生後6カ月以降に発見された難聴児の経緯

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要旨：1997年～2003年に出生し，スクリーニングを受けておらず生後6カ月以降に発見された難聴児31名（男15名，女16名）についてどの時点で発見されたか，その経緯を調べ今後の課題について検討した。発見時の年齢は1歳半以上が80%以上をしめた。発見が生後6カ月以降になった理由として病院で様子をみるようにいわれた児が52%と最も多く，次に健診で見逃された児が39%であった。その他国際結婚が近年増加しており，日本に定住せず，健診も受けずに難聴が見逃されている場合があった。今回の我々が調査の対象とした症例は全て新生児聴覚スクリーニングを受けていなかった。今後スクリーニングが普及すれば生後6カ月以降に発見される難聴児が減少することが期待される。今回の調査結果より難聴児の早期発見には医師・保健師の難聴児に対する正確な知識が不可欠であり，スクリーニングの普及とともに今後一層の啓蒙活動が必要である。

－キーワード－
新生児聴覚スクリーニング，難聴児，母子手帳，健診

はじめに

新生児聴覚スクリーニングの価値が高く評価される源は「生後6カ月までの早期に難聴を発見し補聴すれば3歳時には健聴児の90%に近い言語能力を獲得する」という1998年のItanoの論文による[1～3]。米国ですでに実施されていたこのスクリーニングを日本でも取り入れるため1997年～2000年の間，厚生労働省研究班により20000人を対象としてAABRによる新生児聴覚スクリーニングが行われた[1]。2001年には厚生労働省から全国の都道府県自治体に，いわゆる手上げ方式で呼びかけがあり，岡山，秋田，埼玉，神奈川，大阪，東京などの一部の地域で新生児聴覚スクリーニングが始まった。その後法定化されることなく全国に広まりつつあるが，統一されたスクリーニングの方法が決められておらず，個別に私的に行っている場合が多い[4～6]。結果的に出生した全ての新生児が受けているわけではないため，生後6カ月以降に発見される難聴児があとをたたない。今回我々は生後6カ月以降に発見された難聴児について調査し，今後の課題について検討したので報告する。

対象と方法

対象は1997年以降2003年の間に出生し，東京大学付属病院および関連病院を受診した難聴児31名（男15名女16名）である。前述のItanoの論文[2,3]を基にして生後6カ月以降に発見された症例につき，発見までの経緯，聴力，補聴方法について2004年までの経過を調査した。

結　　果

表1に1997年～2003年に出生し生後6カ月以降に発見された難聴児の症例数を示した（表1）。これらの児はすべて新生児聴覚スクリーニングをうけていない。発見時の年齢は図1に示すように1歳半以上が80%以上を占めている（図1）。次に発見が生後6カ月以降になった理由について調査したとこ

表1　出生した年と調査の対象とした難聴児の数

出生年	難聴児の数
1997年	4名
1998年	3名
1999年	5名
2000年	5名
2001年	8名
2002年	5名
2003年	1名
合計	31名

ろ，1）様子をみるようにいわれた。2）聴こえていると思っていたため母子手帳の聴覚の項目に反応があると記載していた。それが健診の際参考にされ見逃されていた。3）国際結婚のため2カ国語を混同し言葉の発達が悪いのかと考えていた。4）母親が忙しく検査が受けられなかった，の4つの理由があげられた（図2）。そのうち1）の理由が最も多く全体の52％を占めた。さらに発見年齢と難聴の程度について調査した（表2）。両耳の難聴が同程度の症例が30例，左右差が認められた症例が1例であった。また，両親が難聴に気がついてから初めて難聴が診断されるまで6カ月以上を要した症例は31例中16例であった。

今回調査した難聴児のうち発見時ABRにて閾値90dB以上の難聴児24名について2004年の時点での補聴器・人工内耳・手話の割合を図3に示す。

考察

新生児聴覚スクリーニングにより難聴児を早期に発見し療育することが可能となってきた。しかし全例に確実に行われていないこともあり，生後6カ月以降に発見される難聴児があとをたたないのも事実である。その理由と今回我々の調査結果に基づいて今後の対策につき考察する。

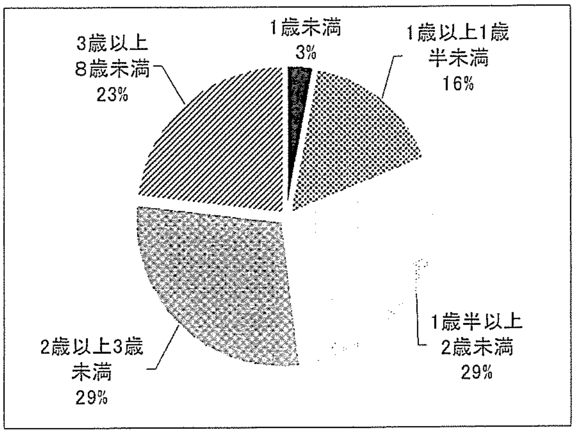
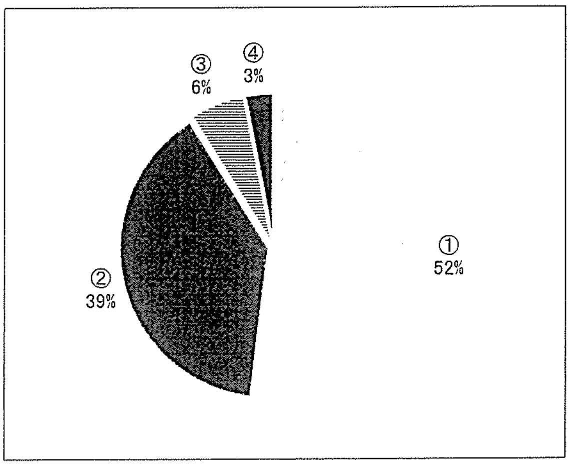


図1　発見時の年齢



①小児科や耳鼻科で様子をみるようにいわれた。（16名　52%）
②母子手帳の聴覚の項目に反応があると記載。
それが健診の参考にされ，見逃された。（12名　39%）
③国際結婚のため2カ国語を混同し言葉の発達が遅いと考えていた。（2名　6％）
④母親が忙しく検査が受けられなかった。（1名　3％）

