery were classified as hard or soft device failure, CI exposure/infection, and CI/electrode migration.

Comparisons between the failure rate of children and adults were performed utilizing Chi-squared test. A non-paired Student *t* test was utilized to compare the means of the interval to re-implantation between the two groups.

RESULTS

A total of 450 cochlear implants were performed during this time, and 23 revision procedures were identified. The 23 revision procedures constituted an overall institution-specific revision rate of 5.4% (23/427). When these results were stratified to children, children demonstrated a revision rate of 7.8% (11/141) and adults revealed a revision rate of 4.2% (12/286) (Fig.1). This difference did not reached statistical significance with a *P* value of 0.14. The mean intervals to revision surgery were 37.6 months in children and 93.8 months in adults (Fig.2). There was a significant difference between two groups ($P = 0.003$).

Hard and soft device failures accounted for 74% of revision procedures. Hard failures comprised 10/23 cases (44%), while soft failures comprised 7/23 cases (30%) (Fig.3). When this was evaluated specifically for children, hard failures comprised 6/11 cases (54%) and soft failures comprised 4/11 cases (36%). Of those children with hard failures as the identified cause, 2/6 (33%) had a specific history of preceding trauma. In adults, hard failures reflected 4/12 cases (33%) and soft failures were 3/12 cases (19%).

In cases that new CI was re-implanted at the same side of cochlea, full insertion of new electrode was achieved in 6/9 (66.7%) in children and in 7/8 (87.5%) in adults.

DISCUSSION

The present study revealed an overall institutional revision rate of 5.4%. When children and adults were evaluated separately, a child revision rate of 7.8% and an adult revision rate of 4.2% were demonstrated, although this difference did not reach statistical significance (*P* value of 0.14). Our data also indicated that the interval to revision surgery was significantly shorter in children than in adults. Previous studies have demonstrated a higher revision incidence in children, presumably due to an increased incidence of head trauma, increased risk of otitis media causing implant infection, and a potential increased risk of electrode migration associated with normal growth of the skull.

The most common indication for revision surgery is hard device failure (42–83%) and a history of antecedent head trauma has been reported in up to 41% of hard failures [1-3], while most often there is no identifiable precipitating event. In this study, 33% (2/6) of children had a history of preceding trauma and the hard device failures comprised a higher proportion of cases in children (54%) than in adults (33%).

CONCLUSIONS

The incidence of revision CI surgery appears to be higher in children than in adults, and the interval to revision surgery is significantly shorter in children than in adults. The most common indication for revision CI surgery is hard device failures and it might be possible that preceding trauma leads to either fracture of the case or loss of the hermetic seal. The potential benefit of revision CI surgery must be

considered carefully for all potential candidates, but patients must understand that it does not always lead to good outcomes.

REFERENCES

1. KD. Brown, SS. Connell, TJ. Balkany, AE. Eshraghi, FF. Telischi, SA. Angeli. Incidence and indications for revision cochlear implant surgery in adults and children. Laryngscope 119: 152-157, 2009.
2. MI. Trotter, S. Backhouse, S. Wagstaff, R. Hollow, RJS. Briggs. Classification of cochlear implant failure and explantation: the Melbourne experience, 1982-2006. Cochlear Implants Int. 10: 105-110, 2009.
3. DM. Zeitler, CL. Bundenz, JT Roland Jr. Revision cochlear implantation. Curr. Opin. Otolaryngol. Head Neck Surg. 17: 334-338, 2009.

FIGURE LEGENDS

Fig.1

Incidence of revision CI surgery

Children demonstrated a revision rate of 7.8% (11/141) and adults revealed a revision rate of 4.2% (12/286). This difference did not reached statistical significance with a *P* value of 0.14.

