on a single kind of image.[1] For the IV method, use of a HYDROPS2 (hybrid of reversed image of magnetic resonance [MR] cisternography and positive perilymph signal by heavily T_2-weighted 3D-FLAIR) image was recently proposed to allow separate visualization of the endolymph, perilymph, and bone on a single kind of image.[13]

The purpose of this study was to evaluate whether the use of HYDROPS2 images can obviate the need to use 3D-real IR images for IT + IV study.

Materials and Methods

Ten patients with clinically suspected Ménière's disease (6 men, 4 women, aged 35 to 68 years) underwent scanning using a 3-tesla MR imaging unit (Verio, Siemens Medical Solutions, Erlangen, Germany) with a 32-channel array head coil. Experienced otolaryngologists diagnosed Ménière's disease based on the 1995 diagnostic criteria of the American Academy of Otolaryngology-Head and Neck Surgery.

All patients received IT administration of 8-fold-diluted gadopentetate dimeglumine (Magnevist, Bayer Co. Ltd., Osaka, Japan) into one ear 24 hours prior to MR scan and single dose (0.1 mmol/kg or 0.2 mL/kg) IV administration of gadodiamide hydrate (Ominiscan, Daiichi-Sankyo Co. Ltd., Tokyo, Japan) for both ears 4 hours prior to MR scan. We have previously described the procedure for IT contrast injection.[14] Because recent study protocols in our institution employ gadopentetate dimeglumine for IT use and gadodiamide hydrate for IV study, we employed them for the present study.

The parameters for heavily T_2-weighted 3D-FLAIR (hT_2W-3D-FLAIR) were: repetition time (TR), 9000 ms; effective echo time (TE), 544 ms; inversion time (TI), 2250 ms; variable refocusing flip-angle echo train, initial flip angle of 180° rapidly decreased to a constant 120°; echo train length, 173; matrix size, 384 × 322; 104 axial, one-mm slice thickness with 180 × 150-mm field of view (FOV); GRAPPA acceleration factor, 2; voxel size, 0.5 × 0.5 × 1 mm; number of excitations (NEX), 4; scan time, 14 min 26 s; readout bandwidth, 434 Hz/pixel; and echo spacing, 5.6 ms.

The parameters for MR cisternography (MRC) by heavily T_2-weighted SPACE (sampling perfection with application-optimized contrast with different flip-angle evolutions) were the same as those used for hT_2W-3D-FLAIR except: TR, 4400 ms with driven equilibrium pulse; NEX, 1.8; and scan time, 3 min 15 s.

The parameters for 3D-real IR were: TR, 6000 ms; effective TE, 181 ms; TI, 1650 ms; 180° flip angle (constant throughout echo train) for the conventional turbo-spin-echo refocusing echo train; echo train length, 27; matrix size, 384 × 384; 30 axial, 0.8-mm-thick slices covering the labyrinth with a 160 × 160 mm FOV; GRAPPA acceleration factor, 2; voxel size, 0.4 × 0.4 × 0.8 mm; NEX, one; scan time, 14 min 32 s; readout bandwidth, 213 Hz/pixel; echo spacing, 13 ms; and reconstruction mode, real.

We obtained MRC for an anatomical reference of total lymph fluid, hT_2W-3D-FLAIR to visualize enhancement of the perilymph while the endolymph showed low signal (i.e., positive perilymph image [PPI]),[15] and 3D-real IR images for separate visualization of the perilymph, endolymph, and bone on a single kind of image.

By subtracting MRC from PPI, we could obtain an image with 3D-real IR-like presentation after IV, an image we termed HYDROPS2.[13] In this study, we generated HYDROPS2 images by subtracting MRC multiplied by 0.05 from PPI on the scanner console according to the method we described previously.[13]

Our medical ethics committee approved this study, and all patients gave written informed consent. We used the data regarding difference in contrast enhancement between the IV side and IT + IV side of these 10 patients in the previously published study.[10] In the current study, we generated HYDROPS2 images and compared them with 3D-real IR images.

In consensus, 2 neuroradiologists graded contrast enhancement of the perilymph in the cochlea, vestibule, and 3 semicircular canals (SCCs) and the degree of EH. They evaluated the presence of contrast enhancement in each semicircular canal separately.

EH was scored as none (0), mild (1), and significant (2) according to the reported criteria.[16] The presence or absence of significant motion between hT_2W-3D-FLAIR and MRC was also evaluated. The apparent double contour of the labyrinth on a HYDROPS2 image was considered the result of motion between scans.

Results

Table summarizes the patients and results of EH grading.

Enhancement of cochlear and vestibular perilymph was recognized in all ears in HYDROPS2 images but only in the IT + IV side in 3D-real IR images, and enhancement of only 22 of 30 semicircular canals could be recognized in the IT + IV side in the 3D-real IR images. In all IV-side ears,

Table. Evaluation of endolymphatic hydrops after intratympanic and intravenous injection of GBCM

Patient No.	Age (years)	Gender	Diagnosis	Side	Hearing level (dB)	EH in the cochlea	EH in the vestibule
1	44	F	Definite MD	R*	68	2	2
				L	15	0	2
2	60	M	Definite MD	R	10	0	0
				L*	55	2	2
3	67	M	Definite MD	R*	65	2	2
				L	35	2	2
4	47	M	Definite MD	R	13	2	2
				L*	47	0	1
5	49	M	Definite MD	R*	50	0	0
				L	13	1	0
6	68	F	Definite MD	R	27	1	1
				L*	38	0	1
7	35	F	Possible MD	R	48	1	1
				L*	48	1	0
8	42	M	Definite MD	R	10	2	2
				L*	67	2	2
9	35	M	Definite MD	R*	87	1	2
				L	12	0	0
10	36	F	Definite MD	R	12	0	0
				L*	38	1	1

EH, endolymphatic hydrops (0 = none, 1 = mild, 2 = significant); GBCM, gadolinium-based contrast material; MD, Ménière's disease
*side with intratympanic GBCM injection
Hearing level is an average of 3 frequencies of 500 Hz, 1 kHz, and 2 kHz.

3D-real IR failed to detect the enhancement of the perilymph in the cochlea, vestibule, and 3 semicircular canals. HYDROPS2 detected perilymph enhancement in all cochleas and vestibules and 58 of 60 semicircular canals but did not demonstrate enhancement in the superior and posterior semicircular canal of the IV side in one patient.

Grades of EH in the IT + IV side agreed completely between HYDROPS2 and 3D-real IR images (Figs.1, 2). No case showed significant motion between scans.

Discussion

In our previous study, the signal intensity ratio of the cochlea against the brain parenchyma was 1.70 ± 0.60 on the IT + IV side and 0.42 ± 0.10 on the IV side, and enhancement was significantly stronger in the IT + IV-side ears than the IV-side ears ($P < 0.001$).[10] The standard deviation was larger for the IT + IV side than the IV side.

The TI value of 3D-real IR in the present study protocol was determined for stronger perilymph enhancement by IT administration.[1] The TI value is determined to be the value between the null point of endo- and perilymph. The degree of contrast enhancement by the IT method varies among patients,[11] so optimal TI value for 3D-real IR obtained after IT might also vary among patients. TI must be longer to compensate for the far weaker enhancement by IV administration. Therefore, a single TI value in 3D-real IR cannot be suitable for both the IT + IV side and the IV side.

The null point of endolymph is nearly constant because there is almost no distribution of GBCM in the endolymph. Therefore, the HYDROPS2 method, based on the subtraction of MRC from hT_2W-3D-FLAIR, is robust for both the IT + IV side and the IV side.

The high sensitivity of hT_2W-3D-FLAIR might also be valuable for potential cases that demonstrate impaired distribution of GBCM by the IT method, a problem reported in 18% of patients in one study.[11] In the present study, there was no significant motion between hT_2W-3D-FLAIR and MRC, but subtraction is susceptible to motion be-

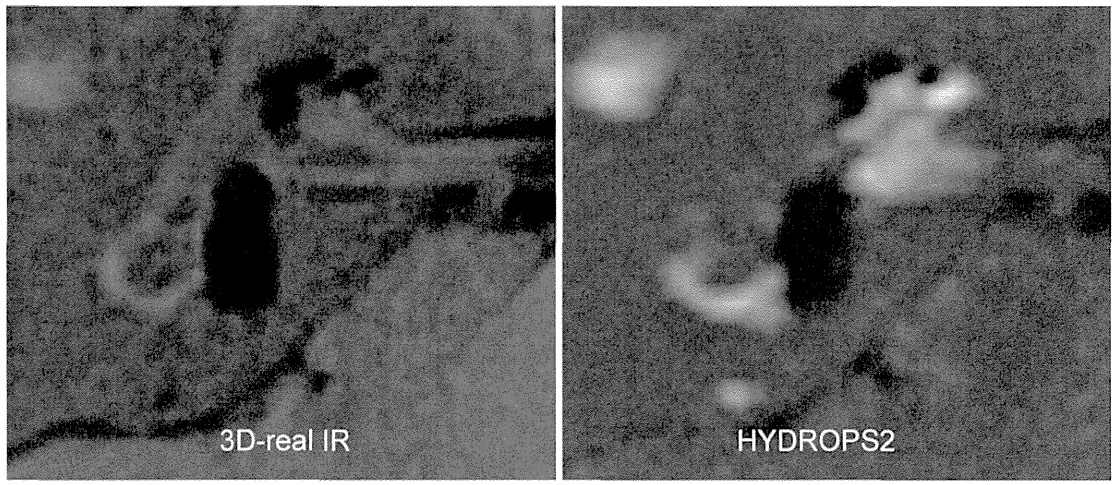

Fig. 1. A 44-year-old man. Intratympanic and intravenous (IT + IV) side. Note the far weaker enhancement of the perilymph on 3-dimensional (3D)-real inversion recovery (IR) than HYDROPS2 (hybrid of reversed image of magnetic resonance cisternography and positive perilymph signal by heavily T_2-weighted 3D-fluid-attenuated inversion recovery [FLAIR]). However, significant endolymphatic hydrops (EH) can be appreciated in the cochlea and vestibule on both images.