図2　難聴の発見が生後6カ月以降になった理由

全体の52％も占める第1の理由は小児科医師，保健師が「言葉の発達には個人差がある」「男の子は言葉の発達が遅い」「3カ月様子をみるように」等と対応し，すぐに精査を勧めなかったことであった。耳鼻科にかかっていたにもかかわらず，「滲出性中耳炎のためである」「鼓膜は正常なので心配ない」と対応されていた症例も認められた。中には音の出るおもちゃを振ったときの子供の反応で聴こえていると判断した症例もあった。視覚が正常であれば反応してしまうため，十分注意して行わなければならない。今回の調査の中で両親が難聴に気がついて医

表2　発見された年齢と難聴の程度について

	発見年齢				
聴力（※1）	～1歳	1歳～1歳半	1歳半～2歳	2歳～3歳	3歳～8歳
ABR 無反応	1名	4名	9名	5名	4名
90dB		1名 (ABR)			
80～90dB				2名（play）	
70～80dB				1名（play）	1名（play）
60～70dB				1名（COR）	
50～60dB					2名(play, オージオ) （※2）
合計	1名	5名	9名	9名	7名

※1　聴力閾値はそれぞれ（　　）内の検査による。
※2　1名は聴力に左右差があり右56.3dB　左93.8dB
その他30名は両耳同程度の聴力である。

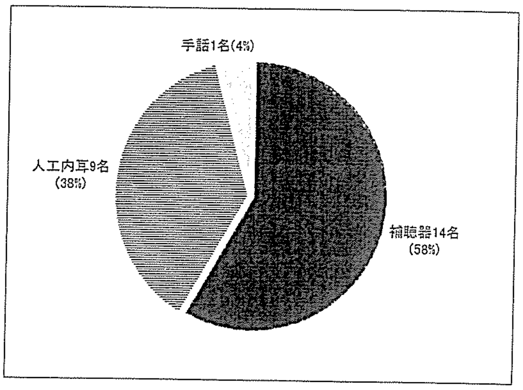


図3　難聴発見時ABRにて閾値90dB以上であった24名について補聴器・人工内耳・手話の内訳　(2004年10月の時点)

師や保健師に相談した際にすぐ適切な精査をすすめていれば早期に発見できた症例は16例と少なくない。またこれまでの論文からも同様の指摘をする報告がある[7,8]。

全体の39%を占める第2の理由は，健診の際母子手帳の聴覚に関する項目について，反応がある，という記載を医師が信頼したため難聴を見逃したことであった。母子手帳の聴覚の項目は両親の主観が入るため，信頼性が高いとはいえない。保健所や小児科医院での健診の際聴力検査を行うのは困難であるが，子供の様子をよく観察し母子手帳を鵜呑みにしないことが大切である。また，今後スクリーニングを全例に行うようになるのであれば，その結果を母子手帳に記載するのも一つの方法である。第1，第2の理由とも児を取り巻くさまざまな事情はあるが，医師，保健師の適切な判断，注意深い観察が必要である。

その他近年国際結婚が増加しているため，家庭の事情で日本に定住せず，乳幼児健診も受けずに難聴が見逃される可能性がある。そして難聴ではなく2つの言語環境による言語発達の遅れと両親が勘違いする場合もある。近年の国際結婚の比率は5%にものぼり，今後注意が必要である。

今回の調査では難聴発見時ABRにて閾値90dB以上であった症例24名中，2004年の時点で補聴器14名，人工内耳9名，手話1名であった。難聴者にとって補聴器，人工内耳，手話，聴覚口話法，指文字を組み合わせたコミュニケーション方法があり，どれを選択するかは難聴の程度や教育施設での教育方針による[1,9]。今後早期発見・早期療育が拡がれば，より良い聴覚言語発達が期待されることを考えると，難聴児が早期に発見され早期療育を行うことができる体制や制度の構築が必要であることを強調したい。

今回の我々の調査では生後6カ月以降に発見された難聴児症例は全て新生児聴覚スクリーニングを受けていなかった。今後スクリーニングが普及すれば，生後6カ月以降に発見される症例は減少することが期待される。しかし出生時にスクリーニングをパスしていても進行性難聴やAuditory Nerve Disease (Auditory Neuropathy) など成長していく過程で難聴が明らかになっていく場合がある[10]。そのため

医師や保健師には，スクリーニングや難聴について正確な知識が必要であり，スクリーニングをパスしていても難聴が少しでも疑われる場合には精査すすめることが必要である。

結　論

今回の調査の結果より，難聴児の早期発見には医師・保健師の難聴児に対する正確な知識が不可欠であり，スクリーニングの普及とともに今後一層の啓蒙活動が必要である。今後新生児聴覚スクリーニングが普及すれば生後6カ月以降に発見される難聴児は減少することが期待される。

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Reasons hearing loss was detected in children more than 6 months after birth

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Screening of newborn infants for hearing loss was started on a trial basis in Japan in 1997, but not all newborns were screened, meaning that many children with hearing loss are diagnosed more than 6 months after birth. To improve this situation we investigated why many children were diagnosed more than 6 months after birth. We reviewed the records of 31 patients with hearing loss (15 males, 16 females) at Tokyo University Hospital born in 1997-2003 who did not undergo newborn screening. In 80% of them the hearing loss was detected more than 18 months after birth. The first reason was that doctors told parents there was no problem, and to wait and see when they grow up. The second reason was nurses told parents there was no problem. If all the newborn underwent screening, fewer children would be diagnosed later. The results show that education of doctors and nurses in regard to children with hearing loss is most important.

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ORIGINAL ARTICLE

Vestibular-evoked myogenic potentials in cochlear implant children

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Abstract

Conclusions. Our results suggest that the sacculi of most children with cochlear implants can easily be damaged, as shown by the absence of vestibular-evoked myogenic potentials (VEMPs) in response to click stimuli. Also, in most of the children, the vestibular nerve was seemingly not stimulated by the cochlear implant. These results suggest that electrical stimulation at the comfortable level can stimulate the cochlear nerve; however, this stimulation did not spread to the vestibular nerve in our children. In some children with Mondini dysplasia or vestibulocochlear nerve abnormality, the vestibular nerve was stimulated when the cochlear implant device was on, because of a VEMP response to electrical stimulation. *Objective.* To clarify the diagnostic value of VEMPs in cochlear implant patients. *Material and methods.* The click-evoked myogenic potentials of 12 children who underwent cochlear implantation surgery were investigated. The latency and amplitude of the VEMP responses were measured. *Results.* Before surgery, 6 of the 12 children showed normal VEMPs, 1 showed a decrease in the amplitude of VEMPs and five showed no VEMP response. After surgery, with the cochlear implant device off, 1 child showed a decreased VEMP and 11 showed no VEMPs. With the cochlear implant device on, four children showed VEMPs and eight did not.

