

ORIGINAL ARTICLE

Ocular vestibular evoked myogenic potentials induced by bone-conducted vibration in patients with unilateral inner ear disease

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Abstract

Conclusion: Patients with vestibular neuritis (VN) with complete canal paresis (CP) showed a higher rate of abnormal ocular vestibular evoked myogenic potential (oVEMP) than those with partial CP. From these results, it is speculated that the superior vestibular nerve function mainly affects oVEMP. Significant correlation was found between the grades of the hearing outcome and oVEMP in sudden sensorineural hearing loss (SSHL). **Objective:** We attempted to correlate the results of oVEMP with the results of cervical VEMP (cVEMP), results of subjective visual vertical (SVV), and clinical course in patients with various vestibular disorders. **Methods:** Twenty-two patients with VN, 65 with SSHL, and 22 with Meniere's disease (MD), were enrolled in this study. We compared the results of oVEMP with those of cVEMP, SVV, and the caloric test. Furthermore, the oVEMP results were compared with the initial hearing threshold, presence of vertigo, and hearing recovery in the patients with SSHL. **Results:** The patients with VN with complete CP showed a higher rate of abnormal oVEMP than those with partial CP. In the patients with SSHL, the hearing recovery rate was lower in the patients with abnormal oVEMP than in those with normal oVEMP.

Keywords: *sacculus, utriculus, otoliths, vestibular neuritis, canal paresis, sudden sensorineural hearing loss, Meniere's disease*

Introduction

Vestibular evoked myogenic potentials induced around the eyes are known as ocular vestibular evoked myogenic potentials (oVEMP) and are useful for the clinical examination of vestibular function. oVEMP is defined as a biphasic negative-positive myogenic response with a very short latency. The cervical evoked myogenic potential (cVEMP) has been used as a test of the vestibulo-collic reflex, particularly the sacculo-collic reflex. However, the origin of oVEMP remains unclear. Curthoys et al. and Govender et al. [1,2] showed that the superior vestibular nerve is the route along which the oVEMP response passes, and not the inferior vestibular nerve. It has been suggested that the primary negative potential of the oVEMP (nI) indicates crossed utricular function [1–3]. As regards examination of

the utriculus, the subjective visual vertical (SVV) test has been recently discussed [4,6].

In the present study, we attempted to correlate the oVEMP results with results of cVEMP and SVV, and the clinical course in patients with representative diseases of the inner ear.

Material and methods

Subjects

From January 2010 to December 2012, oVEMP was measured in 109 cases of unilateral inner ear diseases. A detailed medical history was taken for all patients. The patients were also assessed by cVEMP, SVV, caloric test, and hearing test, evaluated for symptoms of vertigo, and assessed for hearing recovery rate. All the patients were accepted for treatment as inpatients.

Examinations were performed as soon as possible after admission. A patient who described symptoms of vertigo at the onset or during the course of hospitalization was considered positive for vertigo.

Twenty-one healthy subjects including 7 men and 14 women (age range 24–62 years, mean age 32.8 years) from among the resident physicians and co-medical staff were enrolled as normal controls. None had a history of ear disease.

There were 22 patients with vestibular neuritis (VN) (5 women and 17 men; age range 34–68 years, mean age 53.0 years), 65 with sudden sensorineural hearing loss (SSHL) (30 women and 35 men; age range 17–82 years, mean age 48.9 years), and 22 with Meniere's disease (MD) (18 women and 4 men; age range 26–83, mean age 54.3 years).

The diagnostic criteria for VN were as follows: (1) a single attack of continuous vertigo lasting for at least several hours, (2) reduced lateral semicircular canal function (canal paresis (CP) > 20% on the affected side in the caloric test), (3) spontaneous nystagmus, and (4) no cochlear or other neurologic signs.

The diagnostic criteria for SSHL were as follows: (1) sudden unilateral sensorineural hearing loss of at least 30 dB over three frequencies developing within 72 h, (2) exclusion of hearing loss of greater than 30 dB on the pure-tone average of five frequencies (i. e. 0.25, 0.5, 1, 2, and 4 kHz), (3) no other neurological signs, (4) exclusion of acute low-tone sensorineural hearing loss, (5) no history of MD in either ear, (6) no previous otologic surgery, (7) treatment started within 8 days after onset.

