**Table 3**Comparison of the results of VEMP and caloric test in 78 patients with vestibular schwannoma.

kal lamas and the	Correctly identified by VEMP	Incorrectly identified by VEMP	Total
Correctly identified by the caloric test	54	9	63
Incorrectly identified by the caloric test	9	6	15
Total	63	15	78

### 3.3. Comparison of VEMP and the caloric test results

In the present study, the sensitivity of VEMP in VS patients (80.8%) was comparable to that of the caloric test (80.8%; p = 1.00). The specificity of VEMP (52.7%) was slightly lower than that of the caloric test (57.4%); however, there was no significant difference between them (p = 0.07).

The results of VEMP and the caloric test are compared in Table 3. Amongst the 78 patients with VS, 54 (69.2%) were correctly identified by both VEMP and the caloric test, nine (11.5%) were correctly identified by VEMP but incorrectly identified by the caloric test, nine (11.5%) were correctly identified by the caloric test but incorrectly identified by VEMP and six (7.7%) were incorrectly identified by both VEMP and the caloric test. Thus, 72 of the 78 patients (92.3%) were correctly identified by either VEMP or the caloric test.

The mean tumour size was  $24.9 \pm 9.2$  mm in the 54 patients correctly identified by both VEMP and the caloric test,  $13.8 \pm 6.2$  mm in the nine patients correctly identified by VEMP but incorrectly identified by the caloric test,  $21.8 \pm 5.0$  mm in the nine patients correctly identified by the caloric test but incorrectly identified by VEMP and  $15.2 \pm 8.7$  mm in the six patients incorrectly identified by both VEMP and the caloric test. The differences amongst these groups were significant (p = 0.001); therefore, we performed the Bonferroni-adjusted t-test. There was a significant difference in the mean tumour size between the patients correctly identified by VEMP but incorrectly identified by the caloric test and the patients correctly identified by both VEMP and the caloric test (p = 0.003); however, there were no significant differences among the other groups (all p > 0.05).

### 4. Discussion

VEMP is now widely used as part of the test battery to explore vestibular abnormalities and its results have been reported for various diseases including VS (Murofushi et al., 1998; Takeichi et al., 2001; Patko et al., 2003; de Waele et al., 1999; Ohki et al., 2002; Matsuzaki and Murofushi, 2001; Iwasaki et al., 2005a). However, the diagnostic usefulness of VEMP in vestibular abnormalities has not been evaluated according to STARD (Bossuyt, 2003; Bossuyt et al., 2003a,b). We assessed the diagnostic usefulness of VEMP in VS and compared it with the caloric test.

### 4.1. The sensitivities of VEMP and the caloric test

The sensitivity of the VEMP test in patients with VS was 80.8%, which was comparable to that of the caloric test (80.8%). When considering only click VEMP, the sensitivity (59.0%) was lower than that reported in the previous reports, in which they used click VEMP alone and reported sensitivities of 72–80% for VS (Murofushi et al., 1998; Takeichi et al., 2001; Patko et al., 2003). The most probable reason for this discrepancy was the existence of 24 patients showing no click-VEMP response on both sides in the present study. Their ages were significantly higher than those of patients who showed

normal VEMP at least on one side. In fact, it is sometimes difficult to record click VEMP from elderly patients because their SCM contraction is insufficient for recording stable VEMP responses; the previous reports might have excluded such patients (Takeichi et al., 2001; Patko et al., 2003). Furthermore, a decrease in VEMP amplitude with age, which was not associated with any age-related change in static SCM tension, has also been reported (Brantberg et al., 2007; Walgampola and Colebatch, 2005). In contrast, burst VEMP could be obtained in all VS patients except two, which was consistent with the previous reports showing greater responses of burst than click VEMP (Patko et al., 2003; Ushio et al., 2001). The sensitivity of click plus burst VEMP reported in the present study (80.8%) was nearly the same as that in the Patko et al. report (78.8%, 134/170 patients) using both click and burst VEMPs (Patko et al., 2003). They suggested that click VEMP may be more appropriate than burst VEMP for appreciating slight saccular dysfunction and that burst VEMP could be useful for detecting any potential residual saccular nerve function (Patko et al., 2003).

The sensitivity of the caloric test reported in the present study (80.8%) was comparable or lower than that reported in the previous studies; which reported 77–92% sensitivities in VS patients (Furuta et al., 2005; Hulshof et al., 1989; Okada et al., 1991). Since the MRI is now available for medical checkups, the average size of diagnosed VS has significantly decreased (Marangos et al., 2001). The increase in detection of small VS might decrease the sensitivity of vestibular and cochlear function tests.

### 4.2. The specificities of VEMP and the caloric test

In patients with VS, the specificity of VEMP was 52.7%, whereas that of the caloric test was 57.4%. There are two possible reasons for these relatively low specificities. Firstly, we enrolled 803 consecutive patients who visited our vertigo clinic, their chief complaints being vertigo, dizziness or imbalance. They were suspected to have vestibular disorders and underwent vestibular tests including VEMP and the caloric test. This population might show abnormal VEMP and caloric test results more frequently than people who do not display any vestibular symptoms. Such a population bias might have contributed to the relatively low specificity of VEMP and the caloric test. Secondly, unlike auditory brainstem response, which could be specific for retrocochlear lesions such as VS, abnormal VEMP and caloric test results are not specific for retrolabyrinthine lesions; however, they suggest the dysfunction of vestibulo-collic reflexes. In fact, the sensitivities of VEMP and the caloric test were also high in patients with vestibular neuritis, delayed endolymphatic hydrops, sudden hearing loss with vertigo and Ramsay Hunt syndrome. The combined use of galvanic VEMP might have increased the specificities to VS (Murofushi et al., 2002).

### 4.3. Comparison of VEMP and caloric test results

The tumour sizes of VS patients correctly identified by VEMP were not larger than those of patients incorrectly identified by VEMP, whereas the tumours of patients correctly identified by the caloric test were significantly larger than those of patients incorrectly identified by the caloric test, such as auditory brainstem response (Wilson et al., 1992; Godey et al., 1998; Schmidt et al., 2001). Moreover, tumours of patients correctly identified by VEMP but incorrectly identified by the caloric test were significantly smaller than those of patients correctly identified by both VEMP and the caloric test, whereas the tumour sizes of patients correctly identified by VEMP and those of patients correctly identified by both VEMP and the caloric test were not different. These results suggest that the sensitivity of VEMP might be less influenced by the tumour size than that of the caloric test. In other words, VEMP is more sensitive

for detecting a small VS than the caloric test. The inferior vestibular nerve may be more vulnerable than the superior one even in cases of small VS. The rate of tumour growth may be another factor which may influence the results of VEMP and caloric test; however, it was not possible to evaluate it in this study.

In conclusion, although the specificity of VEMP (52.7%) was not very high, the sensitivity of click plus burst VEMP (80.8%) was high and comparable to that of the caloric test. We recommend the use of VEMP as well as that of the caloric test in the assessment of patients with VS.

### **Conflict of interest**

The authors have no conflict of interest.

### References

- Bossuvt PM, Improving the flow of diagnostic information: the importance of STARD for authors and readers. Neurology 2003;61:600-1.
- Bossuyt PM, Reitsma JB, Bruns DE, Gatsonis CA, Glasziou PP, Irwig LM, et al. Standards for reporting of diagnostic accuracy. Towards complete and accurate reporting of studies of diagnostic accuracy: the STARD initiative. Clin Chem
- Bossuyt PM, Reitsma JB, Bruns DE, Gatsonis CA, Glasziou PP, Irwig LM, et al. Standards for reporting of diagnostic accuracy. The STARD statement for reporting studies of diagnostic accuracy: explanation and elaboration. Clin Chem 2003b;49:7-18.
- Brantberg K, Granath K, Schart N. Age-related changes in vestibular evoked myogenic potentials. Audiol Neurootol 2007;12:247-53.
- Clemis JD, Ballad WJ, Baggot PJ, Lyon ST. Relative frequency of inferior vestibular schwannoma. Arch Otolaryngol Head Neck Surg 1986;112:190-4.
- Cohen NL, Lewis WS, Ransohoff J. Hearing preservation in cerebellopontine angle tumor surgery: the NYU experience 1974–1991. Am J Otol 1993;14:423–33. Colebatch JG, Halmagyi GM. Vestibular evoked potentials in human neck muscles
- before and after unilateral vestibular deafferentation. 1992;42:1635-6.
- Colebatch JG, Rothwell JC, Bronstein A, Ludman H. Click-evoked vestibular activation in the Tullio phenomenon. J Neurol Neurosurg Psychiatry 1994a;57:1538-40.
- Colebatch JG, Halmagyi GM, Skuse NF. Myogenic potentials generated by a click-evoked vestibulocollic reflex. J Neurol Neurosurg Psychiatry 1994b;57:190-7.
- de Waele C, Huy PT, Diard JP, Freyss G, Vidal PP. Saccular dysfunction in Meniere's disease. Am J Otol 1999;20:223-32.
- Furuta S, Takahashi S, Higano S, Hashimoto S. Prediction of the origin of intracanalicular neoplasms with high-resolution MR imaging. Neuroradiology
- Godey B, Morandi X, Beust L, Brassier G, Bourdiniere J. Sensitivity of auditory brainstem response in acoustic neuroma screening. Acta Otolaryngol
- Gordon ML, Cohen NL. Efficacy of auditory brainstem response as a screening test for small acoustic neuromas. Am J Otol 1995;16:136-9.
- Hulshof JH, Hilders CG, Baarsma EA. Vestibular investigations in acoustic neuroma. Acta Otolaryngol 1989;108:38-44. Iwasaki S, Takai Y, Ozeki H, Ito K, Karino S, Murofushi T. Extent of lesions in
- idiopathic sudden hearing loss with vertigo: study using click and galvanic

- vestibular evoked myogenic potentials. Arch Otolaryngol Head Neck Surg 2005a;131:857-62. Iwasaki S, Takai Y, Ito K, Murofushi T. Abnormal vestibular evoked myogenic
- potentials in the presence of normal caloric responses. Otol Neurotol 2005b;26:1196-9.
- Komatsuzaki A, Tsunoda A. Nerve origin of the acoustic neuroma. J Laryngol Otol 2001;115:376-9.
- Marangos N, Maier W, Merz R, Laszig R. Brainstem response in cerebellopontine angle tumors. Otol Neurotol 2001;22:95-9.
- Matsuzaki M. Murofushi T. Vestibular evoked myogenic potentials in patients with idiopathic bilateral vestibulopathy; report of three cases, ORL J Otorhinolaryngol Relat Spec 2001;63:349-52.
- McCue MP, Guinan Jr JJ. Spontaneous activity and frequency selectivity of acoustically responsive vestibular afferents in the cat. J Neurophysiol 1995;74:1563-72.
- Murofushi T, Curthovs IS, Topple AN, Colebatch IG, Halmagyi GM, Responses of guinea pig primary vestibular neurons to clicks. Exp Brain Res 1995;103:174–8.
- Murofushi T, Curthoys IS, Gilchrist DP. Response of guinea pig vestibular nucleus
- neurons to clicks. Exp Brain Res 1996a;111:149–52. Murofushi T, Halmagyi GM, Yavor RA, Colebatch JG. Absent vestibular evoked myogenic potentials in vestibular neurolabyrinthitis: an indicator of inferior vestibular nerve involvement? Arch Otolaryngol Head Neck Surg 1996b;122:845-8.
- Murofushi T, Matsuzaki M, Mizuno M. Vestibular evoked myogenic potentials in patients with acoustic neuromas. Arch Otolaryngol Head Neck Surg 1998;124:509-12.
- Murofushi T, Matsuzaki M, Wu CH. Short tone burst-evoked myogenic potentials on the sternocleidomastoid muscle: are these potentials also of vestibular origin? Arch Otolaryngol Head Neck Surg 1999;125:660–4.
- Murofushi T, Takegoshi H, Ohki M, Ozeki H. Galvanic-evoked myogenic responses in patients with an absence of click-evoked vestibulo-collic reflexes. Clin Neurophysiol 2002:113:305-9.
- Ohki M, Matsuzaki M, Sugasawa K, Murofushi T. Vestibular evoked myogenic potentials in patients with contralateral delayed endolymphatic hydrops. Eur Arch Otorhinolaryngol 2002;259:24–6.
- Okada Y, Takahashi M, Saito A, Kanzaki J. Electronystagmographic findings in 147 patients with acoustic neuroma. Acta Otolaryngol Suppl 1991;487:150-6.
- Patko T, Vidal PP, Vibert N, Tran Ba Huy P, de Waele C. Vestibular evoked myogenic potentials in patients suffering from an unilateral acoustic neuroma: a study of 170 patients. Clin Neurophysiol 2003;114:1344–50.
- Robson AK, Leighton SEJ, Anslow P, Milford CA. MRI as a single screening procedure for acoustic neuroma: a cost effective protocol. J R Soc Med 1993;86:455–7. Schmidt RJ, Sataloff RT, Newman J, Spiegel JR, Myers DL. The sensitivity of auditory
- brainstem response testing for the diagnosis of acoustic neuromas. Arch Otolaryngol Head Neck Surg 2001;127:19–22. Slattery 3rd WH, Brackmann DE, Hitselberger W. Middle fossa approach for hearing
- preservation with acoustic neuromas. Am J Otol 1997;18:596-601.
- Takeichi N, Sakamoto T, Fukuda S, Inuyama Y. Vestibular evoked myogenic potential (VEMP) in patients with acoustic neuromas. Auris Nasus Larynx 2001;28(Suppl.):39-41.
- Thomsen J, Nyboe J, Borum P, Tos M, Barfoed C. Acoustic neuromas. Diagnostic efficiency of various test combinations. Arch Otolaryngol 1981;107:601–7.
- Ushio M, Matsuzaki M, Takegoshi H, Murofushi T. Click- and short tone burstevoked myogenic potentials in cerebellopontine angle tumors. Acta Otolaryngol 2001;545(Suppl.):133-5.
- Walgampola MS, Colebatch JG. Characteristics and clinical applications of vestibular-evoked myogenic potentials. Neurology 2005;64:1682–8. Wilson DF, Hodgson RS, Gustafson MF, Hogue S, Mills L. The sensitivity of auditory
- brainstem response testing in small acoustic neuromas. Laryngoscope 1992:102:961-4.