Keywords: *Children, click, cochlear implant, electrical stimulation, sacculus, vestibular-evoked myogenic potential, vestibular nerve*

Introduction

Vestibular-evoked myogenic potentials (VEMPs) in response to click or short tone-burst stimuli have been used as a clinical test for the inferior vestibular nerve [1-4]. It has been suggested [5-7] that VEMPs originate from the otolith organ, particularly the saccule. In VEMPs, galvanic stimulation of the mastoid instead of the use of clicks or short tone bursts can also elicit myogenic responses from the sternocleidomastiod muscle (SCM) [8-10]. Galvanic stimulation of the mastoid is considered to stimulate the most distal portion of the vestibular nerve [8,10], but not the sacculus.

The cochlear function of both ears is impaired in cochlear implant candidates. Patients with cochlear implants can hear speech sounds, which are converted to electrical signals in the speech processor, and these signals are transmitted to the internal receiver under the scalp and conducted to the electrodes in the cochlea. Thus, cochlear nerves that are stimulated electrically convey information to the central auditory system. Cochlear implants may affect the vestibular system by means of either pathologic disruption of the sensory vestibular functions of the labyrinth or fluctuating vestibular vestibulopathy or by electrical stimulation of the vestibular system [11]. However, VEMPs have not yet been studied in cochlear implant patients. The purpose of this study was to determine the presence or absence of VEMPs in cochlear implant children when the device was off or on, and to investigate saccular function in these children.

Material and methods

Subjects

The subjects comprised 12 children (7 boys, 5 girls; mean age 3.8 ± 1.4 years; range 2-7 years) who underwent cochlear implantation (CI) surgery at the University of Tokyo Hospital. Mean pre- and

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postoperative hearing levels were 108.3±14.2 and 45.8±8.4 dB, respectively. As controls, 9 healthy volunteer children (5 boys, 4 girls; mean age 5.1±3.0 years; range 8 months to 10 years) also participated in the study.

Procedure

The children were placed in the supine position. The active electrode was placed over the upper half of the SCM, the reference electrode on the upper sternum and the ground electrode on the midline of the forehead. During recording, the children were instructed to lift their heads up to induce hypertonicity of the SCM.

Recordings

The electromyographic signal from the stimulated side was amplified and averaged using a Neuropack evoked potential recorder (Nihon Kohden Co., Ltd., Tokyo, Japan). Electromyographic activities at a constant level were recorded for each child. Rarefaction clicks (0.1 ms, 95 dB normal hearing level) were presented through headphones (type DR-531; Elega Acous Co., Ltd., Tokyo, Japan). The stimulation rate was 5 Hz, the band-pass filter intensity 20–2000 Hz and the analysis time 50 ms. VEMPs in response to 100 stimuli were averaged twice. VEMPs were recorded both before and after the operation. After the operation, VEMPs were recorded when the device was both off and on.

Measurements

We analyzed the amplitude of the first positive–negative peak, p13–n23, ipsilateral to the stimulated ear, and the latencies of p13 and n23. The average of two runs was taken for the amplitudes and latencies. An absolute value of the VEMP amplitude ratio of <0.5 was considered a decreased VEMP.

Results

Controls

Clear VEMPs were obtained from all the healthy children. The mean±SD amplitude of p13–n23 was 181.0±90.9 μv. The mean±SD latency of p13 and n23 were 10.5±0.5 and 16.1±1.3 ms, respectively.

Patients

All the children underwent CT and MRI of the ear. Four of the 12 children showed abnormalities in the CT or MRI scans, as described below.

Case 2. MRI scans demonstrated that only one branch of the vestibulocochlear nerve appeared in the internal auditory meatus.

Case 3. CT demonstrated Mondini dysplasia, with only one turn in the cochlea and the enlarged basal turn and vestibule forming a common cavity. It was also noted that communication between the internal auditory meatus and cochlea was present. The lateral semicircular canal seemed to form a sac. The superior and posterior semicircular canals were widened (Figure 1).

Case 4. CT demonstrated Mondini dysplasia, with only two turns in the cochlea. There was no distinct visualization of the apical and middle turns in the cochlea, which seemed to form a common sac. The basal turn appeared normal, but showed communication between the internal auditory meatus and cochlea. The vestibular aqueduct was enlarged (Figure 2).

Case 5. CT demonstrated large vestibular aqueduct syndrome (LVAS), but the cochlea and internal auditory meatus appeared normal.

The VEMP results of the CI children are summarized in Table I.

VEMPs and caloric tests before operation. Ten of the 12 children underwent caloric tests with irrigation of ice water. Four children showed normal caloric test results and VEMPs. Four children showed poor responses in the caloric test: one showed a decrease in the VEMP; one showed a normal VEMP; and two showed no VEMP response. Two children showed no response to either caloric or VEMP testing.

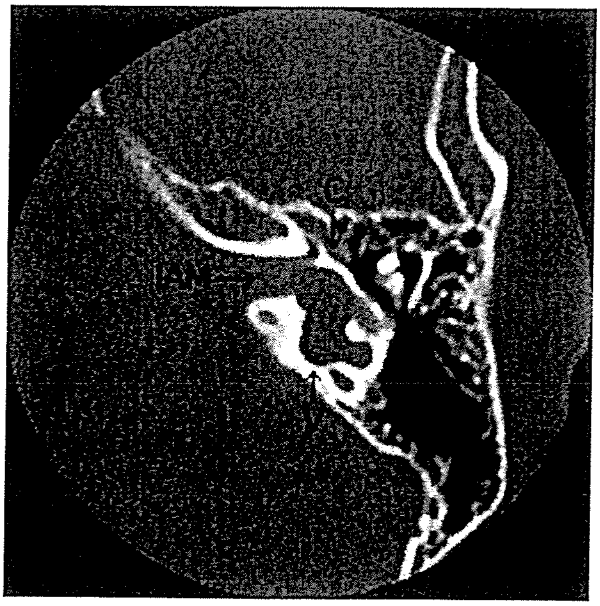

Figure 1. CT scan of Case 3. Left ear of a case of Mondini dysplasia. Note the presence of a common cavity, an enlarged basal turn of the cochlea and communication between the internal auditory meatus and cochlea. C = cochlea; V = vestibule; IAM = internal auditory meatus.