The diagnostic criteria for MD were based on the guidelines proposed by the American Academy of Otolaryngology–Head and Neck Surgery in 1995 [6]: (1) two or more definitive spontaneous episodes of vertigo for 20 min or longer, (2) audiometrically documented hearing loss on at least one occasion, (3) tinnitus or aural fullness in the affected ear, and (4) other causes excluded. The affected ear was identified as the ear in which there was a low frequency hearing loss, and symptoms of fullness were reported.

We classified the pathology into VN as the vertigo-based labyrinthine disorders and SSHL and MD as the auditory-based disorders.

oVEMP measurement

oVEMP was measured using bone-conductive vibration (BCV). BCV was applied to the midline of the forehead at the hairline (a location called Fz). BCV was delivered using a hand-held mini-shaker (Bruel & Kjaer model 4810, Naerum, Denmark). The mini-shaker terminates in a bakelite cap 1.5 cm in diameter. The flat end of this cap was the contact point for the

stimulator on the subject's Fz point. Surface electrodes were placed inferiorly to both eyes after the subject's skin beneath the eyes had been cleaned carefully with alcohol wipes. The active electrode was located over the inferior orbital margin and a reference electrode was placed 2 cm below the active electrode. The ground electrode was on the para-medial forehead.

The subjects were asked to lie in a supine position on the bed with their head supported by a pillow with the chin close to the chest, and to maintain a 30° upward gaze during recording. We placed the target at the point where the subject could examine the upper 30° field of view.

The signals were amplified and bandpass filtered between 20 and 2000 Hz. The stimulus intensity was 115 dB force level, 500 Hz with an analysis time of 40 ms, and 50 responses were averaged for each run. Two or three runs were performed to confirm the reproducibility of the results. In this study, the nI component was measured. The amplitude of nI was measured from baseline to peak.

The *oVEMP* asymmetry was calculated as follows: *oVEMP* signed asymmetry ratio (AR) = $\{(larger\ nI - smaller\ nI)/(larger\ nI + smaller\ nI)\} \times 100$.

In this study, the average of normal subject's AR was 21.7 ± 14.0 . The upper limit of the normal range of the percent *oVEMP* asymmetry was set by the normal subject's AR. The normal mean and range were set as $21.7 \pm 2\ SD$. The upper limit of the normal range was set as 49.7 (mean $\pm 2\ SD$).

cVEMP measurement

cVEMP was recorded in the supine position. The skin over the upper half of the sternocleidomastoid (SCM) muscle was cleaned with alcohol wipes and surface electromyography electrode readings were recorded, with a reference electrode on the upper edge of the sternum and a ground electrode on the forehead. Rarefaction clicks (105 dB nHL, 0.5 ms) were delivered to each ear through a headphone with a stimulation rate of 5 per second. The patients were instructed to continuously raise their head to activate the SCM. The results were evaluated on the basis of comparative ratios between the first positive and first negative (p13–n23) amplitude on the lesion side and that on the healthy side. We defined a ratio of < 0.5 as an abnormal *VEMP* value [5].

SVV measurement

SVV was usually examined at 2 or 3 days after the patients were admitted. SVV was measured using a small rotatable luminous line in the upright body position in a completely darkened room. The patient

was seated in a chair and the head and chin were fixed on a forehead-chin rest in an upright position 50 cm away from the SVV device. The length of the luminous straight line on a computer screen was 15 cm. After the luminous line was randomly tilted automatically, the patient was asked to rotate the bar to the position they perceived as vertical using a hand controller. SVV measurement was performed 10 times for each patient, and the mean was regarded as the measured value.

Based on the results with normal subjects in our institute, the upper limit of the normal range of the SVV tilt was set as $\pm 2.0^\circ$, and SVV tilts outside the range of -2.0° to $+2.0^\circ$ were determined to be pathological.

Caloric test measurement

The caloric test was performed using electronystagmography. The CP level was calculated using the maximal slow phase eye velocity. A CP value of greater than 20% was defined as abnormal. We divided the patients into two groups according to CP severity: complete CP (absence of caloric response) and partial CP (reduced caloric response and a CP of $> 20\%$).