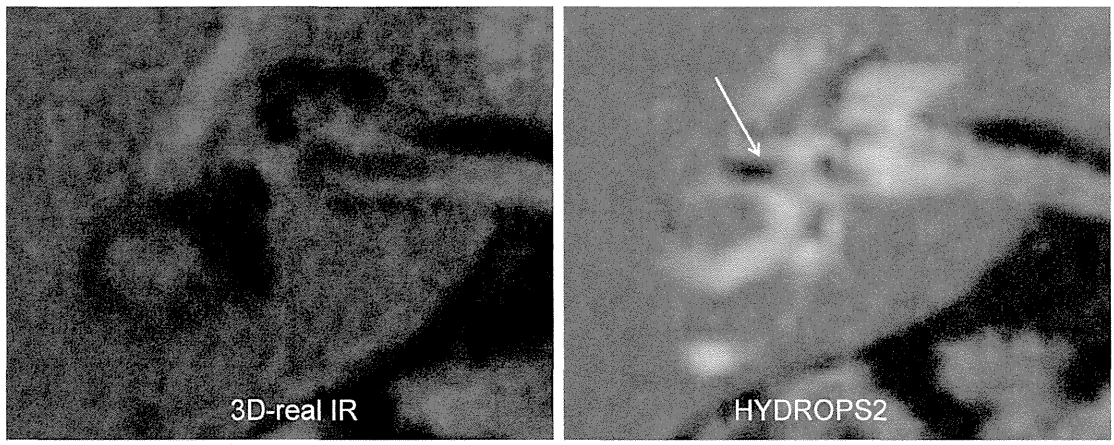

Fig. 2. A 47-year-old man. Intravenous (IV) side. Note that enhancement of the perilymph cannot be recognized on 3-dimensional (3D)-real inversion recovery (IR). Mild endolymphatic hydrops (EH) in the vestibule (arrow) can be appreciated only on the HYDROPS2 (hybrid of reversed image of magnetic resonance cisternography and positive perilymph signal by heavily T_2-weighted 3D-fluid-attenuated inversion recovery [FLAIR]) image.

tween scans.[3,13] This problem might be overcome by the registration program available on most 3D workstations.

Our study is limited by the small number of cases and because most patients had definite MD. Further study that includes more cases of probable and possible MD is necessary to confirm that HYDROPS2 can replace 3D-real IR even in cases with mild EH. Further study is also necessary to evaluate the diagnostic efficacy of HYDROPS2 images when the IV method is used.

Conclusions

The use of HYDROPS2 images might obviate the need for 3D-real IR images in cases utilizing an IT + IV protocol. HYDROPS2 images permit simultaneous evaluation of the IV side and IT + IV side, contributing to the significant shortening of total examination time and possibly reducing the possibility of examination failure due to weak enhancement by impaired permeability of the round window membrane in the IT + IV side.

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3D Real Inversion Recovery MR Imaging for the Visualization of Endolymphatic Hydrops

We read with interest the article by Baráth et al[1] describing the reliability of MR imaging performed 4 hours after intravenous administration of double-dose gadolinium-based contrast agent for the visualization of endolymphatic hydrops in Menière disease. Although we agree with the principal findings of the study, we would like to clarify an important technical point to further increase the practical value of the article. The authors stated that they used a 3D real inversion recovery (3D real IR) sequence using our previously reported method.[2] Real inversion recovery is the method that allows the negative magnetizations before crossing the null point are correctly represented as negative values by the use of phase-sensitive reconstruction.[3] In the MR images shown, endolymphatic fluid shows near zero signal intensity, similar to that of surrounding bone, instead of a negative signal-intensity value as expected on 3D real IR. 3D real IR was intended to separately visualize endolymph, perilymph, and bone on a single kind of image.[2] MR images shown in the article are more like 3D FLAIR than 3D real IR. Clarification of this technical point might be very important for the readers to reproduce this important study.

http://dx.doi.org/10.3174/ajnr.A4126

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FRONTIER

Vestibular evoked myogenic potential

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Abstract

Vestibular evoked myogenic potential (VEMP), is an electromyographic response of vestibular origin evoked by sound, vibration or electrical stimulation. VEMP is widely used as a clinical test of the otolith organs. Nowadays, two kinds of VEMP, cervical VEMP (cVEMP) and ocular VEMP (oVEMP) are clinically used. cVEMP is a test of sacculo-collic reflex while oVEMP is a test of utriculo-ocular reflex. Absence of responses, large interaural asymmetry of amplitudes, prolonged peak latencies, and abnormal thresholds of responses are regarded as abnormal responses. Clinical application to various diseases of the vestibular system was performed. Using VEMP, a new type of vestibular neuritis, inferior vestibular neuritis was established. A prominent feature of VEMP in Meniere's disease is a shift of a preferred frequency in cVEMP. The whole aspects of VEMP findings in patients with benign paroxysmal positional vertigo are not clarified yet. Sensitivity of cVEMP to vestibular schwannoma was 80.0%, while specificity was 52.7%. Concerning diagnosis of superior canal dehiscence syndrome (SCDS), oVEMP to air-conducted sound is the most helpful. Augmentation of oVEMP responses is a prominent feature in SCDS. I also presented "idiopathic otolithic vertigo", which I proposed as a new clinical entity based on VEMP findings. Some patients complained of lateral tilting sensation in the roll plane, or tilting or translational sensation in the pitch plane without rotatory vertigo. Majority of patients with these symptoms had absent or decreased responses of oVEMP and/or cVEMP. I proposed that these patients could be diagnosed as having "idiopathic otolithic vertigo".

Key words: Vestibular evoked myogenic potential; Otolith; Saccule; Utricle; Otolithic vertigo

Core tip: This is a review of Vestibular evoked myogenic potential (VEMP). In this review I presented fundamentals concerning VEMP. Also I showed various types of clinical application of VEMP. Finally I introduced a new clinical entity, idiopathic otolithic vertigo which I poroposed. Idiopathic otolithic vertigo cannot be diagnosed without application of VEMP.

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INTRODUCTION

Vestibular evoked myogenic potential (VEMP) is an electromyographic response derived from the vestibular labyrinth evoked by sound, vibration, or electrical stimulation[1]. VEMP is a clinical test of the otolith organs, sensors of linear acceleration. The otolith organs in human are consisted of the saccule and the utricle. VEMP was first reported by Colebatch and Halmagyi in 1992[2]. Since 1992 many papers concerning VEMP have been published all over the world. At first, VEMP, which was recorded on the sternocleidomastoid muscle (SCM), was performed as a test of otolith-collic reflex[3]. Later, another method, recording around the eyes, has been also adopted as a test of otolith-ocular reflex[4,5]. The former is called cVEMP (cervical VEMP), and the latter is called oVEMP (ocular VEMP). These tests provide different

information concerning the vestibular labyrinth from a caloric test and a head-impulse test (HIT)[6], which are tests of the semicircular canals. In this review I will present fundamentals concerning VEMP.