Figure 2. CT scan of Case 4. Large vestibular aqueduct of the right ear. Note the presence of communication between the internal auditory meatus and cochlea. VA = vestibular aqueduct. See Figure 1 for other abbreviations.

VEMPs before and after CI when the device was off. Six of the 12 children showed normal VEMPs before operation; 1 of these children showed a decrease in the VEMP and 5 showed no VEMP response after CI (Figure 3). Five of the 12 children showed no VEMPs both pre- and postoperatively (Figure 4). One child showed a decrease in the VEMP before operation, but this decrease was abolished after operation (Figure 5).

Comparison of VEMPs when the cochlear implant device was off and on. One child showed a decrease in the VEMP when the cochlear implant device was off and an increase when it was on. Eleven of the 12 children did not show VEMPs when the cochlear implant device was off: 3 elicited VEMP responses (Figures 4 and 5) and 8 showed no VEMP response when it was on (Figure 3).

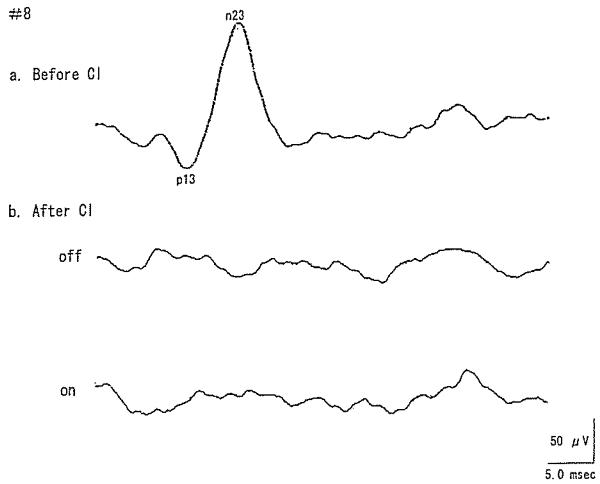

Figure 3. VEMP of Case 8. Normal VEMP before CI, absence of VEMP after cochlear implantation and absence of response on cochlear implant device activation.

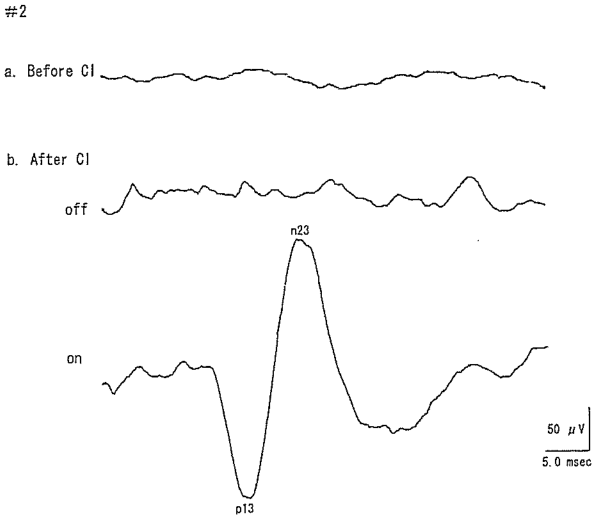

Figure 4. VEMP of Case 2. Absence of VEMP before and after CI and appearance of VEMP response on cochlear implant device activation.

Discussion

Anatomically and phylogenetically, the cochlea and vestibular organs are closely related. They share a continuous membranous structure and have similar receptor cells. Therefore, inner ear diseases are likely to affect not only hearing but also the sense of balance. Regarding the ice water caloric test, our study demonstrated that 6 children (60%) had caloric hypofunction or areflexia and that 4 (40%) were normal. These results are similar to those of Ito [12], who found that, before surgery, 67% of

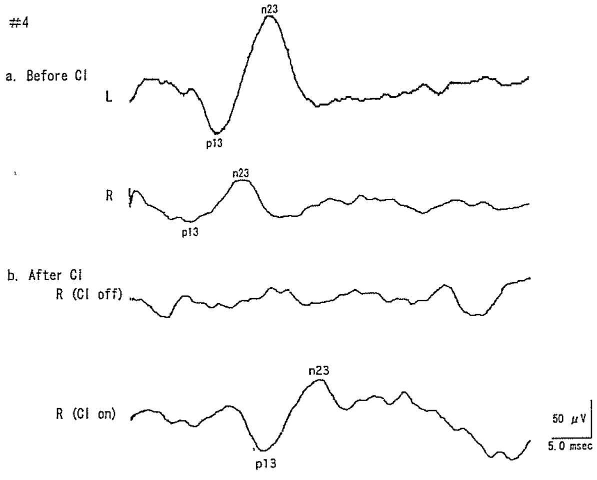

Figure 5. VEMP of Case 4. Decreased amplitude of VEMP before CI in right ear and absence of VEMP after surgery, and appearance of VEMP response on cochlear implant device activation.

Table I. Patient characteristics and data.

				Before CI			After CI			
									VEMP	
Patient No.	Sex	Age at CI (years)	Remarks	Hearing level (dB)	Caloric test	VEMP	Hearing level (dB)	Time lapse	Device off	Device on
1	M	3	Auditory nerve abnormality	111.25	+	+	43.75	2 months	Decreased	+
2	M	2	Mondini dysplasia	83.75		−	67.5	2 months	−	+
3	M	3	Mondini dysplasia	111.25	Poor	−	45	3 years	−	+
4	M	5	LVAS	118.75	Poor	Decreased	45	1 month	−	+
5	M	3	CMV	93.75	+	+	31.25	23 days	−	−
6	F	3		115	−	−	52.5	1 year	−	−
7	F	7		105	−	−	42.5	1 year	−	−
8	F	3		97.5	+	+	42.5	3 months	−	−
9	F	4		97.5	+	+	41.25	2 months	−	−
10	M	5		105	Poor	+	46.25	2 months	−	−
11	F	3		132.5	Poor	−	45	6 months	−	−
12	M	4		128.3		+	47.5	1 year	−	−

CMV = cytomegalovirus.

cochlear implant patients showed hypofunction or the absence of function in the caloric test. Buchman et al. [11] reported that nearly 70% of cochlear implant children had absent or low-intensity responses to caloric irrigation before operation.