Grades of hearing loss and hearing outcome in SSSL

We evaluated the hearing levels of the SSSL patients on the first visit. The hearing level was calculated using five frequencies (0.25, 0.5, 1, 2, and 4 kHz). The grade of hearing was based on the pure-tone average of the five frequencies. The criteria for the evaluation of the grade of hearing were as follows: grade 1, < 40 dB; grade 2, 40–60 dB; grade 3, 60–90 dB; grade 4, > 90 dB. We also evaluated hearing outcome 1 month after the onset as follows. Complete recovery was defined as recovery to a level similar to

that of an intact ear or if all of the five frequencies of hearing level were less than 20 dB. Marked recovery was defined when the average of five frequencies was greater than 30 dB. Slight recovery was defined when the average of five frequencies was 10–29 dB. Unchanged was defined as being within a 10 dB improvement.

Stages of MD

The patients were classified by referring to the guidelines of the Committee on Hearing and Equilibrium in the USA [6]. Stage I included patients whose average pure-tone hearing thresholds (500, 1000, and 2000 Hz) were within 25 dB; stage II, 26–40 dB; stage III, 41–70 dB; and stage IV, > 70 dB.

Statistical analysis

The statistical add-in software for Microsoft Excel 2007 was used for statistical analysis. The Fischer test was employed to test the correlation between *oVEMP* abnormality and the severity of disease, presence of vertigo, *cVEMP* abnormality, and SVV abnormality. The Cochran-Armitage test was used to identify the relationships between *oVEMP* abnormality and hearing outcome. A *p* value of < 0.05 was considered to indicate a statistically significant difference.

Results

We compared the ratio of abnormal *oVEMP* in three inner ear diseases. We compared VN as the vertigo-based labyrinthine disorders, with SSSL and MD as the auditory-based disorders. The ratio of abnormal *oVEMP* was the greatest in VN (68.2%). It was 9.2% in SSSL and 9.1% in MD (Figure 1).

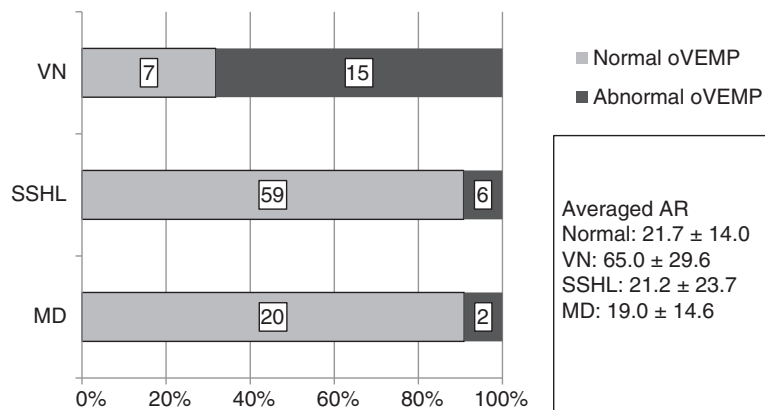


Figure 1. *oVEMP* results for each disease. In the comparisons of each disease, the ratio of abnormal *oVEMP* was greatest in vestibular neuritis (VN), followed by sudden sensorineural hearing loss (SSHL) and Meniere’s disease (MD). AR, asymmetry ratio.

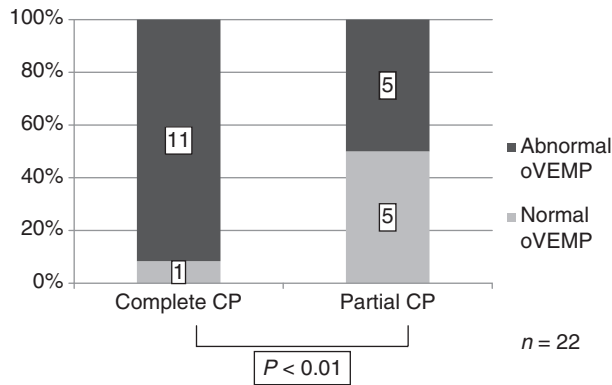


Figure 2. Magnitude of canal paresis (CP) in abnormal and normal oVEMP in patients with vestibular neuritis (VN). The patients with complete CP showed a higher rate of abnormal oVEMP than those with partial CP.