Fig.2

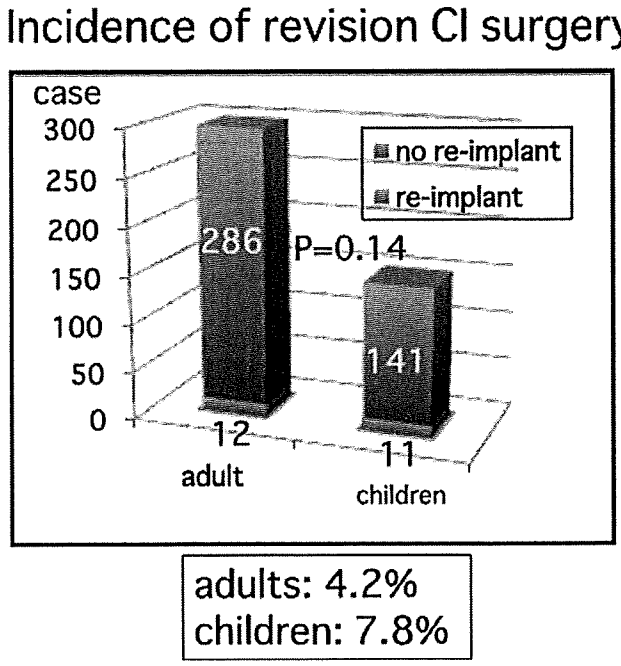
Time interval to revision CI surgery

The mean intervals to revision surgery were 37.6 months in children and 93.8 months in adults. There was a significant difference between two groups ($P = 0.003$).

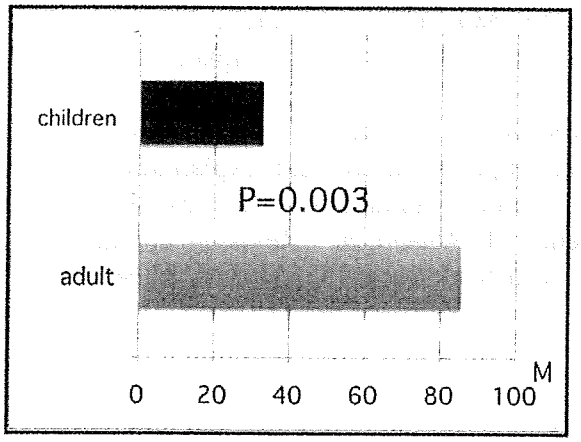
Fig.3

Causes for revision CI surgery

Hard and soft device failures accounted for 74% of revision procedures. Hard failures comprised 10/23 cases (44%), while soft failures comprised 7/23 cases (30%).

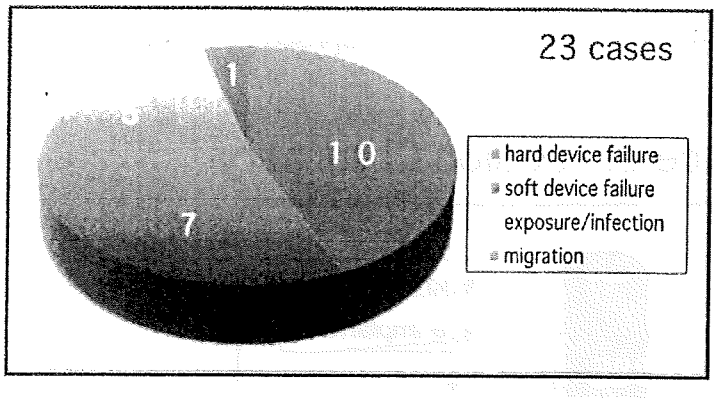


Time interval to revision CI surgery



children: 37.6 months
adults: 93.8 months

Causes for revision CI surgery



hard device failure: 44%
soft divice failure: 30%

Otology & Neurotology
30:812–819 © 2009, Otology & Neurotology, Inc.

