New perspectives on vestibular evoked myogenic potentials

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Purpose of review
Although the vestibular evoked myogenic potential (VEMP) measured from the cervical muscles (cVEMP, cervical VEMP) is well described and has documented clinical utility, its analogue recorded from the extraocular muscles (oVEMP, ocular VEMP) has been described only recently and is currently emerging as an additional test of otolith function. This review will, therefore, summarize recent developments in VEMP research with a focus on the oVEMP.

Recent findings
Recent studies suggest that the oVEMP is produced by otolith afferents in the superior vestibular nerve division, whereas the cVEMP evoked by sound is thought to be an inferior vestibular nerve reflex. Correspondingly, the oVEMP correlates better with caloric and subjective visual vertical tests than sound-cVEMPs. cVEMPs are more complicated than often thought, as shown by the presence of crossed responses and conflicting results of recent vibration studies. Altered inner ear mechanics produced by the vestibular diseases superior semicircular canal dehiscence and Ménière’s disease lead to changes in the preferred frequency of the oVEMP and cVEMP.

Summary
The oVEMP provides complementary diagnostic information to the cVEMP and is likely to be a useful addition to the diagnostic test battery in neuro-otology.

Keywords
otolith, vestibular evoked myogenic potential, vestibulo-collic reflex, vestibulo-ocular reflex

INTRODUCTION
Since its first description in 1992 [1], the vestibular evoked myogenic potential (VEMP) has become a well established vestibular function test. It is a muscle reflex evoked by stimulation of the vestibular organs (typically with loud sound) and recorded from electrodes placed over the sternocleidomastoid (SCM) muscles. It is thought to be primarily a measure of saccular function. The VEMP recorded under these conditions is now often referred to as a cervical VEMP (cVEMP) to distinguish it from the more recently described ocular VEMP (oVEMP). Similar to the cVEMP, which is a manifestation of the vestibulo-collic reflex, the oVEMP is a myogenic reflex of the extraocular muscles that is a form of vestibulo-ocular reflex.

THE PHYSIOLOGICAL BASIS OF VESTIBULAR EVOKED MYOGENIC POTENTIALS
The sound-evoked cVEMP is primarily an ipsilateral reflex consisting of a biphasic positive–negative surface potential with peak latencies at about 13 and 23 ms (Fig. 1) [2,3]. Single motor unit recordings have shown that the basis of this reflex is a short-latency inhibition of the SCM muscle [4]. This evidence supports recent papers describing models of the cVEMP. In terms of signal analysis, the cVEMP can be considered a sound-induced or vibration-induced temporal modulation of electromyographic variance. Several attempts have been made to explain the cVEMP on the basis of a model using a modulation of the sum of motor-unit action potentials as an input [5–7]. The first showed that, in contrast with other evoked potentials (e.g. brainstem auditory evoked potentials or vestibular...
evoked responses), the cVEMP is the result of an interruption of activity and not that of summed synchronized neural action potentials [5]. From subsequent studies [6,7], it became clear that the cVEMP and associated variance modulation is most likely composed of at least two components: a main component of inhibitory nature and at least one minor component of excitatory nature. At present, the iterative model developed based upon deconvolution techniques seems to make it possible to estimate the modulation of motor-unit potentials that underlie any cVEMP. Two functions of time are incorporated into this model: the temporal modulation of the motor unit action potential rate of all contributing motor units (rate component) and the motor unit action potential of an average all contributing motor units (rate component).

In patients with SSCD syndrome, sound-cVEMP thresholds are pathologically low but amplitudes are often in the normal range, whereas sound-oVEMPs have both a low threshold and high amplitude, making them especially useful in diagnosis of this condition.

Addition of VEMPs to the neuro-otological test battery is likely to provide useful information about the function of the otolith organs.