VN

Fifteen of 22 patients showed abnormal oVEMP, 7 of those showed normal oVEMP in VN (Figure 1). The average AR for oVEMP was 65.0 ± 29.6 , which was significantly different from the normal AR.

We performed caloric tests in all VN patients, which revealed complete CP in 12 patients and partial CP in 10 patients. We analyzed whether or not changes in CP severity were related to the oVEMP. There was a significant difference in the rates of abnormal oVEMP between the partial and complete CP (Figure 2). The VN patients with complete CP showed a higher rate of abnormal oVEMP than those with partial CP.

Of 22 VN patients, 6 showed abnormal cVEMP and 16 showed normal cVEMP. We examined whether or not oVEMP results were related to cVEMP. Five of the six patients with abnormal cVEMP showed abnormal oVEMP and one showed normal oVEMP. Ten of the 16 patients with normal cVEMP showed abnormal oVEMP and 6 showed normal oVEMP. However, there was no significant correlation between oVEMP and cVEMP.

Seventeen of 22 patients showed an abnormal SVV. Twelve of 17 patients with an abnormal SVV showed abnormal oVEMP. Three of the five patients with a normal SVV showed abnormal oVEMP. There was no correlation between SVV and oVEMP in the VN patients.

SSHL

Of 65 patients, 6 showed abnormal oVEMP and 59 showed normal oVEMP (Figure 1). The average AR for oVEMP was 21.2 ± 23.7 , which was not significantly different from normal AR.

We examined whether or not oVEMP results were related to cVEMP. Of 65 patients, 27 showed

abnormal cVEMP and 38 showed normal cVEMP. Of the 27 patients with abnormal cVEMP, 4 showed abnormal oVEMP and 23 showed normal oVEMP. Of the 38 patients with normal cVEMP, 2 showed abnormal oVEMP and 36 showed normal oVEMP. There was no significant difference in the rates of abnormal oVEMP between the normal and abnormal cVEMP.

We examined whether or not oVEMP results were related to SVV. Of 65 SSSL patients, 20 showed an abnormal SVV, 39 showed a normal SVV, and 6 patients were not examined for SVV. There was no significant difference in the rates of abnormal oVEMP in those patients with normal and abnormal SVV.

Among the 65 SSSL patients, vertigo occurred in 25 patients. We compared the oVEMP in patients with and without vertigo. There was no significant difference in the rates of abnormal oVEMP in those patients with vertigo and those without vertigo.

SSHL patients were classified into the following four classes based on an initial measurement: grade 1 ($n = 3$), grade 2 ($n = 12$), grade 3 ($n = 23$), and grade 4 ($n = 25$). Abnormal oVEMP was noted in one patient in grade 1, one patient in grade 2, one patient in grade 3, and six patients in grade 4. Figure 3 shows the relationship between oVEMP and grade severity of initial hearing. The rates of abnormal oVEMP tended to be higher in the severe grade, but there was no significant correlation between abnormal oVEMP and grade severity of initial hearing. The SSSL patients with a high grade did not show a higher rate of abnormal oVEMP than those with low grade severity of initial hearing. We also classified SSSL patients into the following categories based on the hearing outcome: complete recovery ($n = 21$), marked recovery ($n = 19$), slight recovery ($n = 12$), and unchanged ($n = 13$). Figure 4 shows the correlations between oVEMP and hearing outcome. We found a significant correlation between hearing outcome and abnormal oVEMP. All patients with complete recovery and marked recovery had normal oVEMP. Abnormal oVEMP was noted in two patients in the slight recovery category and six patients in the unchanged group. The SSSL patients with better hearing recovery showed a lower rate of abnormal oVEMP ($p < 0.01$).

MD

Two of 22 patients with MD showed abnormal oVEMP and 20 showed normal oVEMP (Figure 1). The average AR for oVEMP was 19.0 ± 14.6 , which was not significantly different from the normal AR.