Before operation, the VEMP test demonstrated a decrease in or the absence of VEMP responses in 6 children (50%) and normal responses in 6 (50%). The proportion of abnormal responses was therefore lower for the VEMP than for the caloric tests. These results are in agreement with the caloric test results of Tribukait et al. [13], in which the subjective visual horizontal and VEMPs of deaf children were slightly lower for the otoliths than for the semicircular canals.

Saccule effects of CI

The effects of CI on the vestibular system have been shown in numerous studies. Vestibular symptoms have been reported to occur in 0.33–70% of patients [14]. Ito [12], in a review in which he summarized the results of published electronystagmography studies, demonstrated that caloric responses changed in 71 patients (38%) and vestibulo-ocular reflex responses were reduced in as many as 40% of patients after CI. Mangham [15] reported similar findings for rotational chair testing.

Pathologic analysis of the vestibular apparatus from human temporal bones after CI has been reported [16]. Significant histopathologic damage of the vestibular end-organs was noted in 6 patients (54.5%). Fibrosis of the vestibular apparatus, saccular membrane distortion, osteoanagenesis and reactive neuromas have all been observed in patients who have undergone CI. Involvement of the scala vestibuli, as a result of damage to the osseous spiral lamina or basilar membrane in the cochlear basal turn, correlated strongly with vestibular end-organ damage.

In this study, of 12 children, 5 showed the absence of VEMPs and 2 showed a decreased VEMP amplitude after operation when the cochlear implant device was off. These results show a reduction in saccular function in 7/12 children (58.3%) after CI. Tien and Linthicum [16] suggested that the saccule is more susceptible to damage than the utricle or semicircular canals because of its proximity to the insertion pathway of the electrodes. Basilar membrane penetration was observed in 6/8 cochlear bones when a standard cochleostomy diameter (≈0.8 mm) was used. When the surgical technique was modified by making a slightly larger cochleostomy hole (≈1.8 mm) closer to the round window, the frequency of basilar membrane penetrations was restricted to two of seven bones [17].

Vestibular stimulation as a result of CI

The occurrence of vestibular stimulation as a result of CI has been shown in many studies. Black et al. [18] described two patients who experienced vestibular stimulation on initial activation of their extracochlear implants. Hoffman and Cohen [19] reported 11 patients (0.36%) who experienced device-related dizziness. Wong et al. [20] observed nystagmus in a child after the activation of a multichannel cochlear implant device using increased pulse widths (200 μs) in the monopolar stimulation mode. Bance et al. [21] described a patient who experienced significant vestibular signs during stimulation associated with a loud noise and a "shock-like" sensation. In the same study, it was found that 1/17 patients (5.9%) experienced a totally asymptomatic vestibular stimulation by their implant. Brey et al. [22] evaluated a group of 22 patients by means of pre- and postoperative posturography. In their study, postural stability worsened in one patient and improved in two after CI when the device was activated. Vestibular stimulation is possible in some patients with cochlear implant.

Recently [8,9] it has been shown that galvanic stimulations can also evoke myogenic responses in the SCM, but these myogenic potentials disappear after the activation of a selected vestibular nerve section. Goldberg et al. [23] suggested that galvanic stimulation stimulates the most distal portion of the vestibular nerve and predicted that galvanic-evoked myogenic responses would allow a better assessment of vestibular function, including the differentiation of conditions primarily involving the end-organs from those primarily involving the nerve [9]. Murofushi et al. [10] stated that the recording of galvanic-evoked myogenic responses of the SCM is useful in the differential diagnosis of labyrinthine lesions from retrolabyrinthine lesions in patients without click-evoked vestibulocollic reflexes.

The results of this study indicated that 4/12 children (33.3%) showed VEMPs when the cochlear implant device was activated. Among these four children, one showed decreased VEMPs and two showed no VEMPs before the operation; one showed decreased VEMPs and three showed no VEMPs when the device was off. Although saccular functions were damaged before surgery, VEMP responses were still elicited upon activation of the device. This suggests that VEMPs are induced by activation of the device as a result of stimulation of the vestibular nerve.

Of the 12 children, 8 showed no VEMPs when the cochlear implant device was activated, although 4 showed VEMPs before CI surgery. This finding suggests that electrical stimulation at the C level stimulated the cochlear nerve, but that the stimulation did not spread to the vestibular nerve in these patients.

Although the reasons for these differences are not totally evident, differences in patient selection, surgical procedures, cochlear implant devices, current intensity, stimulation schemes, testing paradigms and anatomical features may all be important factors.

Our study demonstrated that two children with Mondini dysplasia and one child with vestibulocochlear nerve abnormality showed VEMP responses on activation of the cochlear implant device. Sennaroglu et al. [24] reported on vestibular stimulation in the form of nystagmus in a child with a common cavity. Mondini dysplasia in our cases was characterized by the presence of communication between the internal auditory meatus and cochlea. It is possible that cochlear implant device activation may elicit VEMP responses in children with Mondini dysplasia. In one case in our study, only one branch of the vestibular nerve appeared in the internal auditory meatus and showed VEMP responses. This suggests that the vestibular nerve was intact in this child, and that the branch of the vestibulocochlear nerve that was visible on MRI scans was a vestibular nerve.

Finally, we would like to emphasize that VEMP testing is also a useful tool for diagnosing saccular function in cochlear implant patients. The sacculi of most children with cochlear implants were easily damaged, resulting in the absence of VEMP. These results suggest that electrical stimulation at the C level stimulated the cochlear nerve; however, it did not spread to the vestibular nerve in most patients. Nevertheless, it is especially noteworthy that in some children with Mondini dysplasia or vestibulocochlear nerve abnormality, the vestibular nerve can be stimulated by CI.