### ORIGINAL COMMUNICATION

# Novel subtype of idiopathic bilateral vestibulopathy: bilateral absence of vestibular evoked myogenic potentials in the presence of normal caloric responses

Chisato Fujimoto · Toshihisa Murofushi · Yasuhiro Chihara · Mitsuya Suzuki · Tatsuya Yamasoba · Shinichi Iwasaki

Received: 26 January 2009/Revised: 30 March 2009/Accepted: 17 April 2009/Published online: 12 May 2009 © Springer-Verlag 2009

Abstract To characterize clinical features of those patients who showed an absence of vestibular evoked myogenic potential (VEMP) responses in the presence of normal caloric responses bilaterally, we reviewed clinical records of 1,887 consecutive outpatients who complained of balance problems, and identified three patients, who showed absent VEMPs in the presence of normal caloric responses bilaterally with unknown causes. All three patients had episodes of recurrent vertigo without spontaneous, gaze-evoked, or positional nystagmus at the time of examination. They complained of oscillopsia while moving their body or head and showed positive Romberg's signs. Drawing on these cases, we underscore the importance of examining the function of the inferior vestibular nerve system, even with no nystagmus and normal caloric findings, in patients complaining of dizziness or oscillopsia during locomotion.

**Keywords** Evoked potentials · Vertigo · Vestibulopathy · Vestibular function tests

C. Fujimoto (☒) · T. Murofushi · Y. Chihara · M. Suzuki · T. Yamasoba · S. Iwasaki
Department of Otolaryngology, Faculty of Medicine,
The University of Tokyo, 7-3-1, Hongo, Bunkyo-ku,
Tokyo, Japan
e-mail: cfujimoto-tky@umin.ac.jp

T. Murofushi
Department of Otolaryngology, University Hospital,
Mizonokuchi, Teikyo University School of Medicine,
Kawasaki, Japan

### Introduction

The vestibular labyrinth is innervated by the superior and inferior vestibular nerves (SVN, IVN). The SVN innervates the lateral and anterior semicircular canals (LSCC, ASCC), the utricle, and a part of the saccule, whereas the IVN innervates the posterior SCC (PSCC) and most part of the saccule. The caloric test has been used as a clinical test of the LSCC and the SVN system, whereas the vestibular evoked myogenic potential (VEMP) measures the function of the saccule and IVN system [10, 23]. Additionally, the head thrust test can be used to measures the individual SCC function using 3-D magnetic search coil systems [4].

By applying these tests, we have found that selective dysfunction of IVN system, in spite of the spared SVN system, has been reported in Meniere's disease [12], acoustic neuroma [24], sudden deafness with vertigo [19] and selective inferior vestibular neuritis [4]. Some patients who showed abnormal VEMP responses on one side with normal responses on caloric test could not be diagnosed as having an established clinical entity [18].

Idiopathic bilateral vestibulopathy (IBV) is an acquired bilateral vestibulopathy of unknown cause [6]. Absent or markedly decreased response of the LSCC is revealed in the caloric test, the rotation test [3, 6, 26, 29, 31] and the head thrust test [35, 36]. Originally, IBV is not accompanied by cochlear or any other neurological symptoms [6]. The main clinical symptoms are persistent imbalance. In severely affected cases, patients have oscillopsia while moving their body or the head. Some patients with IBV have been reported to show an absence of VEMP [14, 21], suggesting that IBV affects not only the SVN but also IVN systems. However, so far there have been no reported idiopathic cases whose bilateral IVN systems are affected in spite of sparing the bilateral SVN systems.

We identified three patients who showed bilaterally an absence of VEMP responses in the presence of bilateral normal caloric responses. Herein, we reported clinical features of these patients.

### Patients and methods

### **Patients**

We reviewed clinical records of 1,887 consecutive patients visiting Balance Disorder Clinic, the University of Tokyo Hospital, from January 2002 to December 2007. Of these, 1,025 patients underwent both caloric test and VEMP test.

The following were the inclusion criteria: (1) bilateral normal caloric responses and (2) bilateral absence of VEMP responses by both click and short tone burst stimulation. The following were the exclusion criteria: (1) medical history of other neurological disorders, (2) familial history of auditory or vestibular dysfunction, (3) past history of excessive noise exposure, head injury or exposure to ototoxic drugs, (4) sensorineural hearing loss except for presbycusis, (5) the existence of air-bone gap (more than 10 dB) [8], (6) abnormal findings on neurological examinations except for vestibular dysfunction, (7) difficulty in maintaining muscle activity at a sufficient level [electromyographic (EMG) activity >150  $\mu$ V].

### Methods

### Caloric test

Caloric test was performed as reference standard by irrigating the external auditory canal with 2 ml cold and/or ice water for 20 s followed by aspiration of water. Caloric nystagmus was recorded using an electronystagmograph. Canal paresis (CP) was calculated as difference between the maximal slow phase eye velocity for each ear divided by the sum of slow phase eye velocities. The abnormal caloric response is defined as any of the following criteria: (1) CP percentage larger than 20% in caloric test [18]; (2) the maximum slow phase eye velocity smaller than 10°/s bilaterally in caloric test with ice water.

### VEMP test

Electromyographic activity was recorded from a surface electrode placed on the upper half of each sternocleidomastoid muscle (SCM), with a reference electrode on the side of the upper sternum and a ground electrode on the nasion. During the recording, subjects in the supine position were instructed to raise their heads from the pillow to contract SCM. The overall EMG activity of the SCM was

set as the reference level of the tonic contraction. During the recording, EMG activities were monitored on a display, to maintain muscle activity at a sufficient level >150  $\mu V$  in each patient.

The EMG signal from the stimulated side was amplified and bandpass-filtered (20–2,000 Hz). The stimulation rate was 5 Hz, and the time window for analysis was 100 ms (–20 to 80 ms). Rarefaction clicks (0.1 ms, 95 dB nHL) were presented to each ear through headphones (Type DR-531, Elega Acous. Co. Ltd., Tokyo, Japan). Short tone bursts of 500 Hz (95 dB normal hearing level, 135 dB SPL (peak value); rise/fall time, 1 ms; plateau time 2 ms) were also presented. The latencies and amplitudes of the first positive–negative peaks (p13–n23) of the VEMP were evaluated. The average of two runs was taken for the amplitude and latencies. Loss of reproducible p13–n23 in two runs was regarded as no VEMP responses.

#### Results

### Selection of patients

Among 1,025 patients who underwent both caloric test and VEMP test, 19 patients fulfilled the inclusion criteria, but 16 patients were excluded by the exclusion criteria. We finally identified three patients who fulfilled both the inclusion and exclusion criteria. The number of the patients who fell under the exclusion criteria was as follows: two patients in criteria (1), a patient in criteria (2), four patients in criteria (3), eight patients in criteria (4), a patient in criteria (5) and nine patients in criteria (6).

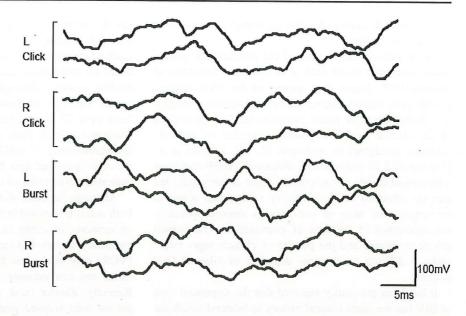
### Case reports

### Case 1

A 71-year-old woman suffered from vertigo attacks lasting for approximately an hour several times a month during 3 years before visiting our clinic. After the first vertigo attack, she began to have dizziness, which became worse gradually, especially while walking. She complained of oscillopsia while moving her head. There were no obvious cochlear or other neurological symptoms related to the dizziness or the vertigo attacks. She had no complaints of headache or changes in strength or sensation. Her medical and family history were unremarkable. She had no history of excessive noise exposure, head injury or exposure to ototoxic drugs.

On examination, she had no spontaneous, gaze-evoked, or positional nystagmus. Her pure-tone hearing levels (the average of hearing levels at 500, 1,000 and 2,000 Hz) were 16.6 dBHL on the right side and 13.3 dBHL on the left

Fig. 1 Absent VEMP on both sides by both click and short tone burst stimulation in Case 1



side. No significant air-bone gaps were present. She showed positive Romberg's sign. Caloric responses were normal in both ears. VEMP tests by both click and short tone burst stimulation showed no response on either side in spite of maintenance of muscle activity at the sufficient level (Fig. 1). There were no abnormal findings in other neurological examinations including sensory and cerebellar examinations.

### Case 2

A 40-year-old woman suffered from vertigo attacks lasting approximately 30 min on four occasions during a month before visiting our clinic. After the first vertigo attack, she began to feel dizziness, which became worse after each vertigo attack. She complained of oscillopsia while moving her body. There were no obvious cochlear or other neurological symptoms related to the dizziness or the vertigo attacks. She had no spontaneous, gaze-evoked, or positional nystagmus. Her pure-tone hearing levels were 10.0 dBHL on the right side and 11.7 dBHL on the left side. No significant air-bone gaps were present. She showed positive Romberg's sign. Caloric responses were normal in both ears. VEMP tests by both click and short tone burst stimulation showed no response on either side in spite of maintenance of muscle activity at the sufficient level.

### Case 3

A 70-year-old woman suffered from recurrent vertigo attacks lasting for several hours approximately once every 2 months during 3 years before visiting our clinic. She

complained of oscillopsia while moving her head. There were no obvious cochlear or other neurological symptoms related to the dizziness or the vertigo attacks. She had no spontaneous, gaze-evoked, or positional nystagmus. Her pure-tone hearing levels were 21.7 dBHL on the right side and 18.3 dBHL on the left side. No significant air-bone gaps were present. She showed positive Romberg's sign. Caloric responses were normal on both ears. VEMP tests by both click and short tone burst stimulation showed no response on either side in spite of maintenance of muscle activity at the sufficient level.

### Discussion

In the present study, we reported three patients with bilateral absent VEMP responses in the presence of normal caloric responses. These cases did not fulfill the criteria of IBV [3, 6, 26, 29, 31], since they showed normal caloric responses. However, given the disease concept of IBV, which was an acquired bilateral vestibulopathy of unknown cause without cochlear or any other neurological disorders, our cases could be considered as one of the subtypes of IBV.

Idiopathic bilateral vestibulopathy has been classified into two types based on their clinical time course: slowly progressive and sequential [6, 35]. The slowly progressive type is characterized by gradually progressive imbalance, whereas the sequential type is characterized by recurrent vertigo accompanied by persistent imbalance. Patients who combined the episode of slowly progressive type and sequential type were also reported [22]. In the present study, all the three cases had episodes of recurrent vertigo,

so they could be classified as the sequential type from their clinical time course.

In the present study, none of the patients had spontaneous nystagmus at the time of examination. Disorders of bilateral IVN system with sparing of the SVN systems should have caused vertical or vertical—torsional nystagmus during the acute phase, because electrical stimulation of the saccule or PSCC produces, vertical or vertical—torsional nystagmus in mammals [9, 11]. Iwasaki et al. [18] reported 40 patients with abnormal VEMP responses with normal caloric test responses. Some of them indicated that the direction of their rotatory vertigo was torsional or vertical, but none of our patients showed spontaneous nystagmus at the time of examination. The normal caloric responses and the paucity of clinical signs might make it difficult to diagnose disorders of bilateral IVN systems.

It has been previously reported that the sequential type of IBV has the same clinical history as bilateral vestibular neuritis [6, 14, 21]. Epidemiologic and pathologic studies showed that an inflammation of the nerve caused by viral infection, such as herpes simplex virus type 1, is a common cause of vestibular neuritis [2, 15, 27]. A subsequent similar attack involving the opposite side can produce bilateral vestibular loss. Although vestibular neuritis usually involves the SVN systems by its conventional definition, a group of patients with vestibular neuritis could selectively involve IVN systems [4, 16]. It is possible that our patients had suffered from the selective inferior vestibular neuritis sequentially. However, in each case of our study, the duration of vertigo was much shorter than that of typical vestibular neuritis, and it is unlikely to regard the cause as bilateral vestibular neuritis. On the other hand, Halmagyi et al. [16] reported that the duration of vertigo attacks of unilateral inferior vestibular neuritis was shorter than that of typical vestibular neuritis. Another possible cause of selective involvement bilateral IVN systems is endolymphatic hydrops in both ears. Patients who have recurrent vertigo attacks without cochlear symptoms have been classified as atypical Meniere's disease [1]. Abnormal VEMP responses in the presence of normal caloric responses are frequently observed in Meniere's disease especially at the early stages [12]. Frequent vertigo attacks of our patients were similar to those of Meniere's disease, and Meniere's disease frequently involves bilateral ears [13, 30, 34]. It is possible that bilateral endolymphatic hydrops in saccular region resulted in absent VEMP responses in the presence of normal caloric responses in our patients.

There have been some reports regarding the effect of age on VEMP amplitude [7, 20, 25, 28, 33] and some of these reports pointed out VEMPs to clicks could be absent in normal healthy subjects, especially in elderly [28, 33].

On the other hand, tone burst stimulation requires lower stimulus intensity to elicit VEMPs in comparison with click stimulation [32]. Using tone burst stimuli, VEMPs could be successfully recorded bilaterally even in elderly healthy control, although the amplitudes tended to be smaller with age [7]. Two of the three patients in our study were over 70 in age, but their absence of VEMPs were confirmed in both click and tone burst stimulation under the maintenance of sufficient muscle activity. Therefore, we considered that their findings of an absence of VEMPs indicated dysfunction of the IVN system.

Although our cases showed normal caloric responses on both sides, it is possible that they might have dysfunction of semicircular canals in response to stimuli with higher frequency. Caloric test can measure vestibulo-ocular reflex (VOR) only in the low frequency [5], whereas the head-thrust test can measure VOR in higher frequency [17]. Recently, Zingler et al. [35] have shown that there are patient who showed pathological head thrust test, even though the caloric test was normal. These patients could have oscillopsia when moving the head. Unfortunately we did not perform head thrust tests or rotational tests in these three patients at the time of examination.