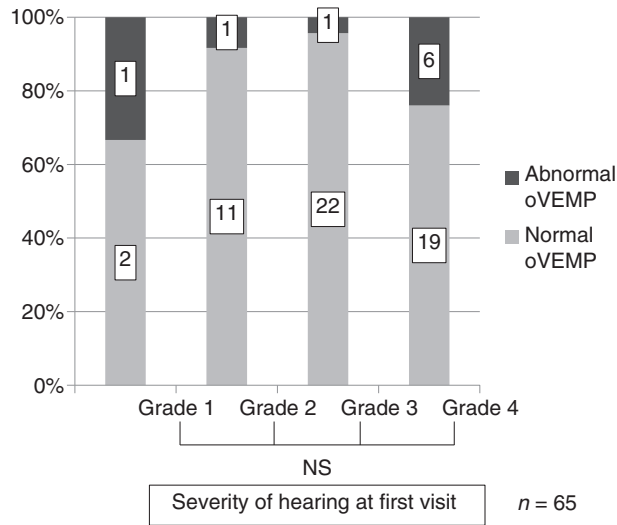


Figure 3. Relationship between oVEMP and severity of hearing at first visit in patients with sudden sensorineural hearing loss (SSHL). There was no significant correlation between abnormal oVEMP and degree of hearing loss at the first visit. The SSLH patients with a high grade at the first visit did not show a higher rate of abnormal oVEMP than those with a low grade of hearing loss. NS, not significant.

We examined whether or not oVEMP results were related to cVEMP. Of 22 patients with MD, 8 showed abnormal cVEMP. Of the 14 patients with normal cVEMP, 1 showed abnormal oVEMP and 13 showed normal oVEMP. Of the 8 with abnormal cVEMP, 1 showed abnormal oVEMP and 7 showed normal oVEMP. There was no significant difference in the rates of abnormal oVEMP in patients with normal and abnormal cVEMP.

We examined whether or not oVEMP results were related to SVV. Of 22 patients, 5 showed abnormal SVV. There was no significant difference in the rates of abnormal oVEMP between patients with normal and abnormal SVV. All of the 17 patients with normal SVV showed normal oVEMP. Of the five patients with abnormal SVV, two showed abnormal oVEMP. There was no significant difference in the rates of abnormal oVEMP between patients with normal and abnormal SVV.

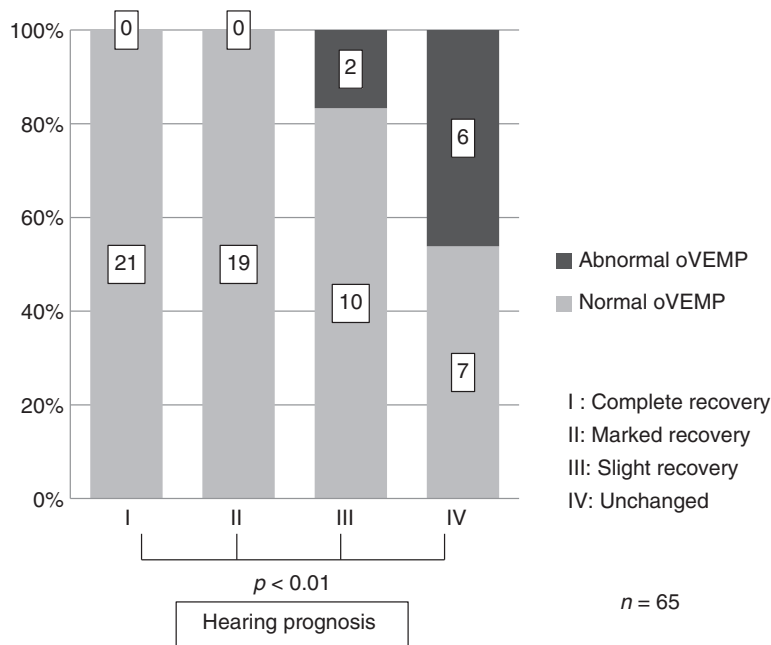


Figure 4. Relationship between oVEMP and hearing prognosis in sudden sensorineural hearing loss (SSHL). The hearing recovery rate was lower in the patients with abnormal oVEMP.