RESPONSIBILITY TO SOUND OF THE MAMMALIAN VESTIBULAR LABYRINTH

For understanding VEMP, responsiveness to sound of the mammalian vestibular labyrinth must be addressed. In 1977 Young *et al*[7] reported responses of the vestibular labyrinth to air-conducted sound (ACS) and bone-conducted vibration (BCV) using squirrel monkeys. They showed vestibular afferents could respond to ACS and BCV. Concerning ACS, saccular afferents showed lower thresholds than other end-organs. Didier *et al*[8] showed that the inferior branch of the vestibular nerve (the inferior vestibular nerve) could respond to sound stimulation using guinea pigs which had destroyed cochlea but preserved vestibular labyrinth by amikacin injection. In 1990s, McCue *et al*[9,10] using cats and Murofushi *et al*[11-13] using guinea pigs showed sound-sensitivity of the mammalian otolith organs using single-unit recording technique. McCue *et al*[10] reported that saccular afferents responded to sound stimulation and that best frequencies of responses were between 500 and 1000 Hz. Murofushi *et al*[12] showed that sound-sensitive otolith afferents could be also tilt-sensitive and were in the caudal part of the superior vestibular nerve as well as the inferior vestibular nerve. Both groups reported that irregularly firing units, which are from type I hair cells, responded to sound well. Their studies confirmed that hair cells in the saccular macula, especially type I cells could respond to sound. McCue *et al*[10] also suggested that preferred frequencies of the saccule were between 500 and 1000 Hz while Murofushi *et al*[13] suggested that the utricle might be also respond to sound. Curthoys *et al*[14] studied responsibilities to BCV. Their study showed that irregularly firing otolith afferents also responded to BCV well.

RECORDING METHODS AND NORMAL RESPONSES OF VEMP

cVEMP

Surface electrodes are used for recording. Active electrodes are placed on the belly of the sternocleidomastoid muscle (SCM) with reference electrodes on the lateral end of the upper sternum. The ground electrode is placed on the nasion. Nowadays 500 Hz short tone bursts (STB) (rise/fall time = 1 ms, plateau time = 2 ms, 125-130 dBSPL, ACS) are usually used as stimuli. Clicks are also applicable. The repetition rate of stimulation presentation is 5 Hz, and the time window for analysis is -20-80 ms. Signals are bandpass-filtered (20-2000 Hz) and 100 responses are averaged. BCV can be also used. Subjects must be instructed to keep contracting their SCM during recording. As methods for contraction, rotation of the neck or raising the head from the pillow is recommended.

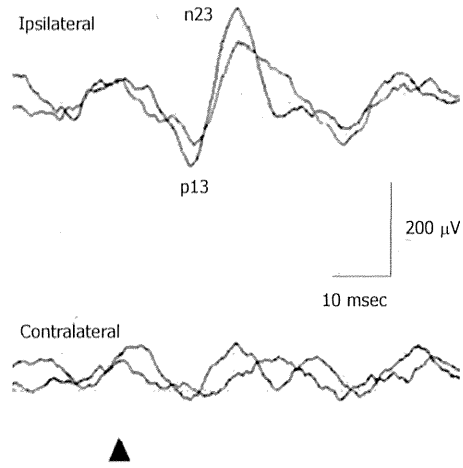

Figure 1 Cervical vestibular evoked myogenic potential waveforms in a healthy subject.

In a healthy subject, to 125 dBSPL 500 Hz ACS STB, the first positive deflection, of which the peak is around 15 ms is recorded in the ipsilateral SCM to the stimulated ear, followed by the negative deflection, of which the peak is around 23 ms (Figure 1). Conventionally, the first positive peak and the following negative peak are called p13 and n23 respectively. Absence of responses, large interaural asymmetry of p13-n23 amplitudes, prolonged peak latencies, and abnormal thresholds of responses are regarded as abnormal responses[1]. Concerning cVEMP, a published guideline should be referenced[5].

For assessment of amplitudes, correction of amplitudes using background muscle activities is desirable. For assessment of interaural asymmetry of amplitudes, percent cVEMP asymmetry has been used[15,16]. Percent cVEMP asymmetry = 100 (CAcu - CAca)/(CAcu + CAca)CAcu(a) = corrected amplitude of p13-n23 on the unaffected (affected) side. The upper limit of percent cVEMP asymmetry in our laboratory is 41.6. The above-mentioned guideline indicated 50.0 as a strict standard of the upper limit of percent cVEMP asymmetry[15]. As latencies can be affected by recording conditions, each laboratory should set their own normal range. The upper limit of p13 latency in our laboratory is 17.7 msec (125 dBSPL 500 Hz STB ACS)[16]. Thresholds lower than 95 dBSPL (500 Hz STB ACS) are definitely abnormal.

It should be taken into consideration that subjects with conduction problems in the middle ear would show absence of responses even though they had normal vestibular function. Air-bone gap more than 15dB makes recording of cVEMP to ACS useless.

oVEMP

Surface electrodes are used for recording. Active electrodes are placed just beneath the lower eye lids with reference electrodes 2 cm below active electrodes[16]. The ground electrode is placed on the nasion. STB of 500 Hz (rise/fall time = 1 ms, plateau time = 2 ms, 125-130 dBSPL, ACS) are standard stimuli. Clicks are not used because healthy subjects frequently show absence of re-

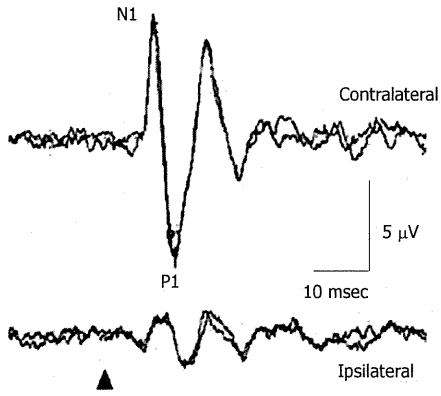

Figure 2 Ocular vestibular evoked myogenic potential waveforms in a healthy subject.

sponses[5]. Instead, BCV are used more frequently for recording oVEMP than cVEMP[17]. The repetition rate of stimulation is 5 Hz, and the time window for analysis is -20-80 ms. Signals are bandpass-filtered (20-2000 Hz) and 100 responses are averaged. Other ranges of bandpass-filter may be used (*e.g.*, 5-500 Hz)[17]. Subjects must be instructed to keep upward gaze during recording (approx. 20 deg).

In a healthy subject, to 125 dBSPL 500 Hz ACS STB, the first negative deflection, of which the peak is around 11 msec, is recorded beneath the contralateral eye to the stimulated ear, followed by the positive deflection, of which the peak is around 15 ms (Figure 2)[16]. Conventionally, the first negative peak and the following positive peak are called N1 and P1. Absence of responses, large interaural asymmetry of N1-P1 amplitudes, prolonged peak latencies, and abnormal thresholds of responses are regarded as abnormal responses. For assessment of interaural asymmetry of amplitudes, percent oVEMP asymmetry has been used[16]. The formula is basically the same as percent cVEMP asymmetry. The upper limit of percent oVEMP asymmetry in our laboratory is 44.3. The upper limit of N1 latency in our laboratory is 13.6 msec (125 dBSPL 500 Hz STB ACS)[16]. As latencies can be affected by recording conditions, each laboratory should set their own normal range. Thresholds lower than 105 dBSPL (500 Hz STB ACS) are abnormal.

Pathways of VEMP

Main pathways related to VEMP are considered as follow (Figure 3). The main neural pathway of cVEMP is uncrossed in the brainstem. cVEMP mainly reflects sacculo-collic reflexes to sound stimulation. Saccular afferents project to the vestibular nucleus through the inferior vestibular nerve. Neurons in the vestibular nucleus (inhibitory) project to the motoneurons in the ipsilateral accessory nerve nucleus through the ipsilateral medial vestibulo-spinal tract[1,18].

The main neural pathway of oVEMP is crossed in the brainstem[5]. oVEMP mainly reflects utriculo-ocular reflexes to sound stimulation[16,19]. Utricular afferents

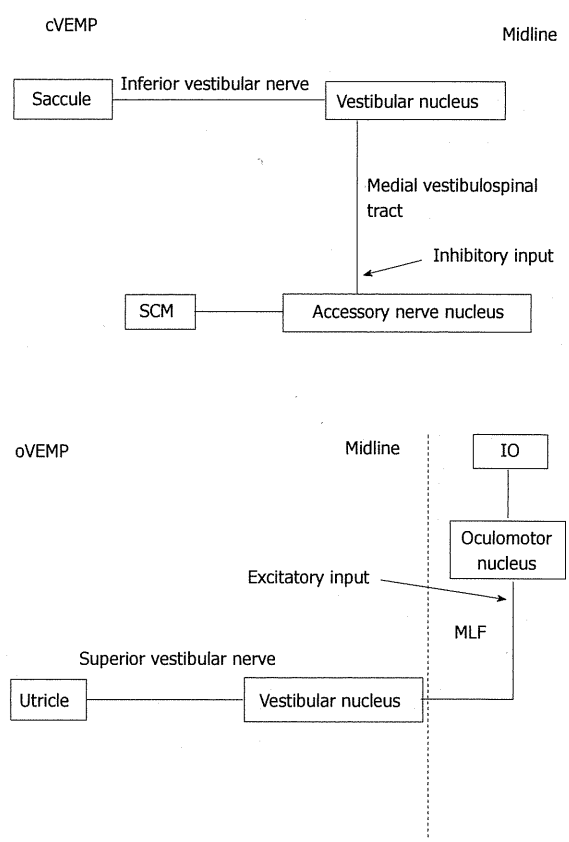

Figure 3 Supposed neural pathway of Cervical vestibular evoked myogenic potential and ocular vestibular evoked myogenic potential. cVEMP : Cervical vestibular evoked myogenic potential; oVEMP: Ocular vestibular evoked myogenic potential; SCM: Sternocleidomastoid muscle; IO: Inferior oblique muscle; MLF: Medial longitudinal fasciculus.

project to the vestibular nucleus through the superior vestibular nerve. Neurons in the vestibular nucleus (excitatory) project to the contralateral oculomotor nucleus through the contralateral medial longitudinal fasciculus (MLF)[20]. oVEMP responses are mainly from the inferior oblique muscle[21]. However, the pathway of oVEMP is still somewhat controversial.