**FIGURE 1.** The cervical vestibular evoked myogenic potential: underlying vestibulo-collic projections and reflex waveforms. (a) The presumed projections from the saccule and utricle to the sternocleidomastoid (SCM) muscles in humans, based on data from animal studies. Kushiro et al. [2] showed that both the saccule and utricle have inhibitory projections to the ipsilateral SCM, whereas the utricle has an additional excitatory projection to the contralateral SCM. (b) Example of cervical vestibular evoked myogenic potentials (cVEMPs) to right-sided sound and vibration stimulation. Two normal variants are shown for sound stimulation. The first (Normal A, 0.1 ms clicks) shows only an inhibitory ipsilateral reflex (p13–n23), and the second (Normal B, 500 Hz tone bursts) shows an inhibitory ipsilateral reflex along with an additional excitatory reflex on the contralateral side (n12–p20). This pattern is seen in up to 40% of normal individuals [3]. For vibration stimulation (500 Hz on the right mastoid), which activates both ears, a typical bilateral response from a normal individual is shown, regardless of whether the stimulus is applied to the healthy side or the affected side. This pattern is sometimes present in patients with unilateral vestibular lesions and suggests that in the absence of input from the healthy (left) ear, the excitatory response from the opposite (right) utricle can be seen. L, left side; R, right side.
stimulus artifact. Responses appear 4.5 ms early. The grey boxes indicate forehead tap stimulation at Fz. Trigger delay makes these side, originating in the opposite healthy ear (following patient with SVN show a response only on the affected left ear (grey traces). For vibration stimulation, and an absent response following stimulation of the healthy right ear (black traces) and an absent response following stimulation of the affected left ear (grey traces). For vibration stimulation, which activates both ears, a typical bilateral n10–p15 response from the normal individual is shown (following 500 Hz 4 ms vibration stimulation at Fz). Data from the patient with SVN show a response only on the affected left side, originating in the opposite healthy ear (following forehead tap stimulation at Fz). Trigger delay makes these responses appear 4.5 ms early. The grey boxes indicate stimulus artifact.

FIGURE 2. The ocular vestibular evoked myogenic potential: underlying vestibulo-ocular projection and reflex waveforms. (a) The proposed projection from the otolith organs to the inferior oblique muscle. Single motor unit recordings have shown that the negative n10 surface potential is produced by increased activity of the inferior oblique muscle, while the inferior rectus becomes active 5 ms later [8*]. A study in cats by Suzuki et al. [9] supports a short-latency projection to the inferior oblique muscle from the utricle. (b) Example of ocular vestibular evoked myogenic potentials (oVEMPs) to right-sided sound stimulation and midline vibration of the forehead. In normal individuals, sound stimulation of the right ear elicits a negative–positive (n10–p15) peak on the contralateral side. Data from a patient with left-sided superior vestibular neuritis (SVN) show a normal contralateral reflex following stimulation of the healthy right ear (black traces) and an absent response following stimulation of the affected left ear (grey traces). For vibration stimulation, which activates both ears, a typical bilateral n10–p15 response from the normal individual is shown (following 500 Hz 4 ms vibration stimulation at Fz). Data from the patient with SVN show a response only on the affected left side, originating in the opposite healthy ear (following forehead tap stimulation at Fz). Trigger delay makes these responses appear 4.5 ms early. The grey boxes indicate stimulus artifact.

OCULAR VESTIBULAR EVOKED MYOGENIC POTENTIAL ORIGINS

Two initial studies of patients with suspected superior vestibular neuritis (SVN) established that oVEMPs evoked by vibration of the forehead are typically asymmetric or absent in SVN [19,20]. The patients were recruited based on abnormal horizontal canal responses on caloric or head impulse testing (HIT) but present sound-cVEMPs, suggesting that there was at least partial dysfunction of the superior vestibular nerve and preservation of the inferior nerve. The same pattern of results has more recently been found for the sound-oVEMP (Fig. 2) [21,22*,23**,24]. As the pattern of oVEMP abnormality in these patients matches that of the horizontal canal (whose fibres travel in the superior
nerve), it suggests that the oVEMP is also produced predominantly by vestibular afferents in the superior vestibular nerve. This approach is promising, but caution is warranted due to possible heterogeneity in disease extent, severity and rate of recovery in vestibular neuritis, not only between patients but also particularly within the same patient. The fact that cVEMPs are the only available clinical measure of saccular function makes them valuable, but at the same time there is no independent measure of saccular function against which they can be judged. To test the origin and diagnostic efficacy of any VEMP in vestibular neuritis, patients would ideally be recruited and classified based only on clinical criteria and the function of the three canals and not VEMPs.

