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Augmentation of Ocular Vestibular-Evoked Myogenic Potentials via Bone-Conducted Vibration Stimuli in Ménière Disease

Ming-Hsun Wen, MD¹, Po-Wen Cheng, MD¹, and Yi-Ho Young, MD²

Abstract

Objective. The asymmetry ratio of ocular vestibular-evoked myogenic potential (oVEMP) >40% is interpreted as augmented or reduced response depending on whether the nI-pI amplitude of the lesion ear is larger or smaller than that of the opposite ear, respectively. This study compared unilateral Ménière disease patients with augmented oVEMPs vs reduced oVEMPs to elucidate the mechanism of augmented oVEMP.

Study Design. Case series with chart review.

Setting. University hospital.

Methods. Forty patients with unilateral definite Ménière disease were enrolled in this study, including 20 patients with augmented oVEMPs and another 20 patients with reduced oVEMPs in the hydropic side. All patients underwent audiometry, caloric test, and oVEMP and cervical VEMP (cVEMP) tests via bone-conducted vibration stimuli. Then, the oVEMP and cVEMP test results were compared with the stage of Ménière disease, respectively.

Results. The augmented group had earlier nI and pI latencies and larger nI-pI amplitude of oVEMPs compared with the reduced group. Caloric test also revealed a significant difference in abnormal responses between the augmented and reduced groups. However, both groups did not differ significantly in the abnormal percentage of cVEMP test results. A significant trend to decline in the prevalence of augmented oVEMPs was noted from stages I to III-IV but not in that of abnormal cVEMPs.

Conclusion. The augmented oVEMPs have earlier latencies and larger amplitudes compared with the reduced oVEMPs, indicating that a relatively larger population of intact utricular afferents is activated during the early stage of Ménière disease.

Keywords

endolymphatic hydrops, Ménière disease, ocular vestibular-evoked myogenic potential, utriculo-endolymphatic valve
probably because the contact enhances the sensitivity of the saccular macula to loud sound. Likewise, augmentation of oVEMP is also observed in Ménière patients. Manzari et al reported that dynamic utricular function in the hydropic ear is enhanced during Ménière attack, as evidenced by augmented oVEMPs, whereas dynamic saccular function in the hydropic ear is decreased, as shown by reduced cVEMPs. It is believable that the dissociation between oVEMPs and cVEMPs in Ménière disease may help to elucidate the mechanism of Ménière attack. Thus, this study compared augmented and reduced oVEMPs in patients with unilateral Ménière disease to elucidate the mechanism of augmented oVEMP.

Patients and Methods

From December 2009 to July 2010, 127 patients with Ménière disease were consecutively encountered at the clinic of the university hospital. Excluding those with probable/possible Ménière disease, absent oVEMPs, bilateral lesion, underlying systemic diseases, and asymmetry ratio <40%, a total of 40 patients with unilateral definite Ménière disease were enrolled in this study. The diagnosis of definite Ménière disease was based on the guidelines proposed by the American Academy of Otolaryngology–Head and Neck Surgery in 1995. The median interval from initial symptoms to diagnosis was 2 months (range, 1 month to 6 years). The augmented group consisted of 20 patients, including 6 men and 14 women, with their ages ranging from 27 to 65 years (mean, 46 years). Right and left ears were affected in 11 and 9 patients, respectively. Likewise, the reduced group also included 20 patients, who were sex, age, and side matched for comparison (Table 1). The time lag between the last vertiginous attack and the testing time varied from 1 week to 2 months.

Prior to treatment, all patients under quiescent state without vertiginous attack received otoscopy, audiometry, caloric test, and oVEMP and cVEMP tests via bone-conducted vibration stimuli. Then, the oVEMP and cVEMP results were compared with the stage of Ménière disease, respectively.

Audiometry

The hearing thresholds were measured by an audiometer (AA67; Rion, Tokyo, Japan). For staging of Ménière disease, the 4-tone average was calculated from 4 frequencies (500, 1000, 2000, and 3000 Hz) of the worst audiogram during the interval of 6 months before treatment. On the other hand, the mean hearing level from 5 frequencies (250, 500, 1000, 2000, and 4000 Hz) was used for interpreting hearing test results. Hearing loss was defined positive when the mean hearing level was >25 dBnHL.