In the present study, all the three patients complained of oscillopsia while moving their body or head, and showed positive Romberg's signs. Through these cases, we advocate that it is important to examine the function of the inferior vestibular nerve system in patients who showed such clinical symptoms even with normal caloric responses.

Conflict of interest statement None.

### References

- (1995) Committee on Hearing and Equilibrium guidelines for the diagnosis and evaluation of therapy in Meniere's disease. American Academy of Otolaryngology-Head and Neck Foundation, Inc. Otolaryngol Head Neck Surg 113:181–185. doi: 10.1016/S0194-5998(95)70102-8
- Arbusow V, Schulz P, Strupp M, Dieterich M, von Reinhardstoettner A, Rauch E, Brandt T (1999) Distribution of herpes simplex virus type 1 in human geniculate and vestibular ganglia: implications for vestibular neuritis. Ann Neurol 46:416–419. doi:10.1002/1531-8249(199909)46:3<416::AID-ANA20>3.0. CO;2-W
- Arbusow V, Strupp M, Dieterich M, Stocker W, Naumann A, Schulz P, Brandt T (1998) Serum antibodies against membranous labyrinth in patients with "idiopathic" bilateral vestibulopathy. J Neurol 245:132–136. doi:10.1007/s004150050192
- Aw ST, Fetter M, Cremer PD, Karlberg M, Halmagyi GM (2001) Individual semicircular canal function in superior and inferior vestibular neuritis. Neurology 57:768–774
- Baloh RW, Honrubia V, Yee RD, Hess K (1984) Changes in the human vestibulo-ocular reflex after loss of peripheral sensitivity. Ann Neurol 16:222–228. doi:10.1002/ana.410160209
- Baloh RW, Jacobson K, Honrubia V (1989) Idiopathic bilateral vestibulopathy. Neurology 39:272–275

- Basta D, Todt I, Ernst A (2007) Characterization of age-related changes in vestibular evoked myogenic potentials. J Vestib Res 17:93-98
- Bath AP, Harris N, McEwan J, Yardley MP (1999) Effect of conductive hearing loss on the vestibulo-collic reflex. Clin Otolaryngol Allied Sci 24:181–183. doi:10.1046/j.1365-2273.1999. 00234 x
- Cohen B, Suzuki JI, Bender MB (1964) Eye movements from semicircular canal nerve stimulation in the cat. Ann Otol Rhinol Laryngol 73:153–169
- Colebatch JG, Halmagyi GM, Skuse NF (1994) Myogenic potentials generated by a click-evoked vestibulocollic reflex. J Neurol Neurosurg Psychiatry 57:190–197. doi:10.1136/jnnp.57. 2.190
- Curthoys IS (1987) Eye movements produced by utricular and saccular stimulation. Aviat Space Environ Med 58:A192–A197
- de Waele C, Huy PT, Diard JP, Freyss G, Vidal PP (1999) Saccular dysfunction in Meniere's disease. Am J Otol 20:223– 232. doi:10.1016/S0196-0709(99)90004-2
- Friberg U, Stahle J, Svedberg A (1984) The natural course of Meniere's disease. Acta Otolaryngol Suppl 406:72–77
- Fujimoto C, Iwasaki S, Matsuzaki M, Murofushi T (2005) Lesion site in idiopathic bilateral vestibulopathy: a galvanic vestibularevoked myogenic potential study. Acta Otolaryngol 125:430– 432. doi:10.1080/00016480410024668
- Furuta Y, Takasu T, Fukuda S, Inuyama Y, Sato KC, Nagashima K (1993) Latent herpes simplex virus type 1 in human vestibular ganglia. Acta Otolaryngol Suppl 503:85–89. doi:10.3109/000164 89309128081
- Halmagyi GM, Aw ST, Karlberg M, Curthoys IS, Todd MJ (2002) Inferior vestibular neuritis. Ann N Y Acad Sci 956:306–313
- Halmagyi GM, Curthoys IS (1988) A clinical sign of canal paresis. Arch Neurol 45:737–739
- Iwasaki S, Takai Y, Ito K, Murofushi T (2005) Abnormal vestibular evoked myogenic potentials in the presence of normal caloric responses. Otol Neurotol 26:1196–1199. doi:10.1097/01.mao.0000194890.44023.e6
- Iwasaki S, Takai Y, Ozeki H, Ito K, Karino S, Murofushi T (2005) Extent of lesions in idiopathic sudden hearing loss with vertigo: study using click and galvanic vestibular evoked myogenic potentials. Arch Otolaryngol Head Neck Surg 131:857–862. doi:10.1001/archotol.131.10.857
- Lee SK, Cha CI, Jung TS, Park DC, Yeo SG (2008) Age-related differences in parameters of vestibular evoked myogenic potentials. Acta Otolaryngol 128:66–72. doi:10.1080/00016480701387 108
- Matsuzaki M, Murofushi T (2001) Vestibular evoked myogenic potentials in patients with idiopathic bilateral vestibulopathy.

- Report of three cases. ORL J Otorhinolaryngol Relat Spec 63:349-352. doi:10.1159/000055772
- 22. Murofushi T (ed) (2009) Vestibular neuropathy and vestibular evoked myogenic potential. Springer, Japan (in press)
- Murofushi T, Curthoys IS (1997) Physiological and anatomical study of click-sensitive primary vestibular afferents in the guinea pig. Acta Otolaryngol 117:66–72. doi:10.3109/00016489709117994
- Murofushi T, Matsuzaki M, Mizuno M (1998) Vestibular evoked myogenic potentials in patients with acoustic neuromas. Arch Otolaryngol Head Neck Surg 124:509–512
- Ochi K, Ohashi T (2003) Age-related changes in the vestibularevoked myogenic potentials. Otolaryngol Head Neck Surg 129:655–659. doi:10.1016/S0194-5998(03)01578-X
- Rinne T, Bronstein AM, Rudge P, Gresty MA, Luxon LM (1995) Bilateral loss of vestibular function. Acta Otolaryngol Suppl 520(Pt 2):247–250. doi:10.3109/00016489509125239
- Schuknecht HF, Kitamura K (1981) Second Louis H. Clerf lecture. Vestibular neuritis. Ann Otol Rhinol Laryngol 90:1–19
- Su HC, Huang TW, Young YH, Cheng PW (2004) Aging effect on vestibular evoked myogenic potential. Otol Neurotol 25:977– 980. doi:10.1097/00129492-200411000-00019
- Telian SA, Shepard NT, Smith-Wheelock M, Hoberg M (1991)
   Bilateral vestibular paresis: diagnosis and treatment. Otolaryngol
   Head Neck Surg 104:67–71
- Thomas K, Harrison MS (1971) Long-term follow up of 610 cases of Meniere's disease. Proc R Soc Med 64:853–856
- Vibert D, Liard P, Hausler R (1995) Bilateral idiopathic loss of peripheral vestibular function with normal hearing. Acta Otolaryngol 115:611–615. doi:10.3109/00016489509139375
- Welgampola MS, Colebatch JG (2001) Characteristics of tone burst-evoked myogenic potentials in the sternocleidomastoid muscles. Otol Neurotol 22:796–802. doi:10.1097/00129492-200 111000-00014
- Welgampola MS, Colebatch JG (2001) Vestibulocollic reflexes: normal values and the effect of age. Clin Neurophysiol 112:1971–1979. doi:10.1016/S1388-2457(01)00645-9
- Wladislavosky-Waserman P, Facer GW, Mokri B, Kurland LT (1984) Meniere's disease: a 30-year epidemiologic and clinical study in Rochester, Mn, 1951–1980. Laryngoscope 94:1098–1102. doi:10.1288/00005537-198408000-00020
- Zingler VC, Cnyrim C, Jahn K, Weintz E, Fernbacher J, Frenzel C, Brandt T, Strupp M (2007) Causative factors and epidemiology of bilateral vestibulopathy in 255 patients. Ann Neurol 61:524–532. doi:10.1002/ana.21105
- Zingler VC, Weintz E, Jahn K, Botzel K, Wagner J, Huppert D, Mike A, Brandt T, Strupp M (2008) Saccular function less affected than canal function in bilateral vestibulopathy. J Neurol 255:1332–1336. doi:10.1007/s00415-008-0887-6

Contents lists available at ScienceDirect

## Clinical Neurophysiology





# Assessment of diagnostic accuracy of foam posturography for peripheral vestibular disorders: Analysis of parameters related to visual and somatosensory dependence

Chisato Fujimoto a,\*, Toshihisa Murofushi a,b, Yasuhiro Chihara a, Munetaka Ushio a, Keiko Sugasawa a, Takuhiro Yamaguchi <sup>c</sup>, Tatsuya Yamasoba <sup>a</sup>, Shinichi Iwasaki <sup>a</sup>

### ARTICLE INFO

Article history: Accepted 7 May 2009 Available online 10 June 2009

Keywords: Posture Vestibule Vestibular diseases Sensitivity and specificity ROC curve

#### ABSTRACT

Objectives: Simple tests to detect peripheral vestibulopathy might be practically useful before conducting elaborate examinations. The purpose of this study was to assess the diagnostic accuracy of foam posturography for peripheral vestibulopathy, with emphasis on visual and somatosensory dependence.

Methods: Two-legged stance tasks were conducted in patients with unilateral (n = 68) and bilateral (n = 16) vestibulopathy and healthy controls (n = 66), under four conditions; eyes open with and without the foam rubber, and eyes closed with and without the foam rubber.

Results: The values of six parameters; the velocity of movement of the center of pressure (COP) and envelopment area tracing by the movement of the COP in eyes closed/foam rubber, the Romberg's ratios of velocity and area with foam rubber, and the foam ratios (ratios of a measured parameter with to without the foam rubber), of velocity and area in eyes closed, were significantly higher in unilateral and bilateral vestibulopathy compared with the control (p < 0.001). The area under the receiver operating characteristic curve for the Romberg's ratio of velocity with the foam rubber was the largest.

Conclusions: Foam posturography detected high levels of visual and somatosensory dependence in patients with vestibulopathy.

Significance: Foam posturography is useful for preliminary assessment of possible peripheral

© 2009 International Federation of Clinical Neurophysiology. Published by Elsevier Ireland Ltd. All rights

### 1. Introduction

The vestibular labyrinth located in the inner ear serves as a sensory organ for angular and linear movements. The semicircular canals (SCCs) respond to angular accelerations, whereas the otolith organs respond to linear accelerations. In the SCC system, the lateral semicircular canal (LSCC), the anterior semicircular canal (ASCC) and the posterior semicircular canal (PSCC) are at almost right angles to each other, and the system can sense angular acceleration in all directions. The otolith organs, which are composed of the utricle and saccule, operate as multidirectional linear accelerometers in the diverse polarization of the

Considering the complexity of the vestibular system, new tests are required for comprehensive evaluation of the function of the receptors in each vestibular end-organ. A number of tests, such as the caloric test and the vestibular evoked myogenic potential (VEMP) test, have been used in the differential diagnosis of vestibular disorders (Colebatch and Halmagyi, 1992; Murofushi et al., 1996, 2003; O'Neill, 1987). However, these tests are time-consuming and demand relatively hard physical tasks for patients. Preliminary tests for vestibular disorders prior to the conduct of detailed examination might be practical.

Posture in human is maintained by muscular actions governed by the processing of the central nervous system. The central processing integrates the information from vestibular, visual, and somatosensory inputs. Posturography measures the position of the center of pressure (COP), which is a good parameter of the position of the center of mass during upright stance. Static posturography measures spontaneous movements of the body on a firm platform (Black and Wall, 1981). Dynamic posturography (moving platform) or posturography while standing on a foam rubber (foam posturography) can change the relative contributions of the visual,

<sup>&</sup>lt;sup>a</sup> Department of Otolaryngology, Faculty of Medicine, The University of Tokyo, 7-3-1, Hongo, Bunkyo-ku, Tokyo, Japan

Department of Otolaryngology, University Hospital, Mizonokuchi, Teikyo University School of Medicine, 3-8-3, Mizonokuchi, Takatsu-ku, Kawasaki, Kanagawa, Japan Department of Clinical Trial Data Management, Graduate School of Medicine, The University of Tokyo, 7-3-1, Hongo, Bunkyo-ku, Tokyo, Japan

<sup>\*</sup> Corresponding author. Tel.: +81 3 5800 8665; fax: +81 3 3814 9486. E-mail address: cfujimoto-tky@umin.ac.jp (C. Fujimoto).

somatosensory, and vestibular inputs, which are used to maintain upright posture under normal circumstances (Furman, 1995; Nashner, 1971; Nashner et al., 1982). Trunk angular sway measured with angular transducers is also used as a clinical test of balance disorder (Allum et al., 2001, 2002).

Previous studies reported that under the condition of standing on foam rubber, patients with unilateral or bilateral peripheral vestibular disorders show more severe balance deficits than healthy controls (Black et al., 1983; Baloh et al., 1998b; Allum et al., 2001). However, the tasks and parameters that can be used in preliminary and simple tests for the diagnosis of peripheral vestibular disorders remain controversial. Although posturography cannot directly evaluate the function of each vestibular end-organ (Baloh et al., 1998a–c, 1994), given it is easy to use and noninvasive, its adaptation for a preliminary test in balance disorders should be discussed in more detail.

The purpose of this study was to assess the diagnostic accuracy of the originally established posturography analysis system with the foam rubber for unilateral and bilateral peripheral vestibular disorders, especially noting the visual and somatosensory dependence in patients with peripheral vestibular damage. We calculated the sensitivity and specificity of several parameters used in foam posturography that could discriminate patients with peripheral vestibular damage from healthy subjects, as well as the construction of receiver operating characteristic (ROC) curve. The strength of this study lies in the validation of these criteria in an independent sample. Several factors threaten the validity of studies of diagnostic accuracy. This inspired the launch of the Standards for Reporting of Diagnostic Accuracy (STARD) initiative (Bossuyt et al., 2003a,b). The objective of the STARD initiative is to improve the quality of studies on diagnostic accuracy. The design of this study followed the guidelines set out in the STARD.