Plasma Vasopressin and V2 Receptor in the Endolymphatic Sac in Patients With Delayed Endolymphatic Hydrops

Tadashi Kitahara, Chie Maekawa, Kaoru Kizawa, Arata Horii, and Katsumi Doi

From the Department of Otolaryngology, Osaka University, School of Medicine, Osaka, Japan

Objective: There are some kinds of sicknesses provoked by inadequate adaptation to physical and/or psychogenic stress in daily life. Delayed endolymphatic hydrops (DEH) is an inner ear disease like Ménière's disease (MD) characterized by episodic vertigo in the setting of preexisting unilateral deafness that especially occurs in civilized people with a stressful lifestyle. Its otopathologic finding was demonstrated to be inner ear endolymphatic hydrops through a temporal bone study in 1976, as in the case with MD in 1938. To elucidate the relationship between stress and the inner ear, we examined the plasma antidiuretic stress hormone vasopressin (pAVP) and its type 2 receptor (V2R) expression in the endolymphatic sac in patients with DEH.

Study Design: A prospective molecular biological study.

Methods: Between 1998 and 2007, we enrolled 20 patients with ipsilateral DEH to examine their pAVP during remission from vertigo attacks. Plasma vasopressin was also examined in 87 patients with unilateral MD and 30 control patients with chronic otitis media. Using the real-time polymerase chain reaction method with tissue samples obtained during surgery, we examined V2R mRNA expression in the endolymphatic sac in 6 patients with ipsilateral DEH, 9 patients with unilateral MD, and 6 control patients with acoustic neuroma.

Results: Plasma vasopressin (1.5 times versus controls; unpaired t test, $p = 0.140$) and V2R mRNA expression in the endolymphatic sac (35.8 times versus controls; unpaired t test, $p = 0.002$) were higher in patients with DEH compared with those with acoustic neuroma. There were no significant differences in pAVP or V2R expression in the endolymphatic sac between DEH and MD. Patients with DEH showed a significantly negative correlation between pAVP and V2R (Pearson test, $r = -0.92$, $p = 0.009$) as in those with MD (Pearson test, $r = -0.68$, $p = 0.043$).

Conclusion: Civilized people are frequently exposed to stress in their daily life, and pAVP can easily become elevated at any time. Therefore, a negative feedback system between pAVP and V2R in the endolymphatic sac may function for inner ear fluid homeostasis against stress-induced increases in pAVP. For the pathogenesis of endolymphatic hydrops resulting in vertigo attacks in patients with DEH as well as MD, pAVP may represent a matter of consequence, but V2R overexpression in the endolymphatic sac could be much more essential as a basis for these diseases. **Key Words:** Delayed endolymphatic hydrops—Endolymphatic sac—Ménière's disease—Stress—V2 receptor.

Otol Neurotol 30:812–819, 2009.

There are some kinds of sicknesses provoked by inadequate adaptation to physical and/or psychogenic stress in daily life. Vertigo attacks of Ménière's disease (MD) due to the inner ear abnormality represent a common example. Delayed endolymphatic hydrops (DEH) due to inner ear abnormality similar to MD is characterized by episodic vertigo in the setting of preexisting unilateral deafness and occurs in people with a stressful lifestyle (1). However, it is very difficult to prove a significant relationship between stress and inner ear abnormality because the definition of stress is too obscure for a scientific analysis of these aspects.

Since the otopathologic finding in DEH was demonstrated to be inner ear endolymphatic hydrops by a temporal bone study in 1976 (2), as in cases with MD in 1938 (3,4), it has gradually become understood that inner ear end organs, including the endolymphatic sac, regulate the fluid homeostatic system via water metabolism–related molecules such as vasopressin and aquaporin (5). Subsequently, it was proposed that the pathogenesis in DEH as well as MD could be inner ear endolymphatic hydrops due to a disorder of water metabolism–related molecules.

Address correspondence and reprint requests to Tadashi Kitahara, M.D., Ph.D., Department of Otolaryngology, Osaka University, School of Medicine, 2-2 Yamada-oka, Suita-city, Osaka 565-0871, Japan; E-mail: tkitahara@ent.med.osaka-u.ac.jp

This study was supported in part by a Health Science Research Grant for Specific Disease from the Ministry of Health, Labour, and Welfare, Japan (2005–2007).

This article will be presented in the next American Neurotology Society meeting.