Clinical application of VEMP

VEMP has been clinically applied to various diseases or conditions which might have abnormal findings in the vestibular system.

Vestibular neuritis

Conventional diagnostic criteria of Vestibular neuritis (VN) were as follow: (1) a single attack of acute spontaneous vertigo lasting at least several hours without accompanying auditory symptoms; (2) absence of other cranial nerve or central nervous system symptoms or signs; and (3) severe canal paresis (CP) on caloric testing (CP more than 50%)[22]. These criteria are good for detection of acute deafferentation of the superior vestibular nerve, but they cannot detect deafferentation of the inferior vestibular nerve. In VN patients diagnosed accord-

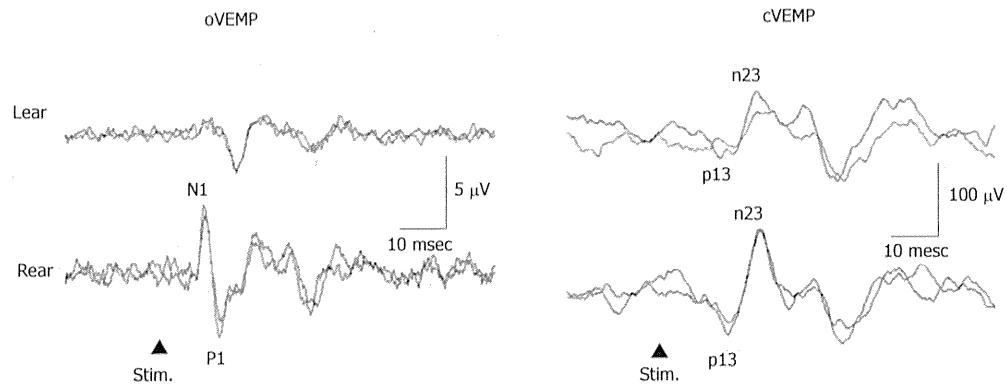

Figure 4 Vestibular evoked myogenic potential responses of a 57-year-old man with episodic lateral tilt sensation diagnosed as having idiopathic otolithic vertigo. He showed absent oVEMP to the left ear stimulation. cVEMP : Cervical vestibular evoked myogenic potential; oVEMP: Ocular vestibular evoked myogenic potential.

ing to these conventional diagnostic criteria, cVEMPs were absent or decreased in amplitudes in one third to half of patients[1,22], while oVEMPs were abnormal in most patients[16]. Patients with absent or highly decreased caloric responses and abnormal cVEMP responses can be regarded as superior and inferior (total) VN, while patients with absent or highly decreased caloric responses but normal cVEMP responses can be regarded as superior VN with spared inferior vestibular nerve functions. This classification lead to a new clinical entity, inferior VN with spared superior vestibular nerve functions[23]. According to retrospective study by Chihara *et al*[23], at the period when 24 patients were diagnosed as total VN and 34 patients were diagnosed as superior VN, 13 patients were regarded as inferior VN. Patients with inferior VN showed tendency of milder and shorter symptoms than patients with total or superior VN. Clinical application of cVEMP enabled us to diagnose patients as having inferior VN. These patients, otherwise, would be left as undiagnosed.

Meniere's disease

One of distinct features of VEMP in Meniere's disease (MD) patients is a shift of a preferred frequency in cVEMP[24,25]. Healthy subjects show the largest amplitudes and the lowest thresholds in ACS cVEMP to stimulation of STB around 500 Hz. On the other hand, MD patients frequently showed a shift of a preferred frequency to 1000 Hz. Node *et al*[26] found that the preferred frequency shift was normalized by dehydration using furosemide. Probably, the frequency shift was caused by endolymphatic hydrops in the saccule. Endolymphatic hydrops in the saccule can be also detected by glycerol-VEMP test. Murofushi *et al*[27] found that 50% of MD patients with abnormal cVEMP prior to glycerol administration showed significant improvement of VEMP responses in 3 h after oral administration of glycerol (1.3 mg/kg body weight) on the affected side.

Benign paroxysmal positional vertigo

The whole aspects of VEMP findings in patients with Benign paroxysmal positional vertigo (BPPV) are not clarified yet. Some investigators reported unilaterally abnormal oVEMP in patients with posterior canal BPPV[28]. Abnormal oVEMPs could be decrease or augmentation of responses. Seo *et al*[28] assumed that reduced responses on the affected side might be from partial degeneration of the utricular hair cells and that augmented responses might be from hypermobility of stereocilia due to detachment of otoconia. On the other hand, Nakahara *et al*[29] reported bilaterally abnormal oVEMP in patients with posterior canal BPPV. They assumed that bilaterally abnormal (= absent) oVEMP might reflect utricular degeneration as a background of BPPV. Further study is required concerning VEMP in BPPV.

Vestibular schwannoma

Majority of patients with Vestibular schwannoma (VS) showed absent or decreased responses on the affected side, while some had prolonged latencies[30,31]. According to Ushio *et al*[31], sensitivity of cVEMP was 80.0%, while specificity was 52.7%. Although it is expected that combined application of cVEMP with caloric tests might be useful for prediction of the nerve origin of VS, Ushio *et al*[32] did not find correlation of results of these tests to the nerve origin. However, Murofushi *et al*[33] reported that a patient with very small VS from the inferior vestibular nerve showed abnormal cVEMP to clicks with normal cVEMP to 500 Hz ACS STB, normal caloric responses, and normal auditory brainstem responses (ABR). Study concerning prediction of the nerve origin of VS using physiological tests should be focused on cases with very small mass. Kinoshita *et al*[34] and Murofushi *et al*[35] reported that oVEMP might be also useful for diagnosis of VS. However, diagnostic values of oVEMP are remained to be clarified.

Superior canal dehiscence syndrome

Dehiscence of the bone overlying the superior (anterior) semicircular canal was first described in 1998 by Minor *et al*[36]. It has been reported that this condition (SCDS) manifests as various vestibular and/or auditory symptoms[36-38]. While detection of dehiscence with computed tomography scans is essential for definite diagnosis, it

has been also reported that augmentation of VEMP responses, especially oVEMP to ACS is marked[37,39,40]. ACS oVEMP might be useful for screening of SCDS in dizzy patients. Zuniga *et al*[40] reported that an n10 (N1 in this paper) amplitude of greater than 9.3 μV and a peak-to-peak amplitude (N1-P1 in this study) of greater than 17.1 μV exhibited 100% sensitivity and specificity for SCDS.

Idiopathic otolithic vertigo

Murofushi *et al*[41,42] reported that some patients complained of lateral tilting sensation in the roll plane, or tilting or translational sensation in the pitch plane without rotatory vertigo. Majority of patients with these symptoms had absent or decreased responses of oVEMP and/or cVEMP (Figure 4). Patients with tilting sensation in the roll plane had tendency to show abnormal oVEMP, while patients with tilting or translational sensation in the pitch plane had tendency to show abnormal cVEMP. Murofushi *et al*[41,42] proposed "idiopathic otolithic vertigo" as a new clinical entity, because the otolith organs are sensors of linear acceleration and dysfunction of them could result in illusion of linear movement[43]. Abnormal VEMP findings may be essential for diagnosis of otolithic vertigo. As a next step, pathophysiology of idiopathic otolithic vertigo should be clarified.

Sensorineural hearing loss

Sensorineural hearing loss itself does not affect cVEMP or oVEMP. Patients with total hearing loss showed normal responses[1,3,44,45].

VEMP is a still developing technique and new discovery is expected. I hope that many clinicians and researchers may be interested in it.

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Guidelines

International guidelines for the clinical application of cervical vestibular evoked myogenic potentials: An expert consensus report

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HIGHLIGHTS

- As more clinical laboratories are publishing data on the cervical vestibular evoked myogenic potential (cVEMP) as a measure of vestibular function, there is a wider range of recording methods and interpretation.
- The variations in methodology and interpretation may be confusing to clinicians and may limit comparisons of cVEMP data across laboratories.
- The purpose of this article is to recommend *minimum requirements* and guidelines for the recording and interpretation of the cVEMP in the clinic and for diagnostic purposes.