### 2. Methods

### 2.1. Participants

Subjects were recruited between December 8, 2006, and October 12, 2007 at the Balance Disorder Clinic, Department of Otolaryngology, the University of Tokyo Hospital. The study was approved by the local ethics committee and conducted according to the tenets of the Declaration of Helsinki, and an informed consent was obtained from each participant. Patients were scheduled to undergo caloric test prior to posturography. Both tests were performed on the same day. Caloric testing was performed as the reference standard by irrigating the external auditory canal with 2 ml ice water for 20 s followed by aspiration. Canal paresis (CP) was calculated as the difference between the maximal slow phase eye velocity for each ear irrigation divided by the sum of slow phase eye velocities. Peripheral vestibulopathy was diagnosed when any of the following two criteria of the caloric test was met: (i) CP percentage >20% (peripheral unilateral vestibulopathy) (Iwasaki et al., 2005); (ii) maximum slow phase eye velocity <7°/s bilaterally (peripheral bilateral vestibulopathy). All subjects with a known history of other neurological or orthopedic disorders, or other abnormal findings on a brief neurological examination, were excluded. Consecutive patients with peripheral vestibulopathy were enrolled after the caloric test. Healthy control subjects were selected from the staff of the University of Tokyo Hospital.

A total of 90 consecutive patients with peripheral vestibulopathy were enrolled after vestibular examination including caloric test. We considered 6 patients were unable to endure our study protocol due to difficulty in standing on hard floor in the upright posture eyes open and were excluded from the study. Thus, 84 patients were enrolled in this study [35 men, 49 women, mean (±SD)

age, 57.4 (±13.9) years, range, 23-84]. Out of the 84 patients, 68 [26 men, 42 women, age, 57.7 (±14.0) years, range, 23-84] were diagnosed as unilateral vestibulopathy, including etiologies of vestibular neuritis (n = 14), acoustic tumor (pre-operative type, n = 6, post-operative type, n = 6), Meniere's disease (n = 4), sudden deafness with vestibular dysfunction (n = 4) and others (n = 34). The other 16 patients [7 men, 9 women, age, 56.4 (±13.9) years, range, 29-71] were diagnosed as bilateral vestibulopathy, including 10 patients who did not show any nystagmus bilaterally and 6 patients who showed nystagmus with maximum slow phase velocity less than 7°/s bilaterally. The mean age of the 66 healthy control subjects (22 men, 44 women) was 56.5 (±14.6) years (range, 24-79). The estimated period after the first episode of balance disorder was less than 14 days in 11 patients, 14-30 days in 13, 1-6 months in 16,  $\geq$ 6 months in 34, and not clear in 5 patients. The remaining 5 patients had no subjective episode of balance disorder.

### 2.2. Posturography test

We used Gravicorder G-5500 (Anima Corp., Tokyo) with foam rubber (Nagashima Medical Instruments, Tokyo). For posturography, we used vertical force transducers to determine instantaneous fluctuations in the COP at a sampling frequency of 20 Hz. A statokinesigram (i.e., the sway path of the COP) was obtained from these vertical forces as changes in electrical signals. The foam rubber material was made of natural rubber, with a tensile strength of 2.2 Kgf/cm², elongation stretch percentage of 100%, density 0.162 g/cm², and thickness of 5 cm. Two-legged stance tasks were performed under four conditions: eyes open with and without the foam rubber, and eyes closed with and without the foam rubber. In each of the four conditions, the distal ends of the big toes of the feet were positioned 45° apart with the heels of both feet close to each other (Fig. 1).

The recording time was 60 s or until the subject required assistance to prevent falling. In the eyes-open condition, the subjects were asked to watch a small, red circle 2 m away from where they were standing in a quiet, well-lit room. Before the test, care was taken to ensure that the platform was at resting level on the floor.

Posturography and caloric tests were administered and evaluated by eight otolaryngologists engaged in medical care at the Balance Disorder Clinic, Department of Otolaryngology, the University of Tokyo Hospital.

### 2.3. Statistical methods

The outcome measures were the mean velocity of movement of the COP for 60 s, which was termed "the velocity", and the envelopment area tracing by the movement of the COP, which was termed "the area". We measured these two variables under four conditions: eyes open with and without the foam rubber, and eyes closed with and without the foam rubber. We calculated the Romberg's ratios of the velocity and area, without and with the foam rubber. The Romberg's ratio was defined as the ratio of a measured value with eyes closed to that with eyes open. We also defined "the foam ratio" as the ratio of a measured value with the foam rubber to without the foam rubber. We calculated the foam ratio of the velocity and the area, with the eyes open and closed.

An overall test for difference among healthy controls, patients with unilateral vestibulopathy and those with bilateral vestibulopathy was performed for each variable using nonparametric Kruskal–Wallis test. The three groups were then compared in pairs for variables that showed a significant difference in Kruskal–Wallis test using nonparametric Steel–Dwass multiple-comparison method. We adopted the variables that showed significant difference between healthy controls and unilateral vestibulopathy patients, and between healthy controls and bilateral vestibulopathy patients, in the Steel–Dwass multiple-comparison method. For patients, in the Steel–Dwass multiple-comparison method.

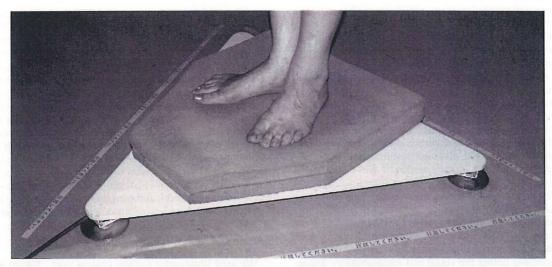


Fig. 1. Position of the feet in the four test conditions. See text for further explanation.

tients who required intervention to prevent them falling under each condition, the most extreme value was set over the maximum among the values recorded by the subjects who were able to stand unaided for 60 s through the trial. For example, the maximal recorded value of Romberg's ratio of velocity with foam rubber was 8.27 in subjects who were able to stand unaided for 60 s through the trial. Then, we pegged the most extreme value, for example, 9.00, which is larger than 8.27. Since we regarded all variables as ordinal variables in non-parametric analyses, subjects with the most extreme value were ranked the highest. To examine the influence of the severity of vestibulopathy on postural control, we described the median and interquartile range (IQR) in each adopted variable in subjects with 20-49%, 50-99% and 100% CP, respectively. An overall test for difference among three groups was conducted using nonparametric Kruskal-Wallis test. For each adopted variable, we constructed receiver operating characteristic (ROC) curve, in which the abscissa was the sensitivity and ordinate was [1 - specificity]. Sensitivity represented the [number of true positive subjects]/[(number of true positive subjects)+(number of false negative subjects)] calculated at each cutoff value. Specificity represented the [number of true negative subjects]/[(number of true negative subjects) + (number of false positive subjects) calculated at each of cutoff value. Then, we calculated the areas under the ROC curve (AUC) to determine the most useful variables. An overall test of difference between four age groups; ≤39 years, 40-54, 55-69 and ≥70 of the healthy controls was performed for each variable adopted, using nonparametric Kruskal-Wallis test.

A *p*-value less than 0.05 denoted the presence of a statistically significant difference. Statistical analyses were conducted using SPSS version 11.0J (SPSS Japan Inc., Tokyo) and R version 2.6.2 (R Development Core Team 2008).

### 3. Results

Fig. 2 shows dot plots of the velocity and area of the movement of the COP under each test condition in healthy controls, and patients with unilateral and bilateral vestibulopathies. In each group, placing the foam rubber on the platform increased the velocity and the area in both the eyes-open and eyes-closed conditions. None of the healthy controls required assistance to prevent falling under any condition. On the other hand, 12 of the 68 (18%) patients with

unilateral vestibulopathy required assistance in tests conducted eyes closed with foam rubber. With regard to patients with bilateral vestibulopathy, 2 of the 16 (13%) and 8 of the 16 (50%) required assistance in eyes open/foam rubber tests and those with eyes closed/foam rubber, respectively.

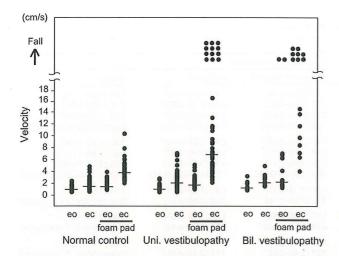
We weighed the velocity, area, Romberg's ratio and the foam ratio between healthy controls and peripheral vestibulopathy patients (Table 1). The values of all variables, except velocity without the foam rubber/eyes open and Romberg's ratio of area without the foam rubber, were significantly higher in the peripheral vestibulopathy group than the control (p < 0.05). Of these variables, six (velocity with eyes closed/foam rubber, area with eyes closed/foam rubber, Romberg's ratios of the velocity and area with the foam rubber, and foam ratios of the velocity and area with eyes closed) were significantly higher in both the unilateral and bilateral vestibulopathy groups than the control group (p < 0.001, each).

Table 2 shows the median and interquartile ranges (IQR) for the above six variables in subjects with 20–49%, 50–99% and 100% CP. No significant differences in the six variables were found among the three groups (Kruskal–Wallis test).

To compare their diagnostic usefulness, we constructed ROC curves for the above six variables and their AUCs were calculated (Fig. 3). An area of 1.0 represents a perfect test; an area of 0.5 represents an uninformative test. All the AUCs were relatively large (>0.7). In particular, the AUCs of the Romberg's ratios of the velocity with the foam rubber, and the velocity with the foam rubber/eyes closed were larger than the other parameters (0.878 and 0.847, respectively).

In the next step, we analyzed the effect of age on the above six variables in healthy controls (Table 3). The velocity in eyes closed/foam rubber, area in eyes closed/foam rubber and foam ratio of the area in eyes closed tended to worsen with age. However, age did not influence the Romberg's ratios of the velocity and area with the foam rubber, and the foam ratio of the velocity in eyes closed. These results suggest that the Romberg's ratio of the velocity with the foam rubber seems the best parameter to identify patients with peripheral vestibular disorders since it showed the largest AUC and was not influenced by age in healthy controls.

The sensitivity and specificity of each variable are listed in Table 4. Based on the ROC curves, the optimal cutoff point of the Romberg's ratio of the velocity with the foam rubber was 2.55. This cutoff point was associated with a sensitivity of 79% (95%CI: 72–84) and specificity of 80% (95%CI, 72–87).



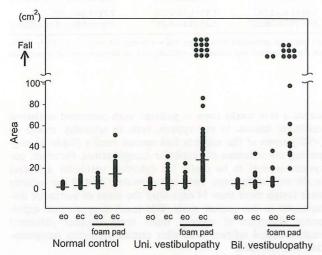


Fig. 2. Dot plots of the velocity and the area in healthy control subjects, patients with unilateral and bilateral vestibulopathies. The dots above the undulating lines represent data of subjects who required assistance to prevent falling. The horizontal lines represent median values. The median values of patients with bilateral vestibulopathy using the foam rubber at eyes closed could not be calculated because 50% (8/16) of the subjects required physical support. eo = eyes open; ec = eyes closed.

### 4. Discussion

In this study, we performed two-legged stance tasks under four conditions in healthy subjects, patients with unilateral vestibulopathy, and patients with bilateral vestibulopathy in order to assess the diagnostic accuracy of foam posturography for peripheral vestibular disorders. The results demonstrated that the values of six variables, including the velocity and area in eyes closed/foam rubber, the Romberg's ratio of the velocity and area with foam rubber, and the foam ratio of the area and velocity in eyes closed, were significantly higher in unilateral and bilateral vestibulopathies than in the healthy controls (p < 0.001). Furthermore, the ROC curves showed that the Romberg's ratio of velocity with foam rubber has the largest (0.878) AUC among the six variables, and the parameter was not influenced by age in healthy controls.

The postural control system involves a complex organization of visual, vestibular and somatosensory inputs, which are related

through the central nervous system to several groups of muscles that act on the musculoskeletal system. Postural control during quiet stance is considered to be based on postural tone and postural reflexes (Massion et al., 2004; Massion and Woollacott, 2004). The vestibular and somatosensory afferents allow the central nervous system to organize balance according to the gravity reference frame and to modulate postural tone by the vestibulospinal loop (Massion et al., 2004; Massion and Woollacott, 2004). In an effort to dissect the different sensory inputs involved in the maintenance of balance, dynamic posturography using a moving platform or foam rubber has been developed to selectively manipulate vision and somatosensation (Baloh et al., 1998b; Nashner et al., 1982). Any increase in body sway measured during standing on a moving platform or foam rubber with eyes closed is considered specific to vestibular disorders, since such patients have asymmetric distribution of postural tone and the role of vestibular inputs becomes more pronounced in the condition with reductions in visual and somatosensory inputs. In this regard, Nashner et al. (1982) reported that the influence of visual and proprioceptive inputs could not be appropriately suppressed in patients with vestibular disorders due to disturbance of information provided by these inputs.

Whether dynamic posturography or foam posturography is useful in clinical diagnosis of peripheral vestibular disorders remains controversial (Allum et al., 2001; Baloh et al., 1998b; Black and Wall, 1981; Evans and Krebs, 1999). Black and Wall (1981) reported that the sensitivity of static posturography is comparable with that of the caloric test and rotational test for detecting Meniere's disease and benign paroxysmal positional vertigo. However, others showed lack of significant differences in Romberg's ratios of sway velocity and sway amplitude in dynamic posturography with foam rubber, between healthy controls and patients with bilateral peripheral vestibulopathy, although the ratios in the latter group was higher than in healthy controls (Baloh et al., 1998b). Some of recent studies have suggested that dynamic posturography is not useful for identifying patients with chronic unilateral vestibulopathy, but modestly useful for identifying patients with acute bilateral vestibulopathy or acute severe unilateral vestibulopathy (Allum et al., 2001; Evans and Krebs, 1999).