Acknowledgements

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A magnetoencephalographic study of Japanese vowel processing

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Magnetic brain responses were recorded to clarify the cortical representation of vowel processing in Japanese. We investigated the peak latencies and equivalent current dipoles of the auditory N1m responses to the Japanese vowels [a], [i], [o], and [u]. In intraindividual analyses for a single participant, well-replicated results for the dipole parameters supported the existence of phoneme-specific cortical maps for vowels. In the interindividual analyses for the eight participants, [a] and [i] elicited significantly earlier N1m responses than [u], and the dipole for [i] was more posteriorly oriented than [a] in the left hemisphere. The results of the current study suggest left hemispheric predominance in vowel processing and that factors associated with a different language system may modify the cortical map. *NeuroReport* 17:1127–1131 © 2006 Lippincott Williams & Wilkins.

Keywords: magnetoencephalography, N1m, phoneme processing, vowels

Introduction

Recently, several studies have examined cortical activity during the processing of vowel sounds by means of magnetoencephalography (MEG) [1–9]. In these studies, N1m (the magnetic counterpart of the auditory-evoked N1 potential) was used as an index of vowel sound processing. Previous studies reported a difference in equivalent current dipoles (ECDs) for N1m responses to vowels and pure tones [2,4], and a latency difference for vowel types [8]. These results were considered to be evidence suggesting the distinct processing patterns of vowels in humans. Some experiments support the notion that the ECD locations for N1m may reflect a distinct cortical representation of vowel sounds [1,3,5,6,9]. The changes in ECD localization for each vowel, which had not even been considered, were surprising to us.

Most of these studies were carried out by using German or Finnish vowels. Developmental research on language acquisition suggests that humans have established prototypes of phonemes in their languages in early childhood and reduced sensitivity to nonnative phonemes [10,11]. Therefore, vowel-sensitive neural substrates, which have been optimized during language learning, may vary across different languages. It is thus essential for a line of research on vowel sound processing to accumulate further information about interindividual variability and intraindividual stability in other languages, such as Japanese, which is characterized by a smaller number of vowels compared with previously studied languages. Research on Japanese phoneme processing has, however, been limited [4]. In the present study, we investigated the cortical representation of Japanese vowels.

The purpose of this study was to demonstrate the cortical representation of Japanese vowels and to examine its similarity with the previous findings in other languages. The stimuli used in this line of research varied across studies. Some employed synthesized vowels [1–4,6,8] or semisynthesized vowels [5] to control the acoustic parameters and to facilitate the examination of formant interaction. In others, naturally spoken vowels were used to investigate the role of phonological features [6] or spectral envelopes [9]. Some psychophysical experiments suggest that spectral cues other than formant frequencies may also be crucial for vowel perception [12]. Thus, we employed digitally recorded vowels spoken by a professional announcer as stimuli. These vowels were well controlled in loudness and pitch, maintaining whole spectral information, which might keep their cortical representation dispersive, and they are purposefully suitable for the present study.

We investigated N1m peak latency and ECD locations for the vowel sounds in a single participant first, because we had to elucidate intraindividual replication to check the reliability of the experimental procedures. We then examined the interindividual consistency in processing Japanese vowels.

Methods

Eight native Japanese speakers (24–57 years old, mean 37, four men and four women) who had normal hearing participated in the experiment. Seven were assessed right-handed with the Edinburgh inventory; laterality quotient ranged from 57.9 to 100, except for one ambidextrous participant whose laterality quotient was 0. One of the right-handed participants (a 28-year-old woman) participated in experiments for intraindividual replication. All participants were fully informed of the methods and techniques of noninvasive MEG recordings before signing a written agreement to participate. The procedure used in the study was approved by the Ethics Committee of the University of Tokyo.

The stimuli were five Japanese vowels ([a], [e], [i], [o], and [u]) separately uttered by a female speaker. The frequencies of the first (F1) and second (F2) formants of these vowels were as follows: [a]: 1140, 1590 Hz; [e]: 590, 2590 Hz; [i]: 390, 3080 Hz; [o]: 600, 1000 Hz; and [u]: 380, 2100 Hz. The waveform of each vowel was trimmed and naturally tapered to have the same duration of 290 ms from voice onset. The five vowels were presented with equal probability in a pseudorandom order, with the stipulation that the same vowel could not appear consecutively. The stimuli were sequenced by the STIM2 system (Compumedics Neuroscan, El Paso, Texas, USA) and delivered binaurally at 70 dB sound pressure level above respective hearing thresholds through ER-3A earphones (Etymotic Research, Elk Grove Village, Illinois, USA) at a stimulus onset asynchrony of 1.5 s. During the experiment, the participants were instructed to look at the gaze point and to press a plastic button with their right forefinger whenever [e] appeared.

Auditory-evoked magnetic fields were recorded in a sound-attenuated magnetically shielded room by the use of VectorView (Elekta Neuromag, Helsinki, Finland), which has 204 planar first-order gradiometers at 102 measurement sites on a helmet-shaped surface that covers the entire scalp. Auditory stimulus-triggered epochs of 1050 ms duration (including a 50-ms prestimulus baseline) were filtered online with a bandpass of 1.0–200.0 Hz and recorded at a sampling rate of 600.0 Hz. Epochs with artifacts exceeding 3 pT/cm in any channel were excluded from averaging. Erroneous epochs were discarded when the participants failed to push the button at [e] or mistakenly pushed it at the other four vowels. In one session, at least 250 artifact-free epochs were recorded per vowel and were selectively averaged for analysis. Eight sessions were repeatedly measured for the single participant, extending over several days. For the rest of the participants, a single session was carried out.

Data analyses were performed on the responses to the vowels [a], [i], [o], and [u]. The averaged waveforms were filtered off-line with a low pass at 40 Hz, and the mean amplitude from −50 to 0 ms in a prestimulus period was defined as the baseline for each channel. The peak latency of the N1m component was determined for each hemisphere by the time point at which the root-mean-square of the selected perisylvian channels (Fig. 1a) reached maximum, from 80 to 140 ms, after the stimulus onset. The sources of each N1m component were modeled separately as a single ECD for each hemisphere. The ECDs were calculated independently for vowels and sessions in each participant at the peak latencies from the same perisylvian channels. The ECDs with goodness of fit above 75% were adopted.