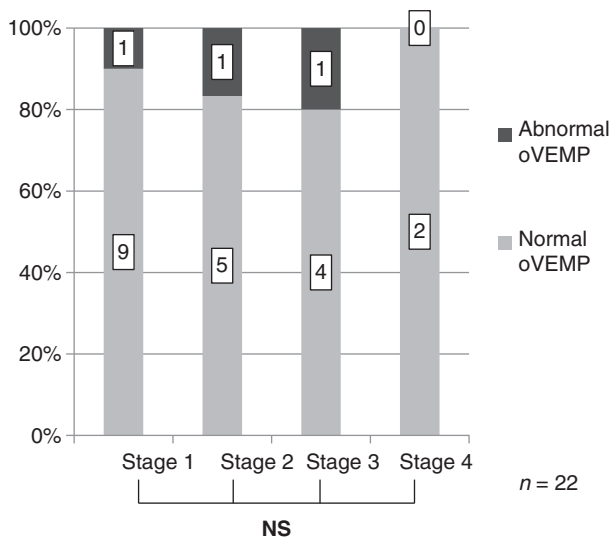


Figure 5. Relationship between oVEMP and stage of Meniere's disease (MD). There was no significant correlation between oVEMP and stage of MD. NS, not significant.

As regards MD, nine patients were classified as stage I, six as stage II, five as stage III, and two as stage IV. Among the six patients classified as stage II, one patient showed abnormal oVEMP. Among the five patients classified as stage III, one patient showed abnormal oVEMP. There was no significant relationship between stage and oVEMP (Figure 5).

Discussion

It is accepted that the ipsilateral p13-n23 of the air-conducted sound (ACS) cVEMP arises from saccular stimulation and measures inferior vestibular nerve function. In humans, oVEMP by BCV stimuli at Fz is suggested to reflect the function of the utricle and superior vestibular nerve [7]. The oVEMP vestibular pathway appeared to be crossed and runs through the superior vestibular nerve. The vestibular origin of oVEMP is not yet fully understood. Iwasaki et al. showed that oVEMP in response to BCV of the midline forehead in patients with unilateral vestibular loss due to removal of the vestibular nerve was greatly reduced or absent on the side contralateral to the unilateral vestibular loss; the average AR for the patients was significantly higher than the average AR for healthy subjects [3]. Manzari et al. showed that oVEMP in unilateral vestibular loss due to removal of the eighth cranial nerve for treatment of vestibular schwannoma and neurectomy for treatment of MD reduced or eliminated n10 on the contralateral side [8]. oVEMP testing is acceptable even to senior patients because the procedure is quite easy. BCV is a modest stimulus that is not painful, is

present for only a very brief time, and requires little effort on the part of the patient who is lying supine. However, few studies have been published about oVEMP in inner ear diseases. We have correlated oVEMP with cVEMP, SVV, the caloric test, and the clinical course in patients with vertigo-based labyrinthine disorders (VN) and auditory-based disorders (SSHL and MD).

We first consider the frequency of abnormal oVEMP in inner ear disease. Shin et al. reported that 73.2% of patients with VN had abnormal oVEMP [9]. Murofushi et al. reported that 100% of patients with VN had abnormal oVEMP, and 45% of patients with unilateral MD showed abnormal oVEMP [10]. In the present study, the ratio of abnormal oVEMP was the greatest in VN, followed by SSLH, and MD (Figure 1). These results indicate that oVEMP reflects the vestibular-evoked response rather than the auditory-evoked response and that superior vestibular function markedly affects oVEMP.

We investigated a vestibular-based labyrinthine disorder, VN. As regards AR, in previous studies [3,8], the AR of the patients with unilateral vestibular loss was significantly greater than the AR of the healthy subjects. In the present study, the results of AR in VN were similar to those of previous studies [2,3]. Most patients with VN had a higher AR than the average AR for healthy subjects; this result was significantly different.

Shin et al. found that oVEMP values were affected in superior VN while cVEMP values were apparently normal, while the opposite held for inferior VN [9]. They proposed that oVEMP responses were the result of utricular activation. Manzari et al. [11] reported that, in 59 patients with inferior vestibular neuritis, the function of the superior vestibular nerve (caloric and head-impulse responses) was within the normal range, cVEMP responses were asymmetrical, and oVEMP responses were normal. They showed that oVEMP and cVEMP differentiated utricular from saccular function [11].

In the present study, patients with complete CP showed a higher rate of abnormal oVEMP values than those with partial CP (Figure 2). CP severity may affect oVEMP results. In other words, oVEMP may reflect the function of the superior vestibular nerve. Although there was no significant relationship between cVEMP and oVEMP, VN patients with abnormal cVEMP tended to show abnormal oVEMP. These results suggest that the patients with both inferior and superior vestibular nerve disorder showed a higher rate of abnormal oVEMP than those with limited superior vestibular nerve disorder. The oVEMP abnormality depends on the severity of vestibular nerve disorder.