In contrast to previous studies using dynamic posturography for evaluation of patients with unilateral vestibulopathy, our study indicated that patients with peripheral vestibulopathy could be clearly distinguished from healthy control subjects without the need to perform complex tasks. There are two possible explanations for the difference between our study and the previously reported studies that did not demonstrate the clinical usefulness of foam posturography in detecting peripheral vestibulopathy. First, we adopted a different supporting base relative to other studies. We instructed the subjects to stand with the distal parts of their feet expanding 45° forward with the heels touching each other (Fig. 1). Most other studies that adopted the two-legged tasks instructed subjects to stand with their feet apart (Black et al., 1983; Furman, 1995). A position that provides narrower supporting base renders subjects more unstable in standing posture and could increase the sensitivity for detecting postural imbalance. The more unstable positions such as standing on toes or one foot using the foam rubber are too physically demanding for the subjects. A moderate and not too demanding loading stimulation could cause a significant difference in our system. We adopted the standing position as modest and not too physically demanding position for subjects, since most patients with vestibulopathy could tolerate all the tasks except for those with eyes closed on the foam rubber. Second, the foam rubber used in the present study could be another factor that significantly affected our results. Differences in the characteris-

**Table 1**Comparison of various parameters in overall and between groups classified by the number of affected ear.

	Posturography	Eyes	Median (IQR)			
			Control	Peripheral vestibulopathy		
				Unilateral + bilateral	Unilateral	Bilateral
Velocity (cm/s)	Static	Open Closed	1.10 (0.84–1.33) 1.69 (1.29–2.14)	1.15 (0.98-1.41) 2.08 (1.69-2.91) <sup>1</sup>	1.12 (0.95-1.42) 2.08 (1.58-2.89) <sup>‡</sup>	1.20 (1.00–1.34) 2.17 (1.82–3.06) <sup>‡</sup>
	Foam	Open Closed	1.64 (1.45-2.01) 3.90 (2.86-4.52)	2.04 (1.60-2.54) <sup>§</sup> 7.16 (4.81-15.86) <sup>§</sup>	1.89 (1.56–2.39)* 6.45 (4.48–11.16) <sup>†</sup>	2.33 (1.82–5.68) <sup>‡</sup> Impossibility of calculation <sup>†</sup>
Area (cm²)	Static	Open Closed	2.21 (1.76–3.13) 3.66 (2.70–5.01)	2.93 (2.21-4.80)§ 5.65 (3.82-9.35) <sup>¶</sup>	2.91 (2.21-4.49) <sup>#</sup> 5.65 (3.69-9.27) <sup>†</sup>	3.67 (1.75-5.76) 5.62 (4.48-13.36) <sup>1</sup>
	Foam	Open Closed	4.71 (3.49–5.98) 14.57 (10.07–19.99)	5.66 (4.48-7.11) <sup>§</sup> 37.25 (18.43-94.22) <sup>§</sup>	5.47 (3.97–6.56) 26.42 (16.67–49.51) <sup>†</sup>	7.02 (5.01–19.96) <sup>‡</sup> Impossibility of calculation <sup>‡</sup>
Romberg's ratio of velocity	Static Foam		1.60 (1.29–1.80) 2.20 (1.97–2.48)	1.86 (1.62-2.21) <sup>¶</sup> 3.32 (2.62-8.14) <sup>¶</sup>	1.82 (1.60-2.18) <sup>†</sup> 3.06 (2.44-4.62) <sup>†</sup>	1.91 (1.61–2.39) <sup>‡</sup> Impossibility of calculation <sup>‡</sup>
Romberg's ratio of area	Static Foam		1.73 (1.21–2.25) 3.48 (2.36–4.23)	1.95 (1.50–2.68) 6.30 (3.94–11.62) <sup>¶</sup>	1.92 (1.50-2.60) 5.13 (3.88-8.45) <sup>†</sup>	2.06 (1.28–3.47) Impossibility of calculation <sup>1</sup>
Foam ratio of velocity		Open Closed	1.56 (1.37–1.78) 2.20 (1.94–2.72)	1.79 (1.52–2.13) <sup>§</sup> 3.27 (2.46–7.85) <sup>¶</sup>	1.75 (1.48-2.12)* 3.11 (2.33-4.03) <sup>†</sup>	1.95 (1.77–2.38) <sup>1</sup> Impossibility of calculation <sup>1</sup>
Foam ratio of area		Open Closed	1.96 (1.49-2.66) 3.49 (2.67-5.02)	1.90 (1.37-2.94) <sup>*</sup> 6.69 (3.52-20.55) <sup>§</sup>	1.83 (1.35-2.35) 5.27 (3.26-9.26) <sup>†</sup>	2.73 (1.64–4.92) Impossibility of calculation

Impossible calculation: the median values could not be calculated because 50% of subjects had to be prevented from falling. IQR = interquartile range. p < 0.05, p < 0.01, p < 0.001 (by nonparametric Kruskal–Wallis test). p < 0.05, p < 0.01, p < 0.001 (between normal control and unilateral vestibulopathy, or between normal control and bilateral vestibulopathy, by Steel–Dwass multiple-comparison method).

tics of the foam rubber such as density and thickness could be critical with respect to the results of the examination. Each research group could have used a different foam rubber with respect to density and height (Allum et al., 2001, 2002; Baloh et al., 1998b; Brandt et al., 1981; Norre, 1993). Not only the density or thickness of the foam, but also other factors such as the tensile strength and elongation percentage could also influence the results. However, details of other factors were not documented in the above reports. There have been some reports concerning the effect of foam properties on postural stability and the properties influence the recorded body movements (Chiang and Wu, 1997; Patel et al., 2008a,b).

Soon after the development of unilateral peripheral vestibular damage, a recovery process known as compensation starts (Curthoys, 2000; Vidal et al., 1998), rearranging signals in the central nervous system to make use of information from a single labyrinth as an adequate input to the vestibulo-ocular and vestibulo-spinal systems. In addition, if the damaged peripheral vestibular function is repairable, functional recovery is expected to vary by several degrees (Aantaa and Virolainen, 1979; Bergenius and Borg, 1983; Okinaka et al., 1993; Silvoniemi, 1988). Fetter et al. (1990) followed the time course of recovery after an acute unilateral vestibular lesion and showed that the postural sway measured by dynamic posturography recovered

within a few weeks even in patients with persistent unilateral vestibular lesions. In our system, even in relatively severe CP (>50%), some of the subjects had normal results (Table 2), suggesting the influence of vestibular compensation. However, our system seemed to be useful for detecting vestibular disorders in the non-acute stage, since approximately 90% of the patients were tested more than 14 days after the onset of vestibular disturbances in the present study. This result suggests that appropriate distortion of sensory input could uncover abnormal vestibulospinal reflexes even after certain vestibular compensation has occurred.

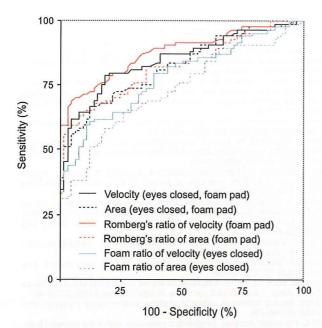
The velocity and the area in eyes closed/foam rubber could indirectly reflect the function of peripheral and central vestibular systems due to reductions in visual and somatosensory inputs. However, these variables were influenced by age in healthy controls (Table 4), a finding similar to that reported in previous studies on the increase in several values of COP with age (Baloh et al., 1998c; Era and Heikkinen, 1985; Masui et al., 2005; Ring et al., 1989; Thyssen et al., 1982). The Romberg's ratio of the velocity with the foam rubber was not influenced by age in healthy controls, and it might be better than the other variables in terms of excluding interindividual variability. The Romberg's ratio might indicate visual dependence in standing posture, and the significant difference in these variables might be due

Table 2

Analysis of six parameters in subjects with 20-49%, 50-99% and 100% canal paresis (CP).

	Posturography	Eyes	Eyes Median (IQR)			Overall comparisons (p-value	
			CP (20-49%), n = 29	CP (50-99%), n = 18	CP 100%, n = 21	sider mad the excellent	
Velocity (cm/s)	Foam	Closed	5.16 (3.88-7.96)	7.55 (4.94-9.95)	7.24 (4.93-fall)	0.223	
Area (cm²)	Foam	Closed	22.16 (12.01-42.58)	30.07 (18.68-54.22)	42.88 (19.51-Fall)	0.092	
Romberg's ratio of velocity	Foam		2.99 (2.54-3.64)	3.05 (2.38-4.62)	3.53 (2.54-fall)	0.083	
Romberg's ratio of area	Foam		4.56 (3.82-7.60)	5.83 (3.24-7.46)	7.33 (4.21-fall)	0.398	
Foam ratio of velocity		Closed	2.64 (2.16-3.49)	3.17 (2.50-3.81)	3.26 (2.35-fall)	0.076	
Foam ratio of area		Closed	3.79 (2.88-7.10)	5.73 (3.60-9.62)	6.43 (3.84-fall)	0.188	

IQR = interquartile range. 14%, 11% and 29% of the patients with 20–49% CP, 50–99% CP and 100% CP, respectively, required assistance to prevent falling. Seventy-five percentile of 100% CP could not be described in each variable (fall).



Valacity (avec alocal from and)	AUC (95% CI)
Velocity (eyes closed, foam pad)	0.847 (0.785-0.908)
Area (eyes closed, foam pad)	0.821 (0.755-0.887)
Romberg's ratio of velocity (foam pad)	0.878 (0.824-0.933)
Romberg's ratio of area (foam pad)	0.822 (0.756-0.887)
Foam ratio of velocity (eyes closed)	0.785 (0.713-0.856)
Foam ratio of area (eyes closed)	0.734 (0.655-0.813)

Fig. 3. ROC curves for the six variables that showed significant difference (p < 0.001) between normal healthy subjects and patients with unilateral vestibulopathy, and between normal healthy subjects and patients with bilateral vestibulopathy by Steel-Dwass multiple-comparison method. Sensitivity represented the [number of true positive subjects]/[(number of true positive subjects)+(number of false negative subjects)] calculated at each cutoff value. Specificity represented the [number of true negative subjects]/[(number of true negative subjects)+(number of false positive subjects)] calculated at each cutoff value. The accuracy of these variables was measured by AUC. An area of 1.0 represents a perfect test; an area of 0.5 represents a uninformative test. All the AUCs were relatively large (>0.7). In particular, the AUCs of the Romberg's ratios of the velocity with the foam rubber, and the velocity the eyes closed/foam rubber were larger than the other parameters (0.878 and 0.847, respectively).

to the higher level of visual dependence in patients with peripheral vestibular disorder.

In conclusion, foam posturography in our analysis system is useful for preliminary assessment of possible peripheral vestibular damage. The Romberg's ratio of the velocity with the foam rubber, which was the largest with regard to the AUC and was not influenced by age in healthy controls, seems the most suitable parameter for assessment of patients with peripheral vestibular disorders. Our results demonstrated higher levels of visual and

**Table 4**Sensitivity and specificity calculated for several standards of the six variables

a, foam pad) (cm/s) 3.0 (1.0-3.0) 39.4 (32.0-44.8) 71.2 (62.9-78.0) 80.3 (72.3-86.6) 90.9 (83.5-95.5) 100.0 (95.2-100.0) am pad) (cm²) 13.6 (9.7-13.6) 33.3 (26.2-38.7) 65.2 (56.7-72.2) 80.3 (71.9-87.0) 90.9 (83.5-95.5) 100.0 (95.3-100.0) elocity (foam pad) 4.5 (2.0-4.5) 57.6 (49.9-63.0)	2.05 3.54 4.37 4.60 5.35 10.55 8.08 11.74 16.71 21.17 24.96 51.59
3.0 (1.0-3.0) 39.4 (32.0-44.8) 71.2 (62.9-78.0) 80.3 (72.3-86.6) 90.9 (83.5-95.5) 100.0 (95.2-100.0) am pad) (cm²) 13.6 (9.7-13.6) 33.3 (26.2-38.7) 65.2 (56.7-72.2) 80.3 (71.9-87.0) 90.9 (83.5-95.5) 100.0 (95.3-100.0) elocity (foam pad) 4.5 (2.0-4.5) 57.6 (49.9-63.0)	3.54 4.37 4.60 5.35 10.55 8.08 11.74 16.71 21.17 24.96 51.59
71.2 (62.9–78.0) 80.3 (72.3–86.6) 90.9 (83.5–95.5) 100.0 (95.2–100.0) am pad) (cm²) 13.6 (9.7–13.6) 33.3 (26.2–38.7) 65.2 (56.7–72.2) 80.3 (71.9–87.0) 90.9 (83.5–95.5) 100.0 (95.3–100.0) elocity (foam pad) 4.5 (2.0–4.5) 57.6 (49.9–63.0)	4.37 4.60 5.35 10.55 8.08 11.74 16.71 21.17 24.96 51.59
80.3 (72.3–86.6) 90.9 (83.5–95.5) 100.0 (95.2–100.0) am pad) (cm²) 13.6 (9.7–13.6) 33.3 (26.2–38.7) 65.2 (56.7–72.2) 80.3 (71.9–87.0) 90.9 (83.5–95.5) 100.0 (95.3–100.0) elocity (foam pad) 4.5 (2.0–4.5) 57.6 (49.9–63.0)	4.60 5.35 10.55 8.08 11.74 16.71 21.17 24.96 51.59
90.9 (83.5-95.5) 100.0 (95.2-100.0) am pad) (cm²) 13.6 (9.7-13.6) 33.3 (26.2-38.7) 65.2 (56.7-72.2) 80.3 (71.9-87.0) 90.9 (83.5-95.5) 100.0 (95.3-100.0) elocity (foam pad) 4.5 (2.0-4.5) 57.6 (49.9-63.0)	5.35 10.55 8.08 11.74 16.71 21.17 24.96 51.59
100.0 (95.2–100.0)  am pad) (cm²) 13.6 (9.7–13.6) 33.3 (26.2–38.7) 65.2 (56.7–72.2) 80.3 (71.9–87.0) 90.9 (83.5–95.5) 100.0 (95.3–100.0)  elocity (foam pad) 4.5 (2.0–4.5) 57.6 (49.9–63.0)	8.08 11.74 16.71 21.17 24.96 51.59
am pad) (cm²) 13.6 (9.7–13.6) 33.3 (26.2–38.7) 65.2 (56.7–72.2) 80.3 (71.9–87.0) 90.9 (83.5–95.5) 100.0 (95.3–100.0) elocity (foam pad) 4.5 (2.0–4.5) 57.6 (49.9–63.0)	8.08 11.74 16.71 21.17 24.96 51.59
13.6 (9.7–13.6) 33.3 (26.2–38.7) 65.2 (56.7–72.2) 80.3 (71.9–87.0) 90.9 (83.5–95.5) 100.0 (95.3–100.0) elocity (foam pad) 4.5 (2.0–4.5) 57.6 (49.9–63.0)	11.74 16.71 21.17 24.96 51.59
33.3 (26.2–38.7) 65.2 (56.7–72.2) 80.3 (71.9–87.0) 90.9 (83.5–95.5) 100.0 (95.3–100.0) elocity (foam pad) 4.5 (2.0–4.5) 57.6 (49.9–63.0)	11.74 16.71 21.17 24.96 51.59
65.2 (56.7-72.2) 80.3 (71.9-87.0) 90.9 (83.5-95.5) 100.0 (95.3-100.0) elocity (foam pad) 4.5 (2.0-4.5) 57.6 (49.9-63.0)	16.71 21.17 24.96 51.59
80.3 (71.9–87.0) 90.9 (83.5–95.5) 100.0 (95.3–100.0) elocity (foam pad) 4.5 (2.0–4.5) 57.6 (49.9–63.0)	21.17 24.96 51.59
90.9 (83.5-95.5) 100.0 (95.3-100.0) elocity (foam pad) 4.5 (2.0-4.5) 57.6 (49.9-63.0)	24.96 51.59
100.0 (95.3–100.0) elocity (foam pad) 4.5 (2.0–4.5) 57.6 (49.9–63.0)	51.59 1.58
elocity (foam pad) 4.5 (2.0–4.5) 57.6 (49.9–63.0)	1.58
4.5 (2.0–4.5) 57.6 (49.9–63.0)	
57.6 (49.9-63.0)	
	2.26
727 (64 4 70 5)	
12.7 (04.4-79.3)	2,45
	2.55
The state of the s	2.74
100.0 (95.2–100.0)	3.10
rea (foam pad)	
4.5 (2.0-4.5)	1.38
57.6 (49.9-63.0)	3.05
	3.86
	4.36
	5.00
100 (95.2–100.0)	7.43
y (eyes closed)	
	1.54
	2.03
	2.30
	2.90
	3.21
100.0 (95.2–100.0)	3.80
eyes closed)	
	1.50
	2.78
	3.27
	5.38
	7.70
	11.42
	72.7 (64.4-79.5) 80.3 (72.2-86.7) 90.9 (83.6-95.5) 100.0 (95.2-100.0) rea (foam pad) 4.5 (2.0-4.5) 57.6 (49.9-63.0) 60.6 (52.1-67.8) 80.3 (71.9-87.0) 90.9 (83.4-95.6) 100 (95.2-100.0) ty (eyes closed) 6.1 (3.1-6.1) 28.8 (21.8-34.2) 56.1 (47.6-63.3) 80.3 (71.8-87.1) 90.9 (83.4-95.6)