Before data acquisition, magnetic resonance imaging (MRI) scans were obtained from all participants. Referenced points (nasion and bilateral preauricular points) and the scalp of each participant were digitized by an Isotrak II system (Polhemus, Colchester, Vermont, USA) to coregister the MEG coordinate system onto the individual MRI. The MEG results were imported into BESA 5.1.2 (MEGIS Software, Gräfelfing, Germany) and transformed into Talairach space by using the interactive link with BESA 5.1.2 and BrainVoyager QX (Brain Innovation B.V., Maastricht, The Netherlands). The MEG results were presented in Talairach coordinates to normalize interindividual anatomical variability in the present study.

Intraindividual analyses of the data for the single participant across eight sessions and interindividual analyses of the data across eight participants were performed. ECD parameters for the N1m responses to each vowel were statistically analyzed in each hemisphere by a repeated-measures analysis of variance and post-hoc Scheffé comparisons. We considered $P < 0.05$ to be statistically significant for these analyses. A Greenhouse–Geisser correction was performed when appropriate.

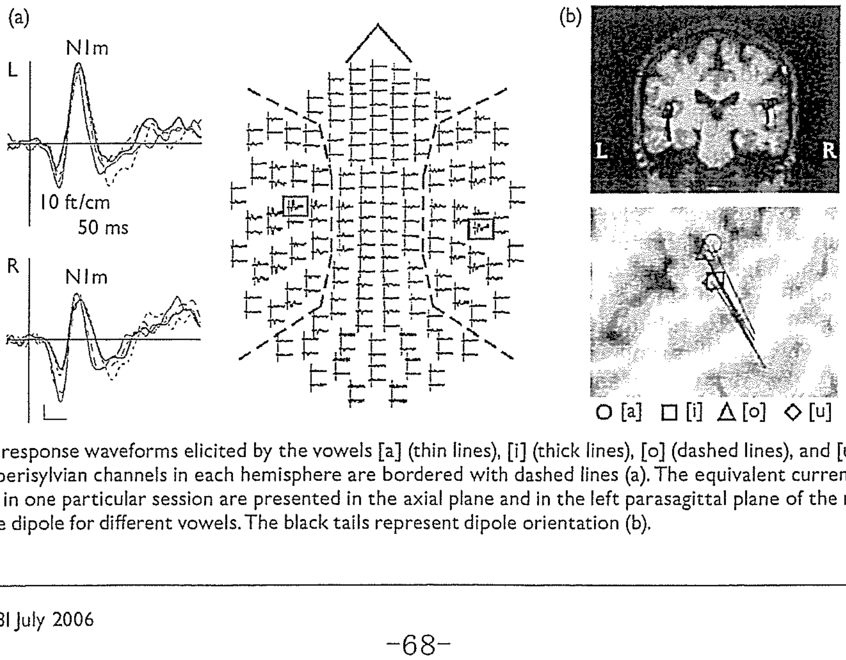

Fig. 1 The averaged N1m response waveforms elicited by the vowels [a] (thin lines), [i] (thick lines), [o] (dashed lines), and [u] (dotted lines) in a representative participant. The perisylvian channels in each hemisphere are bordered with dashed lines (a). The equivalent current dipole locations for N1m from the single participant in one particular session are presented in the axial plane and in the left parasagittal plane of the magnetic resonance image. Each symbol represents the dipole for different vowels. The black tails represent dipole orientation (b).

Table 1 Mean (and SEM) (n=8) of the N1m ECD parameters in intraindividual study

	Left hemisphere					Right hemisphere				
	Latency (ms)	x (mm)	y (mm)	z (mm)	Orientation (deg)	Latency (ms)	x (mm)	y (mm)	z (mm)	Orientation (deg)
[a]	106.4 (0.9)	−43.2 (0.7)	−31.5 (0.8)	10.0 (1.6)	112.7 (1.4)	111.4 (0.9)	54.8 (0.5)	−30.5 (1.1)	12.1 (0.6)	128.9 (2.0)
[i]	111.4 (0.9)	−43.3 (1.2)	−30.5 (0.8)	5.0 (1.1)	117.3 (1.4)	115.1 (1.3)	49.6 (1.0)	−29.3 (1.1)	8.5 (1.6)	128.6 (1.8)
[o]	113.2 (0.9)	−43.9 (0.8)	−30.1 (0.8)	9.7 (1.6)	113.5 (1.1)	118.8 (1.5)	53.9 (1.2)	−29.7 (1.1)	12.9 (1.2)	133.9 (2.4)
[u]	116.3 (0.9)	−42.5 (0.8)	−31.0 (0.7)	2.4 (1.0)	117.2 (1.2)	118.2 (0.9)	50.5 (1.1)	−33.0 (0.7)	5.0 (1.3)	124.4 (1.8)
F-value	31.04	1.07	2.95	26.00	8.01	13.40	10.35	5.76	14.75	6.04
P-value	0.000002	0.37	0.082	0.000025	0.0032	0.0015	0.0025	0.023	0.000067	0.020

Orientation [$=180+\tan^{-1}(Qz/Qy)$]: a downward rotation of the yz-plane projection of the ECD moment (Q) from the y-axis.
ECD, equivalent current dipole.

Table 2 Mean (and SEM) (n=8) of the N1m ECD parameters in interindividual study

	Left hemisphere					Right hemisphere				
	Latency (ms)	x (mm)	y (mm)	z (mm)	Orientation (deg)	Latency (ms)	x (mm)	y (mm)	z (mm)	Orientation (deg)
[a]	103.8 (3.0)	−53.3 (1.2)	−21.5 (5.6)	18.1 (5.9)	111.2 (1.8)	102.6 (3.0)	56.3 (1.0)	− 19.4 (5.9)	15.3 (6.1)	121.5 (3.5)
[i]	102.6 (4.5)	−53.3 (1.4)	−20.7 (5.9)	15.6 (5.7)	118.1 (2.3)	102.0 (3.5)	53.8 (1.6)	− 18.1 (5.3)	16.3 (5.7)	119.3 (5.1)
[o]	108.9 (3.9)	−53.4 (1.8)	−20.8 (5.5)	17.6 (5.7)	113.7 (2.2)	107.6 (3.7)	54.3 (1.7)	− 17.1 (5.1)	16.1 (5.9)	123.2 (5.6)
[u]	111.4 (3.9)	−51.8 (1.2)	−21.2 (5.5)	15.0 (5.4)	114.6 (3.4)	108.2 (2.5)	54.6 (1.6)	− 18.5 (5.4)	14.1 (5.9)	119.9 (4.7)
F-value	6.70	1.69	0.54	3.80	4.96	3.79	1.25	1.69	1.49	0.48
P-value	0.0097	0.22	0.63	0.061	0.017	0.066	0.32	0.22	0.26	0.65

ECD, equivalent current dipole.