ABSTRACT

Background: Cervical vestibular evoked myogenic potentials (cVEMPs) are electromyogram responses evoked by high-level acoustic stimuli recorded from the tonically contracting sternocleidomastoid (SCM) muscle, and have been accepted as a measure of saccular and inferior vestibular nerve function. As more laboratories are publishing cVEMP data, there is a wider range of recording methods and interpretation, which may be confusing and limit comparisons across laboratories.
Objective: To recommend *minimum requirements* and guidelines for the recording and interpretation of cVEMPs in the clinic and for diagnostic purposes.
Material and methods: We have avoided proposing a single methodology, as clinical use of cVEMPs is evolving and questions still exist about its underlying physiology and its measurement. The development of guidelines by a panel of international experts may provide direction for accurate recording and interpretation.
Results: cVEMPs can be evoked using air-conducted (AC) sound or bone conducted (BC) vibration. The technical demands of galvanic stimulation have limited its application. For AC stimulation, the most effective frequencies are between 400 and 800 Hz below safe peak intensity levels (e.g. 140 dB peak SPL). The highpass filter should be between 5 and 30 Hz, the lowpass filter between 1000 and 3000 Hz, and the amplifier gain between 2500 and 5000. The number of sweeps averaged should be between 100 and 250 per run. Raw amplitude correction by the level of background SCM activity narrows the range of normal values. There are few publications in children with consistent results.
Conclusion: The present recommendations outline basic terminology and standard methods. Because research is ongoing, new methodologies may be included in future guidelines.

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Contents

1. Introduction

The cervical vestibular evoked myogenic potential (cVEMP) gained international attention when Colebatch and Halmagyi (1992) described a short latency electromyogram (EMG) response evoked by high-level acoustic stimuli recorded from the tonically contracted sternocleidomastoid (SCM) muscle. The cVEMP has since gained popularity as a clinical test of saccular and inferior vestibular nerve function. In addition to loud (intense) air-conducted sound, cVEMPs can be evoked using bone conducted vibration, head taps, or galvanic stimulation. As more laboratories are publishing data on the cVEMP as a measure of vestibular function, there is a wider range of recording methods and interpretation. The variations in methodology and interpretation may be confusing to clinicians and may limit comparisons of cVEMP data across laboratories. The purpose of this article is to recommend *minimum requirements* and guidelines for the recording and interpretation of the cVEMP in the clinic and for diagnostic purposes. The present recommendations outline basic terminology and standard methods and advocate desirable instrumentation. Because research in this field is ongoing, new methodologies may be included in future guidelines. Therefore, this manuscript will be subject to periodic review.

We have refrained from proposing a single methodology, as clinical use of cVEMPs is evolving and questions still exist about its underlying physiology and its measurement. The development of guidelines by a panel of international experts in the field, however, may provide direction for the accurate and reliable recording and interpretation of cVEMPs.

These recommendations may require revision to keep abreast of the rapid changes in methodology, technology, and knowledge with regards to the neuroanatomy and neurophysiology of cVEMPs.

2. Terminology

To improve communication among scientists and clinicians a standardized nomenclature needs to be adopted (Celesia et al., 1993). The nomenclature in this report is derived from: (1) established use in the last two decades, especially with respect to the development of other vestibular evoked myogenic potentials, and (2) introduction of clarifications in areas where conflicting terms have been used.

Vestibular evoked myogenic potentials are electrical potential differences recorded from muscle in response to vestibular stimulation; they are abbreviated as *VEMPs*. When the VEMP is recorded from the sternocleidomastoid muscle, it is referred to as a *cervical VEMP*, abbreviated to *cVEMP* (Akin et al., 2011; Curthoys, 2010; Rosengren et al., 2011).

Waveform nomenclature is most commonly derived from either of two methods (Chiappa, 1997); (1) the components are numbered in sequence by polarity, for example, N1, N2, N3, and so forth; or (2) the components are labeled according to their polarity and mean latency in normal subjects. Both methods are used in the literature with regards to cVEMPs. Although perhaps the best approach is the use of a method employed by the majority of investigators publishing work in this field, at the moment this does not apply here. Most publications tend to use the second method; however, this committee does not favor either one. With regards to the second method, the response components of cVEMPs are designated with the first major positive peak as p13 and the first major negative peak following p13 as n23 (Fig. 1). The lower case of the letter emphasizes the non-neural origin of the potentials (Yoshie and Okudaira, 1969), as opposed to other neural evoked potentials that usually use an upper case, for example P100 for the visual evoked potential. Of course, the precise peak latency depends on stimulus characteristics. For the purposes of this manuscript, the first major positive peak will be named p13 (P1) and the following major negative peak as n23 (N1). However, laboratories will need to choose either one or the other form of labeling.

3. Neurophysiology

Cervical vestibular evoked myogenic potentials represent a transient alteration of muscle activity. The response likely represents a short period of inhibition on a background of tonic muscle activation (Colebatch and Rothwell, 2004; Wit and Kingma, 2006). cVEMPs are employed routinely in the assessment of the functional

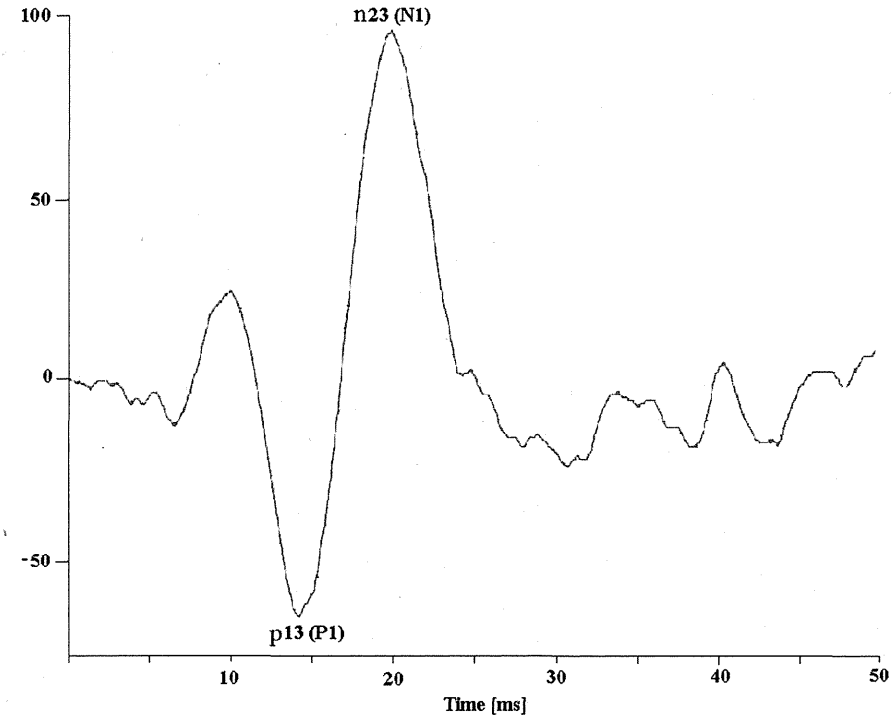

Fig. 1. A normal cVEMP. The raw amplitude of p13 (P1)–n23 (N1) (before correcting for electromyographic activity). In a normal subject this is usually between 20 and 200 μV, with a corrected amplitude between 0.1 and 3.0. The *y*-axis represents amplitude in μV.

integrity of the vestibular pathway, specifically that involving the saccule, inferior vestibular nerve, vestibular nuclear complex, medial vestibulospinal tract and the spinal accessory nerve (Govender et al., 2011; Kushiro et al., 1999). The identities of the specific vestibular nuclei that are involved in this pathway are currently unknown. The major vestibular nuclei (Brodal, 1981) are the superior, medial, lateral (or Deiter's nucleus) and descending (or inferior). It is known from animal studies that primary afferents from the ipsilateral sacculus project to the lateral and descending vestibular nuclei as well as nucleus y (Imagawa et al., 1998; Gacek, 1980; Sato et al., 1997; Wilson et al., 1978). The medial vestibulospinal tract, which is believed to be responsible for transmitting signals to the sternocleidomastoid muscle with respect to cVEMPs (Kushiro et al., 1999), arises mainly from the medial vestibular nucleus (Brodal, 1981; Nyberg-Hansen, 1964) to which the saccule projects only weakly (Kevetter and Perachio, 1986). Despite this discrepancy, saccular projections to the MVST are common (Sato et al., 1997).

4. Basic technology

4.1. Vestibular stimulation

cVEMPs can be evoked using conventional air conducted (AC) sound (Colebatch et al., 1994), bone conducted (BC) vibration (Sheykholeslami et al., 2000) or short duration electrical ("galvanic") stimuli (Watson and Colebatch, 1998). Of the three types of stimuli, conventional AC sound is probably the most widely used, although AC cVEMPs may be absent in patients with conductive hearing loss. All three stimuli require careful and appropriate calibration.