A recent article by Shin et al. [23**] came close to this ideal by recruiting patients based on clinical inclusion and exclusion criteria, the result of clinical HIT in different canal planes and the direction of spontaneous nystagmus (although their criteria for SVN did also include present sound-cVEMPs). Most of their patients with SVN had abnormal sound-oVEMPs, whereas the patients with inferior vestibular neuritis (IVN) had normal sound-oVEMPs but impaired sound-cVEMPs. This pattern of abnormality supports another study of patients with suspected IVN, which showed that most patients with abnormal sound-cVEMP had symmetric vibration-oVEMP [25]. IVN is more difficult to definitively diagnose than SVN, and preferably includes a positive HIT for the posterior canal, as the sound-cVEMP can sometimes be absent in normal individuals, particularly with advancing age. In addition, an isolated cVEMP abnormality should also be interpreted with caution when the background muscle contraction is not known, as it could be the result of underactivation of the SCM muscle.

There is now agreement that both sound-oVEMPs and vibration-oVEMPs originate in the superior division of the vestibular nerve. The greater number of utricular fibres in this division means that a large oVEMP asymmetry is likely to predominantly reflect a utricular lesion. In contrast, it is not yet known what role the fibres from the anterior hook region of the saccule may play in this reflex. Although short-latency sacculo-ocular projections have been shown to be relatively weak [26], several studies have demonstrated their existence (for example [27–30]). Given the different directional sensitivities and physical properties of the two otolith organs, it has been suggested that these properties may render them differentially sensitive to VEMP stimuli delivered with different direction or frequency, and that under some circumstances the oVEMP could reflect saccular function [31]. It is hoped that future studies will determine the function of the sacculo-ocular projections and the conditions under which the saccule contributes to the control of gaze and possibly the oVEMP.

**CERVICAL VESTIBULAR EVOKED MYOGENIC POTENTIAL ORIGINS**

Although it would seem that the projections underlying the cVEMP are well established, new evidence has refocused attention on cVEMP pathways. Animal data on the vestibular projections to the neck muscles show that the saccule has only an ipsilateral inhibitory projection to the SCM, whereas the utricle (and probably also the canals) shares this projection and has an additional excitatory projection to the contralateral SCM [2,32]. Interestingly, in up to about 40% of normal volunteers, the sound-cVEMP consists of a bilateral response, an inhibition (p13–n23) in the ipsilateral SCM and a small excitation (n12–p20) in the contralateral SCM [3] (Fig. 1). In light of the animal data, this suggests that the sound-cVEMP often receives input from other vestibular organs, likely the utricle, especially with increasing stimulus intensity. The crossed response is characteristic of patients with superior canal dehiscence (Fig. 3), although it is not known whether it originates in the utricle or superior canal or both in these patients [33,34]. In practice, it is thought that the saccular contribution to the ipsilateral response is dominant and a sound-cVEMP asymmetry is likely to reflect saccular dysfunction.

In contrast, studies of the vibration-cVEMP show differential patterns of reflex activation with different vibration stimuli. It has recently been suggested that stimulation at the forehead with 500 Hz tone bursts produces normal cVEMPs in patients with SVN and that the saccule is, therefore, responsible for all cVEMPs [35]. In contrast, earlier studies showed that the vibration-cVEMP (evoked by forehead taps with a tendon hammer) was abnormal in SVN patients, suggesting that the superior nerve is indeed important [36]. A more recent study by Govender et al. [22*] produced similar results and showed that cVEMPs evoked by taps delivered laterally to the mastoid were correlated with oVEMPs rather than sound-cVEMPs, again suggesting an origin in the superior nerve and utricle. The reason for this seemingly differential effect of different stimuli is not yet known; however, given the strength of utriculo-collic projections in general [37**], and the role of utricular afferents in compensating for roll tilt of the head, it is not surprising that the utricle may play an important role in the vestibulo-collic reflex.
VESTIBULAR EVOKED MYOGENIC POTENTIALS IN VESTIBULAR DYSFUNCTION

A complementary approach to investigating VEMP origins and diagnostic efficacy has been comparison of VEMPs with established tests of vestibular function in patients with vestibular dysfunction. As expected for a test of superior nerve otolith afferents, the oVEMP appears to be most correlated with subjective visual vertical (SVV) and caloric responses, rather than sound-cVEMPs [38–40]. However, the correlation between SVV and oVEMP is only expected during the acute stage of vestibular loss, as performance on the former test improves over time due to vestibular compensation, while the oVEMP remains abnormal. This is a clear advantage of the oVEMP. Additionally, Valko et al. [41] showed that oVEMPs may also perform better than SVV during eccentric rotation, a test that can detect SVV abnormalities even in cases of chronic vestibular loss.