Results

The behavioral data of a button press revealed that every participant achieved the correct rate of more than 97% (average±SEM: 98.0±0.4), and every participant showed prominent deflections of the N1m responses to each vowel. The responses were well confined in bilateral perisylvian areas (Fig. 1a). The ECDs for N1m were calculated with goodness of fit above 78% (92.2±0.6) and were localized in the superior temporal plane of the MRI of each participant (Fig. 1b).

The averaged ECD parameters obtained from repeated measurements of the single participant are summarized in Table 1. The very small P-values in many parameters mean that the experimental procedures of our study were highly reliable.

The averaged ECD parameters in interindividual analyses are summarized in Table 2. The analysis of variance of the N1m latency revealed a significant difference across vowel types only in the left hemisphere; post-hoc Scheffé comparisons revealed that the vowels [a] and [i] elicited earlier N1m responses than [u]. The ECD orientation across vowel types showed a significant difference only in the left hemisphere; the orientation for [i] was more posteriorly oriented than [a] by approximately seven degrees in the parasagittal plane. In the inferosuperior (z) axis, although it did not reach a significant level, the N1m location for [a] showed a tendency to be superior to those for other vowels. Other ECD parameters were not significantly different across vowel types in either hemisphere. We also examined Euclidean distances between every pair of the vowel ECD locations with and without normalization by the mean distance. No significant difference in distances was, however, observed between any vowel pairs. Furthermore, we compared a displacement of each vowel from the mean ECD location for all vowels with and without normalization by the mean displacement. No significant difference in displacements was, however, detected across vowels. This statistical insignificance was replicated even when the ambidextrous participant was excluded from the analyses.

Discussion

In intraindividual analyses for the single participant, the ECD locations and orientations did show a significant difference in both hemispheres with very small P-values. Well-replicated results confirmed the reliability of the experimental procedures in the present study, and they also supported the existence of cortical maps during the processing of vowels that were pointed out by Eulitz *et al.* [3] in the preceding study.

The interindividual analysis revealed that the N1m latency for [u] was significantly longer than that for [a] in the left hemisphere. The intraindividual analysis showed similar results; the N1m latency for [a] was significantly shorter than those for [i], [o], and [u] in the left hemisphere. Previous studies adopted the N1m component as an index of processing activity in the auditory cortex. N1m latency reflects temporal encoding, which is a critical element of neuronal activity. Roberts *et al.* [13] and Roberts and Poeppel [14] reported that N1m latency for lower-frequency sinusoidal tones was prolonged compared with higher-frequency tones. The results of the studies using vowel stimuli suggested that N1m latency for vowels depends on the position of F1 and can be interpreted in terms of the sinusoidal data [1,8]. Vowel [a] with relatively high F1 elicited an earlier N1m response than [i] or [u], both of which had a relatively low F1. The results of the present study were in line with this notion.

In the present study, the ECD orientation showed the significant main effect of vowels. In the parasagittal plane, the ECD for [i] was more posteriorly oriented than [a] by approximately 7° in the left hemisphere. Preceding studies on the tonotopic organization with pure tones [15–17] and with syllables [7] also found an ECD orientation shift. As the ECD orientation depends on the underlying cortical structure (i.e. the direction of apical dendrites of activated neurons), it contains physiologically important information, which is unique to electromagnetic measurement. The target areas that were focused on in this line of study were characterized by their folded shapes. The ECD rotation suggested that the centroids of vowel processing were close to one another and that they slightly shifted along Heschl's gyrus in the left hemisphere.

It must be noted that in interindividual analyses, the significant main effects in N1m latency and ECD orientation were shown only in the left hemisphere. This may imply left hemispheric predominance in vowel processing [1,5]. It is widely known in the first place that an interhemispheric asymmetry exists in the superior temporal gyrus. The left hemisphere is mainly involved in temporal processing, although the right hemisphere's forte is processing spectral information [18,19]. The greater volumes of white matter in the left hemisphere, which can be attributed to the difference in myelination, explain the rapid processing of auditory stimuli and a left hemisphere dominance for speech [20–22]. The results of the present study suggest that not only spectral but also temporal information processing plays an important role in vowel perception.

In interindividual analyses for the eight participants, a difference in ECD locations across vowels did not reach a significant level. For one thing, the relatively small number of participants might be the cause. We should acknowledge that the number is smaller in our study than those in preceding studies. Furthermore, the characteristics of Japanese might contribute to the results. Some researchers suggested that, in infancy, exposure to particular phonemes leads to neural sensitivity to these phonemes, and consequently the non-native phonemes cannot be discriminated in adults [23–25]. These results may lead to the notion that vowel processing is affected by exposure to a language-specific phonological format in early life. The number of vowels in Japanese is five and is fewer than those in the other languages studied in previous research. If the neural substrates for vowel processing in the auditory cortex are inherently limited, a language with fewer vowels may be allowed to use the same amount of neural substrates with more degrees of freedom. This notion is also applicable to the motor control of articulation. A language with fewer vowels widely allocated in the same F1–F2 space is allowed a relatively coarse control of articulation. The sparse allocation of sensorimotor neural representation of Japanese vowels may consequently result in some interindividual variability and lead to difficulties in identifying consistent ECD locations for each vowel across the participants. This notion does not, however, contradict the existence of an individual cortical map for vowels in Japanese, considering that stable patterns of vowel ECD sources were observed in the single participant.

Conclusion

In the current study, intraindividual replication of the ECD locations and orientations supported the existence of phoneme-specific cortical maps for Japanese. ECD parameters did not, however, reach a significant level except for the ECD orientation in the left hemisphere in the interindividual analyses. Further information on the vowel processing of various languages is awaited because vowel density in the spectral space may be reflected in the cortical map.

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