In particular, the caloric test is an index of superior vestibular nerve function. Although oVEMP is mainly affected by the superior vestibular nerve, it does not always match with the results of the caloric test. This result suggests that induction of oVEMP by BCV may reflect the vestibular function that is solely of the lateral semicircular canal, but rather that of the anterior semicircular canal and utriculus.

We also investigated auditory-based labyrinthine disorders, i.e. SSHL and MD. We first consider SSHL. In histopathologic findings of the cochlea, atrophic changes in the organ of Corti, stria vascularis, and tectorial membrane, as well as a significant decrease in the number of spiral ganglion cells and cochlear nerves have been reported [12]. The utriculus and semicircular canals might be normal or might have only mild lesions. Inagaki et al. [13] reported that the vestibular system changes in cases of sudden deafness with and without vertigo. One of the patients with vertigo had deposits in the utriculus. However, there was no remarkable difference in the density of vestibular hair cells in patients with vertigo and without vertigo [13]. Our finding that there was no significant difference in the rates of abnormal oVEMP in patients with and without vertigo was consistent with previous findings.

In the present study there was no significant correlation between abnormal oVEMP and degree of hearing loss at first visit. However, the hearing recovery rate was lower in the patients with abnormal oVEMP. This result suggests that oVEMP could be used for the prediction of prognosis in SSHL. Iwasaki et al. reported that the absence of cVEMP in 14 of 52 SSHL patients (26.9%) indicates a poor hearing recovery [14]. Our study showed a correlation between abnormal oVEMP and poor hearing recovery. In SSHL patients, abnormal oVEMP may indicate the greater spread of the lesion. The patients with abnormal oVEMP might have extensive vestibular disorders in addition to lesions in the organ of Corti, including stria vascularis and tectorial membrane.

Concerning the pathology of MD, it was reported that there is endolymphatic hydrops and saccular hydrops at the early stage [15]. At the later stages utricular hydrops, ruptures of the membranous labyrinth, fistulae of the membranous labyrinth, collapse of the membranous labyrinth, obstruction of longitudinal flow, and vestibular fibrosis develop. In addition, the level of hearing loss is generally correlated with the degree of hydrops in severe cases. Murofushi et al. showed that ACS oVEMP could be affected in the later stages of MD [10]. If hearing loss progresses, there should be high rates of

abnormal oVEMP. Our results were not comparable to the previous studies [10,16]. Figure 5 shows that there was no difference between the degree of hearing loss and abnormal oVEMP. The small population of patients with MD in the present study may be responsible for the discrepancy in the results.

There was no correlation between SVV and oVEMP in the present study. In previous studies, it was reported that there was a correlation between oVEMP and SVV or SVH (subjective visual horizontal) in MD. Lin and Young showed that the rate of abnormal oVEMPs was 40% in MD, and that a significant correlation existed between SVH and oVEMP test results [16]. The utricular macula as well as the saccular macula is located close to the footplate of the stapes. BCV might stimulate not only utricular maculae, but also saccular maculae. The utricular condition is speculated to affect SVV more than the saccular condition [17]. oVEMP and SVV may share the same utricular reflex pathway, at least in part.

Conclusion

Patients with VN with complete CP showed a higher rate of abnormal oVEMP than those with partial CP. The superior vestibular nerve function mainly contributes to oVEMP. There were no significant differences in the incidence of abnormality between cVEMP and oVEMP in the patients with unilateral inner ear disease. There was no significant relationship between hearing level at first visit and oVEMP. Significant correlation was found between the grades of hearing outcome and abnormal oVEMP in patients with SSHL. oVEMP reflects the vestibular-evoked response rather than the auditory-evoked response and superior vestibular function markedly affects oVEMP.

Acknowledgments

The authors are indebted to the medical editors of the Department of International Medical Communications of Tokyo Medical University for their editing of the English manuscript. This study was supported by a Health and Labor Science Research Grant for Research on Specific Disease (Vestibular Disorders) from the Ministry of Health, Labor and Welfare, Japan (2012).

Declaration of interest: The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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