4.1.1. Air conducted (AC) sound

cVEMPs can be elicited using either click or tone burst stimuli; however normative values will differ. The response amplitude and latency are both affected by the duration of the stimulus, with the largest responses being obtained with stimuli about 7 ms long (Welgampola and Colebatch, 2001b). Because high stimulus levels are necessary to elicit cVEMPs using air conducted sound, safe exposure to the stimulus is a concern. Peak intensities must be limited to safe levels (e.g. 140 dB pSPL) and the total energy delivered to the ear must be within acceptable limits. Longer stimuli carry proportionately larger amounts of energy and therefore may be more effective but the stimulus intensities must be reduced to avoid damage to hearing. The most effective frequencies have been shown to be in the range of 400–800 Hz (Akin et al., 2003; Murofushi et al., 1999; Todd et al., 2000; Welgampola and Colebatch, 2001b) and thus stimuli around 500 Hz are somewhat more efficient than clicks (Rosengren and Colebatch, 2009). Tuning properties may have diagnostic applications, predominantly reported for Meniere's Disease (Lin et al., 2006; Rauch et al., 2004), but also seen in migraine-associated vertigo (Murofushi et al., 2009). Windowing or shaping can concentrate energy around the centre frequency. Stimulus properties will affect the normal values for latency of the p13 (P1) and n23 (N1) peaks, therefore normative observations must be made for each set of stimulus parameters. It is essential that stimulus levels be accurately known if the pathologically low threshold typical of superior canal dehiscence (SCD) is to be recognized, as well as its correction after successful surgery (Welgampola et al., 2008). If tuning properties are to be investigated, the minimum stimulus duration should be at least be a full cycle of the frequency to be studied; otherwise the shortest effective stimulus is probably to be preferred.

Young et al. (1977) showed lower thresholds for saccular receptors than for other vestibular end organs to AC sound and others have confirmed saccular activation (McCue and Guinan, 1994; Murofushi and Curthoys, 1997). Clinical observations in vestibular neuritis are consistent with this view and usually show sparing of cVEMP responses, a consequence of saccular fibers mainly traveling in the inferior division of the vestibular nerve (Murofushi et al., 1996).

4.1.2. Bone conducted (BC) stimulation

Sheykholeslami et al. (2000) were the first to demonstrate that bone vibration or BC sound was also capable of evoking cVEMPs. Recordings from guinea pigs suggest that BC stimulation at 500 Hz preferentially stimulates irregular otolith afferents (Curthoys et al., 2006). The stimulus levels required to activate vestibular afferents are higher than those required for cochlear excitation and a power amplifier such as the 2718 (Bruel and Kjaer) is needed in most cases. Only 20 dB of gain (10*x*) is required and amplifiers with fixed gains are safest. Drive voltages intended for BC oscillators should never be applied to headphones and different styles of connectors for the BC oscillators and earphones as well as separate systems for the two modes of stimulation are essential for safety. High voltage levels can cause harmonic distortion and limit the usable frequency range when delivered to conventional BC oscillators (e.g. B71). Other devices such as "minishakers" can generate wider ranges of frequencies with greater power (e.g. 4810, Bruel and Kjaer).

Tendon taps to the forehead and mastoid also produce cVEMPs (Brantberg et al., 2008; Halmagyi et al., 1995). Skull taps with a tendon hammer equipped with a sensitive trigger (e.g. model 842-116700, Nicolet Biomedical Inc., WI, USA) are a simple technique but inevitably entail some delay with triggering. The wider frequency range of minishakers allows greater flexibility with the nature of the stimulus and non-sinusoidal, impulsive stimuli, such as the "gamma pulse" (Todd et al., 2008) can be an effective means of evoking cVEMPs (Rosengren and Colebatch, 2009). The force pulse used in this methodology has a smooth profile and can be graded in intensity. The responses to impulsive stimuli are little affected by age and have low side to side variability (Rosengren et al., 2011). Ideally, induced acceleration should also be monitored to allow comparison between users and centres. Tendon hammer taps to the mastoid and forehead can evoke responses very similar to a positive (outgoing) gamma pulse applied to the same site (Rosengren et al., 2009).

The use of a BC stimulus avoids the effects of conductive hearing loss which can reduce AC-evoked cVEMPs, as it bypasses the external and middle ear air conducting pathway and stimulates the vestibular apparatus directly via bone vibration. It should be used in addition to and not generally as a substitute for AC sound-evoked cVEMPs. The peak force level (pFL) must be known for any BC stimulus used and the BC stimulus may not excite exactly the same fibers as an AC one. Welgampola et al. (2003) systematically investigated the effect of location and reported that placing the bone conduction oscillator 3 cm posterior and 2 cm superior to the external auditory canal was the most effective location when using a B71 bone conductor. Forehead stimulation is also effective, but requires a stronger stimulator (Iwasaki et al., 2008).

4.1.3. Galvanic (electrical) stimulation

The term "galvanic" is largely historical and was the original description for DC voltages. Watson and Colebatch (1998) showed that a short DC current pulse could evoke a cVEMP. They recorded a positive–negative wave response on the side of the cathode and negative–positive wave response on the side of the anode. Galvanic stimulation is thought to excite irregular vestibular afferents arising from all vestibular receptors (Kim and Curthoys, 2004). Any method of stimulation must meet relevant standards for isolation and electrical safety. Typically currents of 3–4 mA for 1–2 ms are required. Stimulus artifact is a particular problem, one that Watson and Colebatch (1998) were able to overcome by subtracting a recording made while the subject was relaxed from one made during a tonic contraction. The electrical stimulus is thought to act at the most distal part of the vestibular nerves by modulation of the generator potential, thus tonic activity is probably required for the stimulus to be effective. As a consequence it is likely that severe insults to vestibular receptors may affect the response, so electrical excitation may not be a pure test of vestibular nerve and more central function. In acute lesions electrical stimulation may be suitable for separating peripheral from central disorders (Murofushi et al., 2003). The technique may be well suited to investigating central disorders of vestibular function but the technical demands have limited the application of this stimulus to date. This technique will therefore not be described further in this guideline.

4.2. Calibration of auditory stimuli

4.2.1. Air conducted (AC) sound

Due to the high level stimuli needed to elicit cVEMPs via AC, it is essential that audiometric quality headphones (e.g. TDH 49, Telephonics Corp.) or ear inserts are used and that the stimulus levels are calibrated, ideally in dB peak SPL (see Appendix A). Sound level meters typically use both frequency and time weighting. A linear or "C" type frequency weighting is appropriate, and should be specified, for measurements of peak sound pressure level (pSPL). Unlike auditory responses, cVEMPs depend upon the earliest components of the stimulus sound wave, so very fast pressure measurements are essential. Lower absolute stimulus levels can be used with longer duration stimulation, as a consequence of the increase in energy delivered with each stimulus. A good way to compare stimuli is through their energy delivery to the ear, such as measuring L_{Aeq}. A 0.1 ms click of 139 dB peak SPL given at 5/s (Rosengren and Colebatch, 2009) has an $L_{Aeq,1\ s}$ of 105 dB and thus can be presented to each ear for up to 4.8 min and remain within acceptable limits for daily exposure in the workplace (Appendix A). Either clicks or tone bursts may be used to evoke cVEMPs, but the stimuli should be calibrated in dB peak SPL. Ideally the L_{Aeq} should be known and in most cases the effective stimulus with the lowest energy should be used. Other sound reference levels, such as dB nHL, reflect cochlear function and are therefore less suitable.

4.2.2. Bone conducted (BC) vibration

Like the air conducted stimulus, a bone conducted stimulus must also be calibrated, in this case in dB FL (force level), where the reference is 1 μN. The calibration should be stated as the peak force level or RMS (for sinusoids) the former being preferable. Use of dB nHL is less desirable. Only events prior to the generation of the p13 (P1) and n23 (N1) potentials can have an effect, so the force levels in the first 10 or 20 ms are the most relevant. Again a measurement system with a very rapid response is needed.

4.3. Electrodes

cVEMPs should be recorded using good quality surface EMG electrodes with an active electrode placed on the upper third to midpoint of the SCM muscle and a reference electrode placed on or near the sternum. The main response to AC sound occurs ipsilaterally to the stimulated ear but usually recordings are made from both sides simultaneously as short latency crossed responses may be present. BC stimuli, particularly given in the midline, evoke bilateral responses and require bilateral recordings. The common or ground electrode can be placed on the forehead. High quality recordings require matched low electrode impedances. If the SCM electrode is connected to the inverting input to the differential amplifier, then positive potentials are displayed and plotted as downward deflections (e.g., Colebatch and Halmagyi, 2001). In contrast, if the SCM electrode is connected to the non-inverting input, then positive potentials are shown as upward deflections (e.g., Akin and Murnane, 2001). The largest cVEMP amplitudes are obtained when the SCM electrode is located over the midpoint of

the muscle (Sheykholeslami et al., 2001) and over the SCM motor point (Colebatch, 2011).