The standards at which sensitivity and specificity were approximately 100%, 90%, 80%, respectively, are shown. Data in parentheses represent the 95% confidence intervals.

somatosensory dependence in patients with peripheral vestibular disorders in this study paradigm. Further confirmation of the measurement repeatability in this system for other data sets is needed.

### Acknowledgement

This work was supported by Foundation for Total Health Promotion

**Table 3**Overall comparisons of the six variables in four age groups.

	Median age (IQR)	Overall comparisons (p-value)			
	<39 years	40-54 years	55-69 years	70+ years	
Velocity (eyes closed, foam pad) (cm/s)	2.71 (2.41-3.55)	3.47 (2.55-4.30)	3.93 (3.19-4.54)	4.43 (3.69-5.15)	0.005
Area (eyes closed, foam pad) (cm2)	9.98 (7.03-15.77)	13.08 (7.87-16.27)	14.57 (10.99-20.76)	17.77 (14.72-22.02)	0.031
Romberg's ratio of velocity (foam pad)	2.27 (2.02-2.67)	2.10 (1.91-2.41)	2.21 (1.99-2.49)	2.35 (1.94-2.54)	0.801
Romberg's ratio of area (foam pad)	3.04 (1.30-3.74)	3.03 (2.20-3.94)	3.72 (2.55-4.42)	3.88 (2.43-4.50)	0.242
Foam ratio of velocity (eyes closed)	2.00 (1.76-2.68)	2.31 (2.08-2.93)	2.25 (1.97-2.54)	2.16 (1.89-2.99)	0.382
Foam ratio of area (eyes closed)	2.53 (1.71-3.46)	3.44 (2.77-4.51)	3.56 (2.86-4.44)	5.14 (3.34-7.82)	0.037

IQR = interquartile range.

#### References

- Aantaa E, Virolainen E. Vestibular neuronitis; a follow-up study. Acta Otorhinolaryngol Belg 1979;33:401-4.
- Allum JH, Adkin AL, Carpenter MG, Held-Ziolkowska M, Honegger F, Pierchala K. Trunk sway measures of postural stability during clinical balance tests: effects of a unilateral vestibular deficit, Gait Posture 2001;14:227–37.
- Allum JH, Zamani F, Adkin AL, Ernst A. Differences between trunk sway characteristics on a foam support surface and on the Equitest ankle-sway-referenced support surface. Gait Posture 2002;16:264–70.
- Baloh RW, Corona S, Jacobson KM, Enrietto JA, Bell T. A prospective study of posturography in normal older people. J Am Geriatr Soc 1998a;46: 438–43.
- Baloh RW, Fife TD, Zwerling L, Socotch T, Jacobson K, Bell T, et al. Comparison of static and dynamic posturography in young and older normal people. J Am Geriatr Soc 1994:42:405-12.
- Baloh RW, Jacobson KM, Beykirch K, Honrubia V. Static and dynamic posturography patients with vestibular and cerebellar lesions. Arch Neurol 1998b:55:649-54
- Baloh RW, Jacobson KM, Enrietto JA, Corona S, Honrubia V. Balance disorders in older persons: quantification with posturography. Otolaryngol Head Neck Surg 1998c;119:89-92.
- Bergenius J, Borg E. Audio-vestibular findings in patients with vestibular neuritis. Acta Otolaryngol 1983;96:389-95.
- Black FO, Wall C. Comparison of vestibulo-ocular and vestibulospinal screening-
- tests. Otolaryngol Head Neck Surg 1981;89:811-7. Black FO, Wall C, Nashner LM. Effects of visual and support surface orientation references upon postural control in vestibular deficient subjects. Acta Otolaryngol 1983;95:199–210.
- Bossuyt PM, Reitsma JB, Bruns DE, Gatsonis CA, Glasziou PP, Irwig LM, et al. Towards complete and accurate reporting of studies of diagnostic accuracy: the STARD initiative. Ann Intern Med 2003a;138:40-4.
- Bossuyt PM, Reitsma JB, Bruns DE, Gatsonis CA, Glasziou PP, Irwig LM, et al. The STARD statement for reporting studies of diagnostic accuracy: explanation and elaboration. Ann Intern Med 2003b;138:W1-W12.
  Brandt T. Krafczyk S. Malsbenden I. Postural imbalance with head extension;
- improvement by training as a model for ataxia therapy. Ann NY Acad Sci 1981;374:636-49.
- Chiang JH, Wu G. The influence of foam surfaces on biomechanical variables contributing to postural control. Gait Posture 1997;5:239-45.
- Colebatch JG, Halmagyi GM. Vestibular evoked potentials in human neck muscles and after unilateral vestibular deafferentation, Neurology 1992;42:1635-6.
- Curthoys 15. Vestibular compensation and substitution. Curr Opin Neurol 2000;13:27–30.
- Era P, Heikkinen E. Postural sway during standing and unexpected disturbance of balance in random samples of men of different ages. J Gerontol 1985:40:287-95.

- Evans MK, Krebs DE. Posturography does not test vestibulospinal function.
- Otolaryngol Head Neck Surg 1999;120:164–73.
  Fetter M, Diener HC, Dichgans J. Recovery of postural control after an acute unilateral vestibular lesion in humans. J Vestib Res 1990;1:373–83.
- Furman JM. Role of posturography in the management of vestibular patients. Otolaryngol Head Neck Surg 1995;112:8-15.
- Iwasaki S, Takai Y, Ozeki H, Ito K, Karino S, Murofushi T. Extent of lesions in idiopathic sudden hearing loss with vertigo: study using click and galvanic vestibular evoked myogenic potentials. Arch Otolaryngol Head Neck Surg
- Massion J, Alexandrov A, Frolov A. Why and how are posture and movement
- coordinated? Prog Brain Res 2004;143:13-27.

  Massion J, Woollacott M. Posture and equilibrium. In: Bronstein A, Brandt T, Woollacott M, Nutt J, editors. Clinical disorders of balance, posture and gait. 2nd ed. London: Arnold; 2004. p. 1-19.
- Masui T, Hasegawa Y, Matsuyama Y, Sakano S, Kawasaki M, Suzuki S, Gender differences in platform measures of balance in rural community-dwelling
- elders. Arch Gerontol Geriatr 2005;41:201-9.

  Murofushi T, Halmagyi GM, Yavor RA, Colebatch JG. Absent vestibular evoked myogenic potentials in vestibular neurolabyrinthitis. An indicator of inferior vestihular nerve involvement? Arch Otolaryngol Head Neck Surg 1996;122:845-8.
- Murofushi T, Monobe H, Ochiai A, Ozeki H. The site of lesion in "vestibular neuritis": study by galvanic VEMP. Neurology 2003;61:417-8.
- Nashner LM. Model describing vestibular detection of body sway motion. Acta Otolaryngol 1971;72:429–36.
- Nashner LM, Black FO, Wall C. Adaptation to altered support and visual conditions during stance - patients with vestibular deficits. J Neurosci 1982;2:536-44. Norre ME, Sensory interaction testing in platform posturography. J Laryngol Otol
- 1993;107:496-501.
- O'Neill G. The caloric stimulus. Temperature generation within the temporal bone. Acta Otolaryngol 1987;103:266–72.
- Okinaka Y, Sekitani T, Okazaki H, Miura M, Tahara T. Progress of caloric response of
- vestibular neuronitis. Acta Otolaryngol Suppl 1993;503:18-22.
  Patel M, Fransson PA, Lush D, Gomez S. The effect of foam surface properties on postural stability assessment while standing. Gait Posture 2008a;28:649-56.
- Patel M, Fransson PA, Lush D, Petersen H, Magnusson M, Johansson R, et al. The effects of foam surface properties on standing body movement. Acta Otolaryngol 2008:1-9.
- Ring C, Nayak US, Isaacs B. The effect of visual deprivation and proprioceptive change on postural sway in healthy adults. J Am Geriatr Soc 1989;37:745-9
- Silvoniemi P. Vestibular neuronitis. An otoneurological evaluation. Acta Otolaryngol Suppl 1988;453:1-72.
- Thyssen HH, Brynskov J, Jansen EC, Munster-Swendsen J. Normal ranges and reproducibility for the quantitative Romberg's test. Acta Neurol Scand 1982;66:100-4.
- Vidal PP, de Waele C, Vibert N, Muhlethaler M. Vestibular compensation revisited. Otolaryngol Head Neck Surg 1998;119:34-42.

# Ocular Vestibular Evoked Myogenic Potentials to Bone-Conducted Vibration in Vestibular Schwannomas

\*Shinichi Iwasaki, †Toshihisa Murofushi, \*Yasuhiro Chihara, \*Munetaka Ushio, \*Mitsuya Suzuki, ‡Ian S. Curthoys, and \*Tatsuya Yamasoba

\*Department of Otolaryngology, Faculty of Medicine, University of Tokyo, Tokyo; †Department of Otolaryngology, Teikyo University School of Medicine Mizonokuchi Hospital, Kawasaki, Japan; and ‡Vestibular Research Laboratory, School of Psychology, The University of Sydney, New South Wales, Australia

Background: Vestibular schwannoma (VS) arises from either the superior or the inferior vestibular nerve and causes vestibular dysfunction to various degrees. Recently, ocular vestibular evoked myogenic potentials to bone-conducted vibration (oVEMPs to BCV) have attracted much interest as a new clinical test for otolith-ocular pathway function. Because it is unclear whether the oVEMPs to BCV primarily originate from activation of the superior or the inferior vestibular nerve, the results in patients with VS might enlighten us concerning the origin of oVEMPs to BCV.

Objective: To compare the results of 3 clinical tests for vestibular function in patients with VS: 1) oVEMPs to BCV; 2) cervical vestibular evoked myogenic potentials to air-conducted sound (cVEMPs to ACS), which reflect the function of inferior vestibular nerve; and 3) caloric test, which reflect the function of superior vestibular nerve.

Methods: Thirty-six patients with unilateral VS who underwent vestibular tests, including oVEMPs to BCV, cVEMPs to ACS, and caloric tests, were enrolled. The asymmetry ratios of the amplitudes of the oVEMPs to BCV and cVEMPs to ACS and canal paresis on the caloric test were measured.

Results: Among the 36 patients with VS, 31 (86%) showed reduced or absent oVEMPs to BCV. Twenty-eight patients (78%) showed abnormal cVEMPs to ACS, and 31 (86%) showed abnormal caloric responses. The consistency of the results between oVEMPs to BCV and the caloric test was significantly higher than that between oVEMPs to BCV and cVEMPs to ACS (p < 0.02).

Conclusion: Ocular vestibular evoked myogenic potentials to bone-conducted vibration mainly reflect the function of the superior vestibular nerve. Key Words: Air-conducted sound—Bone-conducted vibration—Caloric test—Ocular vestibular evoked myogenic potential—Vestibular schwannoma.

Otol Neurotol 31:147-152, 2010.

Cervical vestibular evoked myogenic potentials (cVEMPs) in response to air-conducted sound have been clinically used to evaluate vestibular function (1) since Colebatch and Halmagyi (2) first reported surface electromyographic (EMG) potentials from the sternocleidomastoid muscles (SCMs) in response to loud air-conducted clicks in 1992. Physiologic and clinical studies have shown that cVEMPs to air-conducted sound reflect the function of the saccule and the inferior vestibular nerve (1,3–5).