In the present study, to elucidate the relationship between stress and the inner ear abnormality, we tested the hypothesis that the plasma antidiuretic stress hormone vasopressin (pAVP) and its type 2 receptor (V2R) in the endolymphatic sac will be increased in patients with DEH compared with controls.

MATERIALS AND METHODS

The use of all the human materials in the present study was approved by the Ethics Committee of Osaka University, School of Medicine (certificate no. 0424).

DIAGNOSIS AND ENROLLMENT

Patients were eligible for enrollment if they had received a clinical diagnosis of DEH or MD according to the 1995 American Academy of Otolaryngology—Head and Neck Surgery criteria (6). These criteria can be briefly described as follows: 1) Repeated attacks of vertigo: a definitive spell is spontaneous vertigo lasting at least 20 minutes. A mixed type of spontaneous nystagmus is observed during attacks. 2) Fluctuating cochlear symptoms: the hearing test usually reveals profound sensorineural hearing loss or deafness in the affected ear (ipsilateral type of DEH) or marked fluctuation of the threshold in the low and middle tone range contralateral to the affected ear (contralateral type of DEH). 3) Exclusion of other causes: to exclude other disorders, a thorough history, neurological, neurotological, and magnetic resonance imaging examinations were performed. Intractable DEH was designated in cases where various forms of medical and psychological management failed for at least 6 months. Medical management included diuretics, β-histine, diphenidol, dimenhydrinate, and diazepam, which were thought to be effective for persistent symptoms in DEH (7).

Patients designated as having intractable DEH had endolymphatic sac drainage, if there was no reason for declination of surgery. The technical details of this surgery were described before (8–10).

LABORATORY EXAMINATION FOR PLASMA VASOPRESSIN

Patients and Controls

Between 1998 and 2007, we enrolled 20 patients at Osaka University Hospital with ipsilateral type of DEH to examine their pAVP level. We also enrolled 87 patients with unilateral MD and 30 patients with chronic otitis media (OM) without any direct inner ear damage. Before collecting blood samples, we were given permission from all the patients with DEH, MD, and OM. Blood samples in all 3 groups were collected in the early morning of the day of surgery. Endolymphatic sac drainage was performed as an inner ear surgery for DEH and MD, and tympanoplasty was performed as a middle ear surgery for OM. There were no significant differences in patients' background (sex and age) among DEH (M/F = 10:10, 36.0 ± 2.5 yr), MD (M/F = 38:49, 47.2 ± 1.4 yr), and OM (M/F = 19:11, 45.4 ± 2.5 yr) except for age (patients with DEH were the youngest of all).

Patients with MD did not have any vertigo attacks and did not take any medicine for endolymphatic hydrops after hospitalization. Patients in all 3 groups took the same kind of nonrestricted meals before surgery and had no water from the morning on the day of surgery. Patients' conditions of medication, meals, and water intake at the collection of blood samples were almost the same in all 3 groups and were thought to have no influence on the pAVP level.

Procedures

The blood for a pAVP assay was transferred into an ethylenediaminetetraacetic acid tube and centrifuged at 4°C, and the separated plasma was stored at −80°C. The pAVP was determined by radioimmunoassay (arginine vasopressin radioimmunoassay kit; Mitsubishi, Tokyo, Japan). The normal pAVP level ranged from 0.3 to 4.2 pg/ml (mean, 2.25 pg/ml) based on the data acquired by blood samples collected at 8:00 to 10:00 AM from 105 healthy subjects with their informed consent (61 men, 44 women) who had no history of vestibular or cochlear disease (11).