4.4. Recording equipment

Previous studies have tended to use bandpass filters of 20–2000 Hz (Murofushi et al., 1996; Welgampola et al., 2008), 30–3000 Hz (Wang et al., 2008), 20–1500 Hz (Basta et al., 2007), 10–1500 Hz (Vanspauwen et al., 2006), and 5–1500 Hz (Ochi et al., 2001) with equally good results. Therefore, the highpass filter should be set between 5 and 30 Hz, while the lowpass filter should be set between 1000 and 3000 Hz. However, the most important point is to describe the range of bandpass filter clearly and to not alter it during the study because this may affect the waveforms of the cVEMP.

Each laboratory should determine the level of gain which allows recording clear waveforms of cVEMP in healthy volunteers. To get a cVEMP, one should not use as high a gain as for neurogenic potentials such as auditory brainstem responses (ABR) which is typically around 100,000. The amplifier gain for cVEMP is usually set between 2500 and 5000 (200–400 μV/V). Artifact rejection is not required.

The sampling rate usually used ranges from 1 to 96 kHz. Most laboratories use between 2.5 and 40 kHz. It may be desirable to adopt a sampling rate between 2.5 kHz (Colebatch et al., 1994) and 40 kHz (Ochi et al., 2001), always ensuring that the sampling rate is at least twice the lowpass cutoff frequency.

The number of sweeps averaged for one run ranges from 25 to 512. Too many sweeps may cause fatigue for subjects, resulting in unclear responses. In our opinion, the number should routinely be between 100 and 250 for each run (Brantberg et al., 2007; Ushio et al., 2009; Versino et al., 2001) unless the response is very clear. Rest periods can be offered within and between runs. The presence of audible or visible neck tremor usually indicates fatigue and a rest period should be offered. Waveforms should be replicated to verify the response presence, particularly when the response is small.

5. Clinical protocol

5.1. General statements

The cVEMP waveform is not mediated by the cochlea (Colebatch et al., 1994; Itoh et al., 2001). The presence of the response is independent of the degree of sensorineural hearing loss, and cVEMPs can be recorded in patients with profound sensorineural hearing loss (Colebatch et al., 1994; Ozeki et al., 1999; Wu and Young, 2002). Although cVEMPs may be absent in some patients with low-frequency hearing loss related to Ménière's disease or idiopathic sudden sensorineural hearing loss (Hong et al., 2008; Wu and Young, 2004), the absence of the cVEMP in these patients suggests involvement of the saccule and/or inferior vestibular nerve rather than the cochlea.

Air conduction-elicited cVEMPs require a normal middle-ear conductive mechanism to convey the stimulus to the vestibular end organs. Thus, air-conducted cVEMPs are typically reduced or absent in patients with even mild to moderate conductive hearing loss due to attenuation in the level of sound transmitted to the inner ear (Bath et al., 1999; Wang and Lee, 2007). In patients with conductive hearing loss, bone-conduction stimuli may be used to elicit cVEMPs (Sheykholeslami et al., 2000; Welgampola et al., 2003; Yang and Young, 2003). In addition to bone conduction stimulation, cVEMPs can be recorded in patients with conductive hearing loss by tapping on the forehead with a tendon hammer (Halmagyi et al., 1995; Yang and Young, 2003).

There are few contraindications to cVEMP, and most patients tolerate the test procedure easily. Because the response is mediated via the sternocleidomastoid muscle, head rotation and/or elevation is necessary to activate adequately the sternocleidomastoid muscle. Patients with limited mobility of the neck, or neuromuscular disorders affecting the SCM, may not be able to cooperate for cVEMP testing. Because cVEMP thresholds to air conduction stimuli are obtained at high stimulus levels, patients with hyperacusis may have difficulty tolerating the acoustic stimulus. It may be possible to test such subjects with BC stimuli as the auditory sensation levels (SLs) are much lower.

Because the cVEMP is produced by inhibitory inputs to the sternocleidomastoid muscle (SCM) of vestibulo-collic reflexes (Colebatch and Rothwell, 2004), contraction of the SCM is essential (Murofushi and Kaga, 2009; Rosengren et al., 2010). Two methods have been adopted for contraction of the SCM. One is the elevation method. In this method, subjects are asked to raise their heads from a bed or a chair in the supine position or in the semi-recumbent position. For the rotation method, subjects are asked to rotate their heads toward the contralateral side to the stimulated ear. This method can be used in the sitting position as well as in the supine position. Some laboratories have adopted a combined method in which the patient rotates and lifts the head in the supine position (Seo et al., 2008). A few laboratories have used a pushing method in which subjects are asked to push their heads to something (e.g. a cushioned bar) (Kingma and Wit, 2011). Any of these methods to contract the target muscle may be adopted; however, one should bear in mind that the rotation method only allows recording of responses in the unilateral muscle (because the other muscle is relaxed). Although bilateral activation can be used, it is difficult to monitor EMG activity in this situation (for example acoustically) as two muscles are being activated at the same time. In this latter situation, electrophysiological EMG monitoring is required from each muscle separately to normalize the response.

5.2. Monitoring of EMG activity

Correction of raw amplitudes by the level of background SCM muscle activity makes the range of normal values narrower (Karino et al., 2005; Welgampola and Colebatch, 2001c), as it has been shown that *the larger the amount of muscle contraction the larger the cVEMP amplitude* (Colebatch et al., 1994). It is therefore important that the electromyographic (EMG) activity of the SCM is monitored in some way. Ideally, observations should be made at the same level of activation in all subjects, so that little adjustment is then needed. Measuring mean rectified (or root mean squared, RMS, a similar but not identical measure: Colebatch, 2009) EMG allows monitoring of the level of contraction and normalization for it (normalized amplitude = raw peak to peak amplitude divided by mean rectified EMG or RMS). Indirect measures (e.g. using a blood pressure cuff: Vanspauwen et al., 2006) also help ensure a similar level of activation within and between subjects. In most laboratories, to maintain muscle contraction, muscle activation is monitored through the display of electromyographic activity. Some laboratories give subjects feedback of the level of muscle activity using an LED light (Kingma and Wit, 2011). It is desirable that average rectified or RMS muscle activity is kept between 50 and 200 μV in adult subjects (Murofushi et al., 1998; Krause et al., 2009). In children including babies, average background muscle activities may be weaker (Young et al., 2009). It is desirable to keep muscle activity levels as constant as possible to get the most reproducible responses.

5.3. Measurement of cVEMPs

Normative values. We recommend that each laboratory establish or confirm its own normal values. Normal values obtained from other institutions should be utilized only if equivalent stimulation and recording methods are employed and only after testing the validity of the adopted normal values on a number of locally gathered subjects. The measurements between the two groups should be similar.

Normative values are influenced by age and possibly by gender. Thus a laboratory and/or manufacturer establishing normal values should gather data from age-matched individuals of the two sexes. It is desirable that a total of at least 10 subjects be collected for each decade. The boundaries of normals are usually set at 2.0 or 2.5 standard deviations above and below the mean value when the distribution is normal. For amplitude, the values of which may be skewed, the distribution should either be normalized first (for example by converting the values to their logarithms) before defining upper and lower limits or specialized statistics be used that do not depend on the normal distribution. Ideally studies will become available that will allow criteria to be set based upon measured sensitivity and specificity for vestibular diseases.

The amplitude asymmetry ratio (AR) is the most common parameter used in the interpretation of cVEMP testing. The AR is usually calculated as:

$$\text{Asymmetry Ratio}(\%) = 100(A_L - A_S)/(A_L + A_S)$$

in which Al equals the larger p13–n23 amplitude and As equals the smaller p13–n23 amplitude. The asymmetry ratio is expressed as a percentage and always positive, similar to Jongkees' formula for caloric responses and an AR over 50% is certainly abnormal, with reported mean values ranging from 7.2% to 23.1% (Lee et al., 2008; Nguyen et al., 2010; Shin et al., 2013) and an upper limit of normal of 32% (Wang et al., 2010). It is important to realize that the above formula is not equivalent to calculations based upon right vs left sided values – which can also be used but will give both positive and negative values, with a zero mean. Unilateral or bilateral absence of responses is an extreme example of amplitude changes.

The cVEMP threshold is the lowest stimulus level for which a reproducible p13–n23 wave is detected. This is determined by increasing sound level in steps of 5–10 dB from a level of around 100 dB pSPL, A very large response raises the possibility of superior canal dehiscence syndrome (SCDS) but while highly suggestive, is not enough alone to prove this diagnosis. Such a finding should prompt an examination of the threshold for the response. Other causes of a vestibular "third widow" such as a fistula or dehiscence of the posterior semicircular canal (Aw et al., 2010; Cremer et al., 2000) may also substantially lower the normal VEMP threshold. Latency of the positive and negative peaks should also be measured. Prolonged latencies may indicate the presence of a brainstem abnormality (Shimizu et al., 2000).