Caloric Test

A bithermal caloric test was conducted. Canal paresis was defined as a greater than 25% difference between maximum slow-phase velocity (SPV) measurements for each ear, when compared with the sum of SPVs from each ear. If no response was elicited, the participant underwent an ice-water (0°C, 10 mL) caloric test to further confirm the caloric areflexia.

oVEMP Test

The participant was in a sitting position. Two active electrodes were placed around 1 cm below the center of the 2 lower eyelids. The other 2 reference electrodes were positioned about 1 to 2 cm below the active ones, and 1 ground electrode was placed on the sternum. During recording (Smart EP 3.90; Intelligent Hearing Systems, Miami, Florida), the participant was instructed to look upward at a small fixed target >2 m from the eyes. The electromyographic (EMG) signals were amplified and bandpass filtered between 1 and 1000 Hz. The stimulation rate was 5 Hz. The duration of analysis of each response was 50 ms, and 30 responses were averaged for each run.

The operator held the vibrator by hand so that the axis of the connected bakelite cap perpendicularly delivered a repeatable tap with little pressure on the participant’s skull at Fz. The input signal was a half-cycle 500-Hz sine wave, with the initial peak driving voltage about 8 V, equivalent to a 128-dB force level.
The initial negative-positive biphasic waveform comprised peaks nI and pI. Consecutive runs were performed to confirm the reproducibility of peaks nI and pI, and oVEMPs were deemed to be present. At our laboratory, the norm for the latency of peak nI was 11.4 ± 0.8 ms. Those with the nI latency exceeding 13.0 ms were defined as having a delayed response, and those with an asymmetry ratio >40% were interpreted as having an abnormal response.

**cVEMP Test**

Each participant was in a supine position. Two active electrodes were placed on the upper half of the sternocleidomastoid (SCM) muscles; 1 reference electrode was positioned on the suprasternal notch, and a ground electrode was situated on the forehead. The other settings were the same as in the oVEMP test, except that the vibrator delivered a repeatable tap on the participant’s head at inion. To measure background muscle activity, participants were given feedback of the level of EMG activity in their SCM muscles during data collection and were required to keep a background muscle activity of at least >50 µV. The participants elevated their heads during testing. A total of 50 responses were averaged and recorded bilaterally.

The first positive and second negative polarities of the biphasic waveform were termed waves p13 and n23, respectively. At our laboratory, the norm for the latency of p13 was 14.4 ± 1.3 ms, and we defined a latency of peak p13 >17.0 ms as delayed cVEMPs. In addition, those with an asymmetry ratio >33% were defined as having an abnormal response.

**Statistical Methods**

The mean age, latencies, and amplitudes of oVEMPs between the augmented and reduced groups were compared by unpaired t test. The abnormal percentages of the physiological test between the 2 groups were analyzed by Fisher exact or χ² test. Prevalence of augmented oVEMPs or abnormal cVEMPs in relation to Ménière stage was evaluated by the Cochran-Armitage trend test. A significant difference indicates a P value <.05.

This study was approved by the institutional review board of the College of Medicine, National Taiwan University Hospital, and each participant signed the informed consent to participate.

**Results**

**Audiometry**

On the basis of the arithmetic mean of the pure-tone thresholds at 0.5, 1.0, 2.0, and 3.0 kHz, 20 patients of the augmented group were classified as stage I in 12 ears, stage II in 5 ears, and stage III in 3 ears. In contrast with reduced group, stage I was observed in 3 ears, stage II in 9 ears, stage III in 7 ears, and stage IV in 1 ear, exhibiting a significant difference (P < .05, Fisher exact test).

On the other hand, mean hearing level from 5 frequencies (250, 500, 1000, 2000, and 4000 Hz) was used for interpreting hearing test results. Accordingly, 5 ears with stage I and all 25 ears with stages II to IV had a mean hearing level >25 dBnHL. Thus, an abnormal percentage of mean hearing level in a total of 40 hydropic ears (both groups) was 75% (30/40).

In comparison, 12 (60%) of 20 ears in augmented group vs 18 (90%) of 20 ears in the reduced group showed hearing loss; both groups did not reach a significant difference (P > .05, Fisher exact test; Table 1).

**Caloric Test**

In the augmented group, the caloric test identified normal responses in 18 ears and abnormal responses in 2 ears (10%), including canal paresis in 1 and caloric areflexia in 1. In the reduced group, normal responses were noted in 10 ears and abnormal responses in 10 ears (50%), including canal paresis in 4 and caloric areflexia in 6. Both groups revealed a significant difference in terms of abnormal percentage of caloric test (P < .05, Fisher exact test). In total, the abnormal rate for the caloric test in 40 hydropic ears was 30% (12/40).