MOLECULAR EXAMINATION FOR VASOPRESSIN RECEPTOR

Patients and Controls

Before surgery, we obtained permission for collection of the endolymphatic sac tissue during surgery from 6 of 20 patients with ipsilateral DEH and from 9 of 87 patients with unilateral MD mentioned. We also prepared 6 patients with acoustic neuroma (AN) without any direct endolymphatic sac damage as controls. Tissue samples from a part of the endolymphatic sac in groups, DEH, MD, and AN, were collected during surgery (endolymphatic sac drainage for DEH and MD groups and acoustic neuroma removal surgery for the AN group). There were no significant differences in patients' background (sex and age) among DEH (M/F = 3:3, 34.8 ± 4.2 yr), MD (M/F = 4:5, 47.9 ± 4.9 yr), and AN (M/F = 3:3, 53.0 ± 6.5 yr) except for age (patients with DEH were the youngest of all).

Tissue Preparation

For real-time polymerase chain reaction (PCR; DEH = 1–6, unilateral MDs = 1–9, ANs = 1–6) and Western blotting (DEH = 4–6, MDs = 7–9, ANs = 4–6), tissues were obtained from the endolymphatic sac during endolymphatic sac drainage for DEH and MD groups or from AN removal surgery for the AN group, placed immediately in chilled phosphate-buffered saline (PBS; pH 7.3) and frozen with dry ice powder.

Real-Time PCR

Total RNA Extraction

Total RNA was extracted from dissected frozen tissues using Trizol reagents (Gibco/BRL, Alameda, CA, USA).

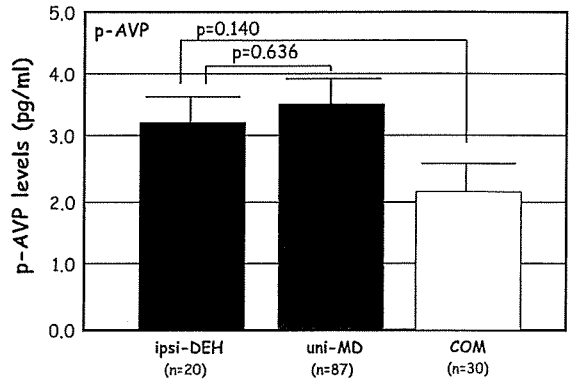


FIG. 1. Plasma vasopressin levels in patients with DEH compared with control patients. Plasma vasopressin was 1.5 times higher in patients with ipsilateral DEH (ipsi-DEH; n = 20; 3.10 ± 0.58 pg/ml) than in control chronic otitis media (COM) patients (n = 30; 2.11 ± 0.38 pg/ml) during the early morning of the day of surgery, although this difference was not statistically significant (unpaired *t* test, $p = 0.140$). There were no significant differences between the pAVP levels in patients with ipsi-DEH and unilateral MD (uni-MD; n = 87; 3.47 ± 0.35 pg/ml; unpaired *t* test, $p = 0.636$).

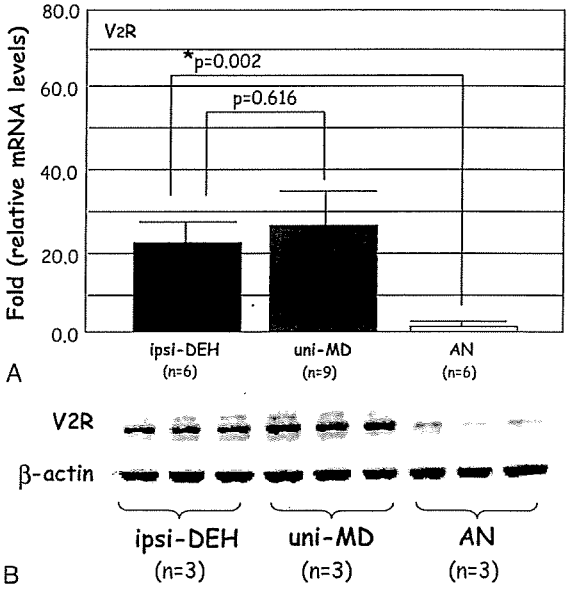


FIG. 2. V2 receptor mRNA and protein expression levels in the endolymphatic sac in patients with DEH compared with control patients. *A*, V2 receptor mRNA expression in the endolymphatic sac was 35.8 times significantly higher in patients with ipsilateral DEH (ipsi-DEH; n = 6; 22.21 ± 5.28-fold) than in control AN (AN) patients (n = 6; 0.62 ± 0.10-fold) as evaluated by real-time PCR (unpaired *t* test, $*p = 0.002$). There were no significant differences between the V2R mRNA expression levels in patients with ipsi-DEH and unilateral MD (uni-MD; n = 9; 27.86 ± 8.19-fold; unpaired *t* test, $p = 0.616$). *B*, V2R protein expression in the endolymphatic sac was also higher in patients with DEH and MD than in control AN patients as evaluated by Western blotting.