6. Clinical report of results

Clinical reports should ideally contain basic information about the: (1) patient; (2) clinical status; (3) technical data; (4) normative values; (5) results; (6) interpretation.

(1) Patient information should include: name, age, gender and patient identification number.
(2) The clinical question and symptoms to be addressed should be provided.
(3) Technical data. The following stimulus parameters should be reported: stimulus type and level (SPL), rate of presentation, frequency of stimulus if tone is used.
(4) Normative values. The laboratory normal values for amplitude and latency of the p13 (P1) and n23 (N1) should be reported. Normal values should include the criteria for normality.
(5) Results. The report should include the amplitude and latency of the cVEMPs for each ear. Representative waveforms of the response should, where possible, be provided with calibration signals for time and amplitude, particularly for research reports.
(6) Interpretation. The interpretation of cVEMP results usually requires knowledge of the patient, the condition being investigated, the technique used and the findings on other vestibular tests. If cVEMPs are absent or the asymmetry ratio >50%, then conductive hearing loss should be ruled out. Hearing loss itself can be an indicator of pathology, particularly if asymmetrical, but sensorineural hearing loss is otherwise irrelevant to the cVEMP. Hearing thresholds for sound and tuning fork tests should be recorded and audiometric findings for AC and BC stimuli be included, if available. The findings on other vestibular tests, in particular caloric testing, greatly enhance the interpretation of VEMP findings. The cVEMP is not a substitute for methods that assess canal function and combining it with caloric testing improves diagnostic sensitivity (Zapala and Brey, 2004).

The latency of p13 (P1) and n23 (N1) and the amplitude difference between p13 (P1) and n23 (N1) of cVEMPs for each ear and for each type of stimulus should be reported. The latency of the p13 (P1) and n23 (N1) peaks is important as a prolonged latency can occur with central lesions such as Multiple Sclerosis (Shimizu et al., 2000).

When an abnormality is reported it should be specified whether it was present for each type of stimulation if more than one type is used or if it was limited to one or two stimulation types.

Age is an important variable – over the age of 60 cVEMPs may be small or absent in normal subjects (Welgampola and Colebatch, 2001a). The results should therefore be interpreted with caution and with reference to the laboratory's own experience and normative dataset.

Tuning of the cVEMP to AC stimuli normally shows a peak from 400–800 Hz (Akin et al., 2003; Murofushi et al., 1999; Welgampola and Colebatch 2001b). Changes in tuning may indicate pathology affecting the saccule (Kim-Lee et al., 2008; Rauch et al., 2004). Assessing tuning requires observations to be made using tone bursts at several frequencies and may be a useful additional parameter to record.

cVEMPs are a very effective means of diagnosing SCD, with sensitivity and specificity of over 90% (Brantberg and Verrecchia 2009; Zhou et al., 2007). A clue may be the large size of the response or a prominent response on the opposite side "crossed response", but making a confident diagnosis of canal dehiscence requires the demonstration of a pathologically low threshold for the VEMP. This does not necessarily require that the actual threshold be measured; rather it is sufficient to show a response at stimulus levels that are normally too low to evoke responses (Brantberg and Verrecchia, 2009). It may be appropriate to do a form of screening on all patients, that is, to attempt to record cVEMPs at low stimulus levels. If the cVEMPs are absent, then the patient passes screening. If cVEMPs are present, then further testing to establish the threshold should be considered. Thresholds greater than 10 dB below the limit of normal suggest the presence of a third window in the vestibular apparatus, usually SCD.

7. Suggested specific protocols

The following standardized protocols are suggested as the minimum requirement to obtain reliable and reproducible cVEMPs (summarized in Table 1).

The following criteria should be adhered to:

7.1. Recording

The recommended filtering is: high pass 5–30 Hz, and low pass 1000–3000 Hz.

Table 1
Recommended cVEMP recording parameters.

cVEMP Recording parameters	
Number of channels	1[a] or 2
Amplifier gain	5000*x*
Low pass filter	5–30 Hz
High pass filter	1000–3000 Hz
Sample rate	2500–10,000 Hz[b]
Sweep time	100 ms
Artifact rejection	Off
Number of sweeps	100–250
Active electrode	Midpoint to upper third of SCM muscle
Reference electrode	Sternoclavicular junction
Ground electrode	Forehead or upper chest

[a] If one channel it must be the SCM ipsilateral to the stimulated ear.
[b] Sampling rate should always be at least twice the High Pass Filter setting.

A montage consisting of one derivation is sufficient for recording cVEMPs. Automatic artifact rejection should be turned off.

The following montage is suggested: Midpoint to upper third of the SCM muscle (active electrode) against sterno-clavicular junction (indifferent electrode), placed bilaterally and symmetrically. If the active is the inverting input the waveform will show negative potentials as upwards deflections and the reverse if it is the non-inverting electrode. Bilateral electrodes allow detection of crossed responses which may occur with unilateral AC stimuli and both crossed and bilateral responses following BC stimuli.

The ground or common electrode should be placed on the forehead or upper chest.

An analysis time of 100 ms is recommended with averaging of 100–250 individual trials. At least two averages should be obtained and superimposed to verify reproducibility of the results.

7.2. Stimulation

The committee recommends the use of air-conducted sound. Bone-conducted sound can be used in addition to air-conducted sound, but not to replace it.

The following parameters are suggested for air-conducted sound stimulation. The recommended values of the stimulus are:

- 400–600 Hz tone burst (or other frequencies if tuning is being assessed) or 0.1 ms clicks.
- Duration of tone burst stimulus: up to 7 ms (more than one cycle during the plateau time).
- Sound level: 120–135 dB pSPL, maximum 140 dB pSPL.
- L_{Aeq} should ideally be no more than equivalent to a continuous sound of 85 dB over 8 h (i.e. an $L_{Aeq,8\ hrs}$ of 85 dB).
- The usual rate is 5 Hz (2–10 Hz: slower rates prolong the test unduly).
- Unilateral stimulation is less loud subjectively and allows detection of both uncrossed (p13 n23) and also crossed responses. It also means that the level of contraction can be optimized for a single (ipsilateral) SCM.

The following parameters are suggested for bone-conducted stimulation. The recommended values of the stimulus are:

- Sound frequency: 100–500 Hz or impulsive (e.g. tendon hammer or similar stimulus).
- Location: mastoid or forehead application.
- Maximum intensity: 150 dB peak FL* (=31.6 N peak). *The safety of this type of BC stimulation has not been formally investigated and this should be regarded as an interim recommendation only.

8. Cervical vestibular evoked myogenic potentials in pediatrics

cVEMP characteristics vary with age (Picciottti et al., 2007; Sheykholeslami et al., 2005). There are few publications, however, that have used this technique in children with consistent results, and therefore no formal guidance on its application in children based on experience can be given at this time. This is shown by the fact that there is no agreement as to when the measured parameters reach adult values, with reports ranging from 3 years of age with respect to latencies and amplitude ratios between the two ears of p13 (P1) and n23 (N1) (Picciottti et al., 2007), to 23 years of age with respect to mean p13 latency (Chang and Young, 2007). One report has shown that when the neck length reaches 15.3 cm then adult values can be used (Wang et al., 2008).

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Appendix A. Measurement of sound exposure

Sound exposure is measured both in terms of peak exposure and cumulative exposure. The IEC (609645-3) recommends the use of peak to peak equivalent SPL for measuring short duration acoustic test signals. This will give a higher value than simple onset to largest peak measures. However, current legislative requirements specify, and most sound level meters measure, onset to peak SPL and this is the value we continue to use. (The peak to peak SPL intensity can at most be only 6 dB greater than the onset to peak value and should be specified if used.)

L_{Aeq} is formally defined in the ISO standard as the total "A" weighted sound energy delivered to the ear over a given time period and is the common means by which cumulative sound exposure is measured. The "A" refers to frequency weighting (i.e. filtering) but both C and linear weightings are also used. L_{Aeq} will thus vary with waveform, intensity and stimulus rate. L_{Aeq} always implies a time period over which it has been measured and, if unqualified, a duration of 1 s is assumed. Safe sound exposure is often expressed in terms of L_{Aeq} and an 85 dB L_{Aeq} over 8 h is a common limit for workplace exposure (=85 + 44.6 = 129.6 dB energy delivery compared to 20 μPa for 1 s). Thus an 85 dB $L_{Aeq,8\ hrs}$ is equivalent to a 105 dB $L_{Aeq,1\ s}$ stimulus given for 24.6 dB seconds = 4.8 min, which, for a stimulus given at 5 Hz, would allow 1440 stimuli to be presented to each ear (Rosengren and Colebatch, 2009).

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