**oVEMP Test**

The oVEMP test obtained augmented (Figure 1) and reduced (Figure 2) responses in all hydropic ears of the augmented and reduced groups, respectively. The mean nI and pI latencies of the augmented group were 8.1 ± 0.3 ms and 12.1 ± 0.7 ms, respectively, which differed significantly from those of the reduced group (P < .01, unpaired t test; Table 2). Likewise, the mean nI-pI amplitude was significantly larger in the augmented group than in the reduced group (P < .01; Table 2).
The cVEMP test of the augmented group revealed normal responses in 6 ears and abnormal responses in 14 ears (70%), including reduced response in 1, delayed responses in 1, and absent responses in 12 ears. In contrast, the reduced group revealed normal responses in 7 ears and abnormal responses in 13 ears (65%), including delayed responses in 2 and absent responses in 11. Abnormal percentages observed on the cVEMP test did not significantly differ between the augmented and reduced groups ($P > .05$; Table 1).

Unlike the oVEMP test, the mean $p_{13}$ latency, $n_{23}$ latency, and $p_{13}-n_{23}$ amplitude did not significantly differ between the 2 groups ($P > .05$; Table 2). In total, the abnormal rate for the cVEMP test in 40 hydropic ears was 68% (27/40).

Ménière Stages vs VEMP Responses

Forty hydropic ears were divided into 3 groups based on the Ménière stage to investigate the VEMP responses as a function of advancing stage. Accordingly, stage I consisted of 12 ears with augmented oVEMPs and 3 ears with reduced oVEMPs; stage II, 5 augmented ears and 9 reduced ears; and stage III, 3 augmented and 8 reduced ears. The prevalence of augmented oVEMPs exhibited a significant trend to decline from stage I to stages III-IV ($P < .01$, Cochran-Armitage trend test; Table 3).

In cVEMP responses, stage I consisted of 4 ears with normal cVEMPs, 10 ears with absent cVEMPs, and 1 ear with delayed cVEMPs; stage II, 5 normal ears and 9 abnormal ears (absent in 8 and delayed in 1); and stages III to IV, 4 normal ears and 7 abnormal ears (absent in 5, delayed in 1, and reduced in 1). Unlike oVEMPs, no significant trend was observed in the prevalence of abnormal cVEMPs from stage I to stages III-IV ($P > .05$, Cochran-Armitage trend test; Table 4).

Discussion

In this study, the stages of Ménière disease were significantly earlier in the augmented group than in the reduced group (Table 1). In addition, the abnormal rates in the caloric test were 10% in the augmented group and 50% in the reduced group, which further confirms that the augmented oVEMP occurred in the early stage, whereas the reduced oVEMP occasionally.

**Figure 1** illustrates the VEMP results in a 56-year-old woman with Ménière disease in the right ear. The $n_{1}-p_{1}$ amplitudes of oVEMPs were 22.1 $\mu$V for the right (hydropic) ear and 7.1 $\mu$V for the left (opposite) ear, respectively, indicating an augmented oVEMP in the hydropic ear, with an asymmetry ratio of 51%. In contrast, the $p_{13}-n_{23}$ amplitudes of cVEMPs were 55 $\mu$V in the right (hydropic) ear and 125 $\mu$V in the left (opposite) ear, indicating a reduced cVEMP in the hydropic ear with an asymmetry ratio of 39%.

**Figure 2** illustrates the VEMP results in a 49-year-old woman with Ménière disease in the left ear. Reduced oVEMPs and absent cVEMPs were observed in the left (hydropic) ear, whereas the right (opposite) ear showed normal oVEMPs and cVEMPs.
occurred in the late stage since canal paresis was noted in 50% of Ménière patients after the first decade. In the early stage (stages I-II) of Ménière disease, augmented oVEMPs (Figure 1) may be attributed to a mechanical, biochemical, or some other reversible cause. However, in the late stage (stages III-IV), there are permanent morphological changes in the sense organs (eg, loss of hair cells associated with a collapsed otolithic wall onto the otolithic membrane), leading to reduced oVEMPs (Figure 2). However, one may ask why the augmented oVEMP is associated with reduced cVEMP in the hydropic ear during the Ménière attack (Figure 1).

Based on the hypothesis of “efferent specificity” proposed by Curthoys, oVEMPs by bone-conducted vibration primarily originate from the utricular macula, whereas cVEMPs originate from the saccular macula. As the histopathological finding of Ménière disease is endolymphatic hydrops, it is interesting to investigate whether the dissociated VEMP results correlate with the waxing and waning of hydrops. For instance, a mechanical factor such as swelling/distortion of the hydrops in the utricle or saccule may cause augmentation/reduction of VEMP responses.