Briefly, samples were homogenized in 0.8 ml of Trizol reagent. Chloroform was then added, and the mixture was centrifuged to separate the RNA phase from the DNA phase. The RNA phase was used for RNA precipitation using isopropyl alcohol. The RNA samples were rinsed with ethanol and dissolved with RNase-free water. Finally, the RNA samples were treated with RNase-free Dnase I (Roche, Nutley, NJ, USA) to remove contaminated genomic DNAs before reverse transcription.

Reverse Transcription of RNA

The reverse transcription mixture included 10 μl of 10× PCR Taq Gold buffer II (Applied Biosystems, Inc., Foster City, CA, USA), 30 μl of 25 mmol/L $MgCl_2$, 4 μl of 25 mmol/L of each deoxynucleotide triphosphate, 5 μl of 100 μmol/L of random primers (Gibco/BRL), 2 μl of RNasin (Applied Biosystems), 1.25 μl of Super-Script II (Applied Biosystems), and 5 μl (250 ng) of DNA-free total RNA in a final volume of 100 μl. The mixture was incubated at 25°C for 10 minutes, 48°C for 30 minutes, and 95°C for 5 minutes in a 9600 Thermocycler (Applied Biosystems).

Reverse Transcription–PCR

Samples with reverse transcriptase were forwarded for PCR (95°C for 12 min and, 35 cycles at 95°C for 15 s, and 60°C for 1 min) and electrophoresed on 1.5% agarose gel to check the results of reverse transcription–PCR. Samples without reverse transcription were also forwarded for PCR as negative controls to make sure of no genomic DNA contamination.

TABLE 1. *Raw data for 6 patients with DEH (A) and 9 patients with MD (B)*

	pAVP, pg/ml	V2R mRNA, fold	V freq, per mo	H level, dB	Duration, mo
(A)					
Ipsi-DEH 1	1.0	40.74	2.0	115.0	36
Ipsi-DEH 2	1.4	25.11	1.0	100.0	60
Ipsi-DEH 3	1.7	28.54	1.3	101.3	18
Ipsi-DEH 4	4.7	18.78	4.3	112.5	45
Ipsi-DEH 5	6.9	18.33	4.0	115.0	30
Ipsi-DEH 6	11.6	1.76	1.0	115.0	60
(B)					
Uni-MD 1	0.5	64.78	1.0	30.0	34
Uni-MD 2	0.8	69.28	1.0	45.0	60
Uni-MD 3	1.3	13.72	1.3	66.3	84
Uni-MD 4	2.0	20.18	3.3	60.8	98
Uni-MD 5	2.7	1.90	1.7	70.0	48
Uni-MD 6	2.7	32.38	7.3	57.5	18
Uni-MD 7	3.5	29.52	8.0	66.5	30
Uni-MD 8	4.2	17.32	4.0	60.0	48
Uni-MD 9	6.0	1.70	2.0	58.5	60

The raw data for 6 patients with ipsilateral DEH (ipsi-DEH) and 9 patients with unilateral MD (uni-MD) include the pAVP level, V2R mRNA expression level in the endolymphatic sac, vertigo frequency (V freq), hearing level (H level), and duration of disease (Duration) before surgery. In both ipsi-DEH (*Pearson test, $r = -0.92$, $p = 0.009$) and uni-MD patients (**Pearson test, $r = -0.68$, $p = 0.043$), there were significantly negative correlations between pAVP and V2R mRNA expression in the endolymphatic sac.