Address correspondence and reprint requests to Shinichi Iwasaki, M.D., Department of Otolaryngology, Faculty of Medicine, University of Tokyo, 7-3-1 Hongo, Bunkyo-ku, Tokyo 113-8655, Japan; E-mail: iwashin-tky@umin.ac.jp

This study was supported by The Foundation for Total Health Promotion.

Recent studies have shown that short-latency, initially negative surface EMG potentials can be recorded from around the eyes in response to air-conducted sound (ACS) and bone-conducted vibration (BCV) (6,7). These potentials, called ocular vestibular evoked myogenic potentials (oVEMPs), are considered to represent vestibular function mediated by crossed vestibulo-ocular pathways because they are present in patients without hearing but absent on the contralateral side in those with unilateral vestibular loss (8,9). The oVEMPs have the advantage that the subjects do not have to contract the SCMs during recording so they can be easily recorded from the elderly, children, and patients with cervical spondylosis (8–11).

The oVEMPs in response to BCV can be recorded from most normal subjects when BCVs are delivered to the midline of the forehead at the hairline (Fz) by a powerful bone-conduction vibrator with subjects looking up during the recording (8–10). Physiologic studies using guinea pigs showed that moderate BCV activates irregular otolithic primary vestibular neurons that originate in the utricular maculae (12). The oVEMPs to BCV are thus likely to reflect the function of the utriculo-ocular pathway.

Vestibular schwannoma (VS) is a benign tumor arising from the superior or inferior vestibular nerve. It has been reported that patients with VS show various extents of vestibular dysfunction, including decreased or absent responses on caloric tests and cVEMPs to ACS (13). The cVEMPs to ACS have been used as a clinical test of the saccular afferents, whereas the caloric test has been used as a clinical test of the lateral semicircular canal afferents. Afferents from the lateral semicircular canals and the utricle course in the superior vestibular nerve, whereas afferents from the saccule course in the inferior vestibular nerve. We reasoned that if the oVEMPs to BCV mainly reflect the function of the utricular afferents, then the results in patients with VS should coincide with those of the caloric test rather than cVEMPs to ACS.

In the present study, we examined the correlation of the results of oVEMPs to BCV, the caloric test, and cVEMPs to ACS in patients with VS and compared them with the size and the nerve origin of the tumor.

### MATERIALS AND METHODS

### **Patients**

Data were retrospectively collected from 36 patients (21 men, 15 women; mean  $\pm$  standard deviation [SD] age, 54  $\pm$  12 yr; range, 33–73 yr) who visited our dizziness clinic and were diagnosed as having untreated unilateral VS based on contrast-enhanced magnetic resonance imaging (MRI) of the brain from January 2007 to December 2008. All patients underwent vestibular tests, including oVEMPs to BCV, cVEMPs to ACS, and the caloric test. Among these VS patients, 34 patients underwent surgical resection and had their tumors neuropathologically confirmed to be VS. For patients who underwent surgery, we used the results of vestibular tests performed preoperatively. We included patients that did not undergo surgery because the exclusion of these patients might have caused some bias concerning the patient's age and the size of tumor.

All procedures were in accordance with the Helsinki declaration and were approved by the University of Tokyo Human Ethics Committee, and all patients gave informed consent for the use of their clinical data.

### **Vestibular Function Tests**

The methods for recording oVEMPs to BCV were described in detail elsewhere (9–11). Briefly, the subjects lay supine on a bed, with their head supported by a pillow and with surface EMG electrodes placed on the skin 1 cm below (active) and 3 cm below (indifferent) the center of each lower eyelid. The ground electrode was placed on the chin. During testing, the subject looked up approximately 25 degrees above straight ahead and maintained their focus on a small dot approximately 1 m from their eyes. The signals were amplified by a differential amplifier (bandwidth, 0.5–500 Hz), and the unrectified signals were averaged (n = 50) using Neuropack  $\Sigma$  (Nihon Kohden, Tokyo, Japan).

Otology & Neurotology, Vol. 31, No. 1, 2010

The BCV stimuli were 4-millisecond tone-bursts of 500-Hz vibration delivered by a handheld 4810 mini-shaker (Bruel and Kjaer, Naerum, Denmark) fitted with a short rod terminated in a bakelite cap 1.5 cm in diameter, which was placed on the forehead at the hairline, in the midline (Fz). These stimuli caused BCV at the mastoids with a peak acceleration of approximately  $0.4 \times g$  as measured by linear accelerometers on the skin over the mastoid (10). The stimulation rate was 3 Hz, and the time window for analysis was 50 milliseconds. The responses to 50 stimuli were averaged twice.

We analyzed the amplitude of the first negative peak (n10) from the baseline to the peak. We calculated the asymmetry ratio for n10 amplitude (oVEMP AR) with the following formula using the n10 amplitude beneath the eye ipsilateral to the affected side  $(A_a)$  and beneath the eye ipsilateral to the unaffected side  $(A_n)$ :

oVEMP AR% = 
$$100 \times [(A_a - A_u) / (A_a + A_u)]$$

The upper limit of normal oVEMP AR was set at 27.3 (10). When no reproducible n10 were present in 2 runs, we regarded them as "no response." When reproducible n10 were present and the AR (%) was greater than the normal upper limits, we regarded them as "decreased response." We included both "decreased" and "no" responses as "abnormal" responses.

To record cVEMPs, the EMG electrodes were placed at symmetric sites over the upper half of the SCM, with reference electrodes on the side of the upper sternum. The ground electrode was placed on the nasion. During the recording of cVEMPs, the subjects were instructed to raise their heads to activate the SCM, and the EMG activities of the bilateral SCMs were monitored to confirm normal muscle activities. The signals from the stimulated side were amplified by the differential amplifier (20-2,000 Hz), and the unrectified signals were averaged (n = 100). Air-conducted clicks (0.1 ms; 95 dBnHL) or short tone-bursts (500 Hz; 4 ms; 95 dBnHL) were delivered through headphones. The patients were instructed to contract the SCM during testing by lifting their head off the pillow. During the recording, EMG activities were monitored on a display to maintain muscle activity at a sufficient level greater than 150 μV in each patient. We analyzed the first biphasic responses (p13-n23) on the ipsilateral SCM to the stimulated side. We calculated the asymmetry ratio for the amplitude of cVEMPs (cVEMP AR) with the following formula using the amplitude of p13-n23 on the affected side  $(A_a)$  and that on the unaffected side  $(A_n)$ :

cVEMP AR% = 
$$100 \times [(A_u - A_a) / (A_u + A_a)]$$

On the basis of results from normal subjects (13,14), the upper limit of normal cVEMP AR was set to 34.1 for click-VEMP (13) and 34.0 for burst-VEMP (mean + 2 SDs, respectively) (14). When no reproducible p13-n23 was present in 2 runs, we regarded it as "no response." When reproducible p13-n23 was present and the AR (%) is greater than the normal upper limits, we regarded it as "decreased response." We included both "decreased" and "no" responses as "abnormal" responses.

Caloric tests were performed using 4°C ice water (2 ml; 20 s). This method of caloric stimulation is easier to perform than bithermal irrigation with water at 30°C and 44°C, and has been shown to have a high sensitivity and specificity for detecting canal paresis (CP) based on Jonkees' formula (15). Percentage CP was calculated with the following formula using the

**TABLE 1.** Results of oVEMP, caloric, and cVEMP tests in 36 patients with VS

	Absent on 1 side	Decreased on 1 side	Absent on both sides	Normal
oVEMP to BCV	27 (75)	4 (11)	0 (0)	5 (14)
Caloric test cVEMP to ACS	17 (47) 25 (69)	14 (39) 3 (8)	0 (0) 2 (6)	5 (14) 6 (17)

Number (%) of patients are shown.

maximum slow-phase eye velocity of the induced nystagmus responses on the affected side  $(MSEV_a)$  and on the unaffected side  $(MSEV_u)$  using an electronystagmograph in the supine position (head up 30 degrees):

$$CP (\%) = 100 \times (MSEV_u - MSEV_a) / (MSEV_u + MSEV_a)$$

A value of CP > 20% was regarded as abnormally decreased on the affected side. When both the  $MSEV_a$  and  $MSEV_u$  were less than 10 degrees per second, it was regarded as a decreased response on both sides.

### **Evaluation of Tumor Size**

Axial and coronal T1-weighted MRI with contrast medium (gadolinium diethylene triamine pentaacetic acid) and axial T2-weighted MRI were performed using a fast spin echo program with 1.5 T unit, 3.0 mm in thickness at intervals of 3.3 mm before surgery. Maximum diameter of VS was measured and used as a tumor size.

### Statistical Analyses

Statistical analyses were performed using SPSS statistical software (SPSS, Chicago, IL, USA). The frequency of patients showing abnormal responses in each vestibular test was compared using the  $\chi^2$  test or Fisher's exact test. Mean tumor size in patients with normal and abnormal responses in the vestibular tests and mean tumor sizes in patients with superior VS and inferior VS were compared using Mann-Whitney U test. A difference of p < 0.05 was considered significant.

### RESULTS

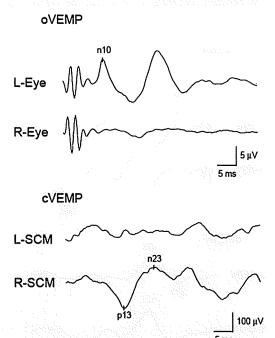
Initial negative potentials that peaked at approximately 10 milliseconds (n10) could be recorded from the eye ipsilateral to the affected side in all 36 patients with VS in the oVEMPs to BCV. On the side contralateral to the VS, 27 patients (75%) did not show oVEMP responses, and 4 patients (11%) showed decreased responses. The remaining 5 patients (14%) showed normal responses on both sides. As a result, 31 (86%) of the 36 patients showed abnormal oVEMPs on the contralateral eye to the affected side (Table 1).

For cVEMPs to ACS, 28 patients (78%) showed abnormal responses (decreased responses in 3 patients; no response in 25 patients) solely on the affected side, whereas 6 patients (17%) showed normal responses on both sides. Two patients (6%) showed no cVEMP response on either side.

In the caloric test, 31 patients (86%) showed decreased or absent responses on the affected side, whereas the remaining 5 patients (14%) showed normal responses on both sides.

There were no significant differences in the abnormal ratios among oVEMPs to BCV, cVEMPs to ACS, and the caloric test (p > 0.5).

Twenty-five patients (69%) showed abnormal results in all 3 vestibular tests (Fig. 1), whereas only 1 patient (3%) showed normal results on all of them. There were 10 patients (28%) who showed inconsistent results among the 3 vestibular tests (Table 2). Among them, 4 patients (Patients 1–4) showed abnormal results in both the oVEMPs to BCV and caloric tests but showed normal cVEMPs to ACS on both sides (Fig. 2). Three patients (Patients 5–7) showed normal results in both the oVEMPs to BCV and caloric tests but showed abnormal cVEMPs to ACS. Thus, 7 (70%) of the 10 patients showed consistent results between the oVEMPs to BCV and caloric tests and showed inconsistent results only in the cVEMPs to ACS. Of the 3 remaining patients,



Caloric test: 33% canal paresis in the left ear.

FIG. 1. Ocular vestibular evoked myogenic potentials to bone-conducted vibration (oVEMP to BCV; upper panel), cVEMP to ACS (lower panel), and the caloric test in a 39-year-old man with VS in the left ear. The n10 response of the oVEMP to BCV was absent in the right eye, whereas the p13-n23 response of the cVEMP to ACS was absent in the left. Caloric testing showed 33% CP on the left-ear stimulation. L-eye indicates response recorded from the left SCM; R-eye, response recorded from the right eye; R-SCM, response recorded from the right SCMs.

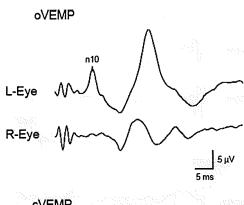
Otology & Neurotology, Vol. 31, No. 1, 2010

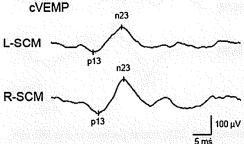
TABLE 2. Test results of patients who showed inconsistencies among oVEMP to BCV, caloric test, and cVEMP to ACS

	PTA (dB)								
Patient no.	Age, sex	Affected side	oVEMP to BCV (AR%)	Caloric test (CP%)	cVEMP to ACS (AR%)	Affected side	Healthy side	Tumor size (mm)	Nerve origin
1	41 F	L	Abnormal (100)	Abnormal (100)	Normal (6.7)	78.3	5	26	Inferior
2	49 F	R	Abnormal (100)	Abnormal (100)	Normal (13)	35	11.7	25	Superior
3	33 F	L	Abnormal (55)	Abnormal (33.3)	Normal (2.1)	18.3	10	24	Superior
4	66 M	R	Abnormal (100)	Abnormal (73.8)	Normal (6.4)	36.7	30	7	Unknown
5	57 M	L	Normal (7.3)	Normal (4.8)	Abnormal (100)	23.3	10	21	Unknown
6	46 F	L	Normal (16.7)	Normal (4.2)	Abnormal (100)	60	16.3	22	Inferior
7	64 M	L	Normal (6.7)	Normal (18.5)	Abnormal (38.2)	60	16.3	10	Unknown
8	66 M	L	Abnormal (41.3)	Normal (18)	Normal (5.1)	75	13.3	8	Unknown
9	60 M	R	Normal (1.5)	Abnormal (33.3)	Normal (11)	45	8.3	14	Superior
10	64 M	L	Normal (12.5)	Abnormal (40)	Abnormal (100)	76.3	17.3	18	Superior

F indicates female; Inferior, inferior vestibular nerve; L, left; M, male; PTA, average of the pure-tone threshold for tones at 500 Hz, 1, and 2 kHz; R, right; Superior, superior vestibular nerve.

2 showed abnormal results only in the oVEMPs to BCV (Patient 8) or caloric test (Patient 9). Only 1 patient showed normal oVEMPs but abnormal cVEMPs and caloric responses (Patient 10). The consistency of the results between oVEMPs to BCV and the caloric test





Caloric test: 100% canal paresis in the left ear.