One proposed mechanism of Ménière attack is membrane rupture theory, typically in Reissner’s membrane. Another is membrane distension theory, in which the utricular or saccular membrane herniates into the semicircular canal. Although membrane rupture is undeniably a contributing factor, especially when those patients present grave accidents for hours, rupture of Reissner membrane fails to explain why vertigo is induced when high potassium concentrations in the endolymph bypass the saccule and enter the semicircular canal. Hence, Ménière attack must be precipitated by saccular hydrops because next to the cochlea, the saccule is the second most important part for the development of endolymphatic hydrops. In addition, abnormal cVEMPs observed in most (67%) patients during Ménière attacks are further indication of the participation of the saccule. Restated, rupture or distortion of the saccular hydrops during Ménière attack may cause an elimination or reduction of cVEMPs.

Konishi observed that the utriculo-endolymphatic (UE) valve opens for several days after hydrops formation begins and then closes because of the compression caused by increasing hydrops (Figure 3). The UE valve, first reported by Bast in 1928, exists at the junction between the utricle (U) and the utricular duct. In contrast, the saccular duct, which is between the saccule (S) and endolymphatic duct, does not contain a valve.

### Table 3. Ménière Stage vs oVEMP Responses

<table>
<thead>
<tr>
<th>Ménière Disease</th>
<th>No.</th>
<th>Augmented oVEMPs, No. (%)</th>
<th>Reduced oVEMPs, No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage I</td>
<td>15</td>
<td>12 (80)</td>
<td>3 (20)</td>
</tr>
<tr>
<td>Stage II</td>
<td>14</td>
<td>5 (36)</td>
<td>9 (64)</td>
</tr>
<tr>
<td>Stages III-IV</td>
<td>11</td>
<td>3 (27)</td>
<td>8 (73)</td>
</tr>
<tr>
<td>P value</td>
<td></td>
<td>&lt;.01</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviation: oVEMP, ocular vestibular-evoked myogenic potential.

### Table 4. Ménière Stage vs cVEMP Responses

<table>
<thead>
<tr>
<th>Ménière Disease</th>
<th>No.</th>
<th>Normal cVEMPs, No. (%)</th>
<th>Abnormal cVEMPs, No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage I</td>
<td>15</td>
<td>4 (27)</td>
<td>11 (73)</td>
</tr>
<tr>
<td>Stage II</td>
<td>14</td>
<td>5 (36)</td>
<td>9 (64)</td>
</tr>
<tr>
<td>Stages III-IV</td>
<td>11</td>
<td>4 (36)</td>
<td>7 (64)</td>
</tr>
<tr>
<td>P value</td>
<td></td>
<td>&gt;.05</td>
<td></td>
</tr>
</tbody>
</table>

Abnormal cervical vestibular-evoked myogenic potentials (cVEMPs) indicate absent, reduced, or delayed responses.

### Figure 3. Diagram of the membranous labyrinth. The utriculo-endolymphatic valve exists at the junction between the utricle (U) and the utricular duct. In contrast, the saccular duct, which is between the saccule (S) and endolymphatic duct, does not contain a valve.
In this study, abnormal percentages of hearing, cVEMP, oVEMP, and caloric tests in 40 hydropic ears were 75% (30/40), 68% (27/40), 100% (40/40), and 30% (12/40), respectively (Table 1). This decreasing order of abnormal percentages in function of the cochlea, saccule, utricle, and semicircular canals opposes the declining sequence of hydrops formation in temporal bone studies and physiological testing.\(^{4,5}\) However, if augmented oVEMP is interpreted as a normal response, an abnormal percentage of oVEMPs turns out to be 50% (20/40), compatible with the utricle as the third frequent site for hydrops formation with equivalent information in the latency and amplitude between the 2 modes. Thus, BCV stimulation mode is not the cause for absent cVEMPs.

Ming-Hsun Wen, performed VEMP and wrote paper; Po-Wen Cheng, performed VEMP; Yi-Ho Young, supervised study.

**Limitation of the Study**

Patients in this study were selected to have augmented/reduced oVEMPs in the beginning, which could not reflect the entire population of Ménière patients. As augmented oVEMPs occur after saccular membrane rupture, it may explain why more than half of the ears showed absent cVEMPs. In addition, one may ask whether various stimulation modes affect the cVEMP results. Wang et al\(^ {12}\) reported that cVEMPs by bone-conducted vibration (BCV) mode generate a higher response rate in Ménière ears than those by air-conducted sound (ACS) mode, with equivalent information in the latency and amplitude between the 2 modes. Thus, BCV stimulation mode is not the cause for absent cVEMPs.

**Author Contributions**

Ming-Hsun Wen, performed VEMP and wrote paper; Po-Wen Cheng, performed VEMP; Yi-Ho Young, supervised study.

**Disclosures**

**Competing interests:** None.

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**References**