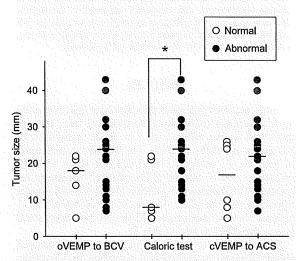
FIG. 2. Ocular vestibular evoked myogenic potentials to boneconducted vibration (oVEMPs to BCV; upper panel), cVEMPs to ACS (lower panel), and the caloric test in a 41-year-old woman with VS in the left ear (Patient 1 in Table 2). The n10 response of the oVEMP to BCV was absent on the right, whereas the cVEMPs to ACS showed normal responses on both sides. The caloric test showed 100% CP on the left ear.

Otology & Neurotology, Vol. 31, No. 1, 2010

was significantly higher than that between oVEMPs to BCV and cVEMPs to ACS (p < 0.02).

Tumor sizes measured on MRI ranged from 5 to 43 mm (mean  $\pm$  SD, 20.5  $\pm$  9.0 mm). Mean tumor sizes of the patients with abnormal responses were larger than those with normal responses on oVEMPs to BCV, caloric test, and cVEMPs to ACS. However, the difference was significant only on the caloric test (p < 0.05 on caloric test, p > 0.1 on both oVEMPs to BCV and cVEMPs to ACS; Fig. 3).

Among the 34 patients who underwent surgical resection of VS, the nerve origin of the tumor was identified in 23 patients by neurosurgeons. Among them, 12 (52%) were originated from the superior vestibular nerves, whereas 11 (48%) were originated from the inferior vestibular nerves (Table 3). There were no significant



**FIG. 3.** Dot plots of the tumor sizes between patients with VS showing normal responses and those showing abnormal responses in oVEMPs to BCV, caloric test, and cVEMPs to ACS. The horizontal lines represent median values. The difference was significant only in the caloric test (p < 0.05).

TABLE 3. Nerve origin of the tumor and results of vestibular tests

		No. (%) patients with abnormal response				
Nerve origin of the tumor	n	oVEMPs to BCV	Caloric test	cVEMP to ACS		
Identified in surgery Superior VN Inferior VN			12 of 12 (100) 10 of 11 (91)	8 of 12 (67) 10 of 11 (91)		
Not identified Not operated	11 2					

VN indicates vestibular nerve.

differences in abnormality ratios between patients with superior VS and those with inferior VS on oVEMPs to BCV, caloric test, or cVEMPs to ACS (p > 0.3).

### DISCUSSION

We compared the results of oVEMPs to BCV, cVEMPs to ACS, and the caloric test in patients with VS in the present study. We showed that the sensitivity of the oVEMPs to BCV is comparable to those of cVEMPs to ACS and the caloric test for detecting vestibular dysfunction in patients with VS, and that the results of the oVEMPs to BCV mostly coincided with those of the caloric test rather than those of cVEMPs to ACS.

The oVEMP, which was first reported by Rosengren et al. (6) in 2005, is a surface EMG potential recorded from beneath the eyes in response to ACS and BCV (6-11). The oVEMPs probably reflect extraocular EMG activity, especially of the inferior oblique muscle, because they become larger if the subject looks up, activating the inferior oblique and superior rectus muscles and bringing the inferior oblique muscles close to the recording electrodes (6,10). Chihara et al. (16) reported that patients without any intraorbital content did not show oVEMP responses, but a patient without eyeballs but with preserved extraocular muscles showed normal oVEMP responses (15). These findings suggest that oVEMPs should originate from the extraocular muscles. When strong BCV such as brief taps with a tendon hammer or short tone bursts of 500 Hz by a powerful bone-conducted vibrator is delivered to the midline of the forehead at the hairline, a short latency-negative component with a latency of 10 milliseconds (n10) can be recorded from both eyes in unselected normal subjects (8-10). The amplitude of n10 responses decreases, and its latency increases with age, but the amplitude is almost identical in both eyes in healthy subjects (10).

The n10 is considered to be of vestibular origin because patients with bilateral vestibular loss but normal hearing do not show n10 potentials to BCV (6). On the other hand, patients without hearing but with residual vestibular functions show typical n10 responses (8). The n10 is not due to the blink response or facial nerve activation because patients with unilateral vestibular loss but preserved facial nerve function on both sides show absent

oVEMP responses on the contralesional side (9). Conversely, patients with unilateral facial palsy without vestibular disorders show symmetric oVEMP responses (16).

The origin in the vestibular labyrinth of oVEMPs to BCV remains to be clarified. However, there are some reasons to assume that oVEMPs might reflect the function of the contralateral utricular maculae. Suzuki et al. (17) showed that electric stimulation of the nerve from the utricular maculae in cats activates the inferior oblique muscle on the contralateral side. Physiologic studies in guinea pigs have shown that moderate BCV selectively activates irregular otolithic primary neurons, most of which are in the superior division of the vestibular nerve and originate from the utricular maculae (12). On the other hand, in cats and guinea pigs, strong ACS selectively activates the otolithic primary vestibular neurons that are located in the inferior division of the vestibular nerve and originate from the saccular maculae (3,4). Saccular afferents act via inhibitory neurons in vestibular nuclei to inhibit cervical motoneurons (18). On the basis of these findings, cVEMP to ACS is considered to reflect the function of the ipsilateral saccular maculae and is widely used as a clinical test to evaluate the saccule and the inferior vestibular nerve (1).

Vestibular schwannoma is a benign tumor arising from the superior or inferior nerve, and it produces dysfunction of the nerves by compressing the nerve fiber and obstructing the blood supply to the nerves (19,20). We hypothesized that if the oVEMPs to BCV mainly reflect the function of the utricular afferents, the results should mostly coincide with those of the caloric test rather than with cVEMPs to ACS. In the present study, among the 10 patients with inconsistent results in the 3 vestibular tests, 7 (70%) showed corresponding results between oVEMPs to BCV and the caloric test, whereas only 1 patient (10%; Patient 9) showed correspondence between oVEMPs to BCV and cVEMPs to ACS (Table 2). These results are partially consistent with our hypothesis. Interestingly, in the 3 patients (Patients 8-10) who showed inconsistent results between oVEMPs to BCV and the caloric test, either their AR% scores of oVEMPs to BCV or their CP% scores were relatively low, suggesting that damage to the superior vestibular nerve caused by VS was incomplete. Another possible explanation is that VS affected various parts of the vestibular end-organ and the vestibular nerves through obstruction of the blood supply to the inner ear. Telischi et al. (21) showed using distortion product acoustic emissions that approximately 60% of VS patients had cochlear damage.

In the present study, the abnormal ratios on oVEMPs to BCV, caloric test, and cVEMPs to ACS did not show clear correlation with the nerve origin of the tumor, which were identified by neurosurgeons. This result is consistent with results of other previous studies (19,20,22). Ushio et al. (20) reported that the results of the caloric test, cVEMPs to ACS, and auditory brainstem responses did not show correlations with the nerve origin of the tumor in 109 patients with VS. Extension of schwannoma develops not only inwardly but also outwardly, so it could produce

Otology & Neurotology, Vol. 31, No. 1, 2010

dysfunction of the nerve from which it originates and the adjacent nerves by compressing them. Thus, VS can affect all the nerves in the internal auditory canal. In fact, despite the high sensitivity of auditory brainstem responses for detecting VS (23,24), it rarely arises from the cochlear nerve.

In conclusion, this study showed that approximately 80% of patients with VS had abnormal oVEMPs to BCV. The sensitivity for detecting vestibular dysfunction in VS using this method was comparable to those for cVEMPs to ACS and the caloric test. The results of the oVEMPs to BCV mostly coincided with those of the caloric test rather than those of cVEMPs to ACS, suggesting that the oVEMPs to BCV mainly reflect the function of the superior vestibular nerves. The same hypothesis was recently proposed by clinical and neurophysiologic oVEMP studies (25,26). From a clinical point of view, the oVEMP has some advantages over the cVEMP. Recording oVEMP only requires subjects to look up for short trials, whereas recording cVEMP requires sustained contraction of the neck muscles, which is physically demanding, especially in more senior subjects. The oVEMP can identify the affected side in 1 patient in a single examination by comparing the responses from 1 eye with the responses from the other eye to the simultaneous stimulation of both labyrinths. Thus, the oVEMPs to BCV could provide patients with VS additional useful information regarding the function of the utricle and the superior vestibular nerve systems.

Acknowledgment: The authors thank Ann Burgess for critically reading this manuscript.

### REFERENCES

- Welgampola MS, Colebatch JG. Characteristics and clinical application of vestibular-evoked myogenic potentials. *Neurology* 2005; 64:1682-8.
- Colebatch JG, Halmagyi GM. Vestibular evoked potentials in human neck muscles before and after unilateral vestibular deafferentation. Neurology 1992;42:1635-6.
- McCue MP, Guinan JJ Jr. Acoustically responsive fibers in the vestibular nerve of the cat. J Neurosci 1994;14:6058-70.
- Murofushi T, Curthoys IS, Topple AN, Colebatch JG, Halmagyi GM. Responses of guinea pig primary vestibular neurons to clicks. Exp Brain Res 1995;103:174-8.
- Murofushi T, Halmagyi GM, Yavor RA, Colebatch JG. Absent vestibular evoked myogenic potentials in vestibular neurolabyrinthitis; An indicator of inferior vestibular nerve involvement? Arch Otolorymon Head Neck Sura 1996:122:845-8.
- us; An muraor of interior vestioniar nerve involvement? Arch Otolaryngol Head Neck Surg 1996;122:845–8.

  6. Rosengren SM, Todd NPM, Colebatch JG. Vestibular-evoked extraocular potentials produced by stimulation with bone-conducted sound. Clin Neurophysiol 2005;116:1938–48.
- Todd NPM, Rosengren SM, Aw ST, Colebatch JG. Ocular vestibular evoked myogenic potentials (OVEMPs) produced by air- and bone-conducted sound. Clin Neurophysiol 2007;118:381-90.

- Iwasaki S, McGarvie L, Halmagyi GM, et al. Head taps evoke a crossed vestibulo-ocular reflex. Neurology 2007;68:1227–9.
- Iwasaki S, Smulders YE, Burgess AM, et al. Ocular vestibular evoked myogenic potentials in response to bone-conducted vibration of the midline forehead at Fz. A new indicator of unilateral otolithic loss. *Audiol Neurotol* 2008;13:396–404.
- Iwasaki S, Smulders YE, Burgess AM, et al. Ocular vestibular evoked myogenic potentials to bone conducted vibration of the midline forehead at Fz in healthy subjects. Clin Neurophysiol 2008;119:2135-47.
- Chihara Y, Iwasaki S, Ushio M, Murofushi T. Vestibular-evoked extraocular potentials evoked by air-conducted sound: another clinical test for vestibular function. *Clin Neurophysiol* 2007;118: 2745-51.
- Curthoys IS, Kim J, McPhedran SK, Camp AJ. Bone conducted vibration selectively activates irregular primary otolithic vestibular neurons in the guinea pig. Exp Brain Res 2006;175:256-67.
- Murofushi T, Matsuzaki M, Mizuno M. Vestibular evoked myogenic potential in patients with acoustic neuromas. Arch Otolaryngol Head Neck Surg 1998;124:509–12.
- Murofushi T, Matsuzaki M, Wu CH. Short tone burst-evoked myogenic potentials on the sternocleidomastoid muscle: are these potentials also of vestibular origin? Arch Otolaryngol Head Neck Surg 1999;125:660-4.
- Schmal F, Lubben B, Weiberg K, Stoll W. The minimal ice water caloric test compared with established vestibular caloric test procedures. J Vestib Res 2005;15:215-24.
- Chihara Y, Iwasaki S, Ushio M, et al. Ocular vestibular-evoked myogenic potentials (oVEMPs) require extraocular muscles but not facial or cochlear nerve activity. Clin Neurophysiol 2009;120: 581-7.
- Suzuki JI, Tokumasu K, Goto K. Eye movements from single utricular nerve stimulation in the cat. Acta Otolaryngol 1969;68: 350-62.
- Kushiro K, Zakir M, Sato H, et al. Saccular and utricular inputs to single vestibular neurons in cats. Exp Brain Res 2000;131:406-15.
- Tsutsumi T, Tsunoda A, Noguchi Y, Komatsuzaki A. Prediction of the nerves of origin of vestibular schwannomas with vestibular evoked potentials. Am J Otol 2000;21:712-5.
- Ushio M, Iwasaki S, Chihara Y, Kawahara N, Saito N, Murofushi T. Is the nerve origin of the vestibular schwannoma correlated with vestibular evoked myogenic potential, caloric test, and auditory brainstem response? Acta Otolaryngol. In press.
- Telischi FF, Roth J, Stagner BB, Lonsbury-Martin BL, Balkany TJ. Patterns of evoked otoacoustic emissions with acoustic neuromas. Laryngoscope 1995;105:675-82.
- Suzuki M, Yamada C, Inoue R, Kashio A, Saito Y, Nakanishi Y. Analysis of vestibular testing in patients with vestibular schwannoma based on the nerve of origin, the localization, and the size of the tumor. *Otol Neurotol* 2008;29:1029-330.
- Wilson DF, Hodgson RS, Gustafson MF, Hogue S, Mills L. The sensitivity of auditory brainstem response testing in small acoustic neuromas. *Laryngoscope* 1992;102:961–4.
- neuromas. Laryngoscope 1992;102:961-4.
  24. Schmidt RJ, Sataloff RT, Newman J, Spiegel JR, Myers DL. The sensitivity of auditory brainstem response testing for the diagnosis of acoustic neuromas. Arch Otolaryngol Head Neck Surg 2001; 127:10-22
- Iwasaki S, Chihara Y, Smulder YE, et al. The role of the superior vestibular nerve in generating ocular vestibular-evoked myogenic potentials to bone conducted vibration at Fz. Clin Neurophysiol 2009;120:588-93.
- Todd NPM, Rosengren SM, Colebatch JG. A utricular origin of frequency tuning to low-frequency vibration in the human vestibular system? *Neurosci Lett* 2009;451:175–80.

Otology & Neurotology, Vol. 31, No. 1, 2010