VEMPs have their clearest role in diagnosis of superior semicircular canal dehiscence (SSCD) and other ‘third window’ disorders, in which it is well documented that the sound-cVEMP has a characteristically low threshold. Shortly after the introduction of the oVEMP, it became clear that this new reflex showed even greater abnormality in SSCD patients: a low threshold and a reliably high amplitude (Fig. 3) [42,43*]. Although the sound-cVEMP is often large in SSCD, there is significant overlap of amplitude with the normal range, thought to be because the inhibitory nature of the cVEMP makes it susceptible to saturation at high intensity. As the n10 oVEMP peak is an excitatory reflex [8*], it is probably not prone to such saturation effects. New evidence suggests that a midline vibration stimulus produces similar results to sound stimulation for both cVEMPs and oVEMPs, suggesting that this stimulus could also be useful in diagnosis [44*]. Although it is thought that VEMPs from the dehiscent labyrinth are enhanced partly due to activation of superior canal afferents, a recent case report provided evidence that VEMPs can still be abnormal even with dysfunction of the superior canal [45]. This demonstrates that otolith receptors are indeed abnormally stimulated in SSCD, but does not rule out concomitant canal activation.

The altered mechanical properties of the labyrinth in patients with SSCD lead to interesting changes in the preferred frequency, or tuning, of both cVEMPs and oVEMPs. In normal individuals, the sound-cVEMP is maximal at frequencies around 400–800 Hz, and new evidence has shown that the normal sound-oVEMP has very similar tuning [43*]. In contrast, the normal vibration-cVEMP and oVEMP have a lower preferred frequency, closer to 100 Hz [49,50*]. In contrast to normal individuals, frequency tuning studies in SSCD patients have shown broader tuning curves for both reflexes, with the sound-cVEMP tending to tune downwards and the sound-oVEMP upwards [43*]. This high-frequency enhancement of the oVEMP to sound and vibration is preserved when patients are tested with stimulus intensities closer to threshold, suggesting that they are related to mechanical changes within the dehiscent labyrinth and an altered pattern of receptor activation, rather than being a simple consequence of stimulating far above threshold [51]. A consequence of the broader tuning is that higher frequencies may separate patients from controls better than the more commonly used 500 Hz stimulus [43*]. The altered VEMP tuning

![Figure 3. Typical pattern of vestibular evoked myogenic potential seen in patients with superior canal dehiscence. The black electrodes show the sites where the dominant responses are recorded for each reflex: the ipsilateral sternocleidomastoid (SCM) muscle for the cervical vestibular evoked myogenic potential (cVEMP) and the contralateral inferior oblique muscle for the ocular vestibular evoked myogenic potential (oVEMP). Stimulation of the dehiscent ear produces a large inhibitory (p13–n23) response in the ipsilateral SCM and an excitatory (n12–p20) response in the contralateral SCM. A very large oVEMP can be recorded from the eye opposite the dehiscence. Both of these reflexes typically have a threshold below the normal range. SCD, superior canal dehiscence.](image-url)
returns to normal after resurfacing of the superior semicircular canal [52].

Similar tuning changes can be seen in patients with Ménière’s disease, a very different type of vestibular disorder, but one that is also thought to produce changes in the mechanical properties of the labyrinth. Previous research has established that the sound-cVEMP in patients with Ménière’s disease has higher frequency tuning than in controls (for example [53]). Recent studies have shown that this is also true of the sound-oVEMP [47,54,55]. Apart from the tuning shift, the sound-oVEMP also shows lower mean amplitudes and higher rates of abnormality in Ménière’s disease compared to control groups, sometimes exceeding the performance of the sound-cVEMP [56,57,58*]. However, data from normal individuals show that the sound-oVEMP has a higher threshold than the sound-cVEMP, thus care should be taken when comparing rates of abnormality across these reflexes [57,59].

**CONCLUSION**

Current evidence supports an origin primarily in the ipsilateral saccule for the sound-cVEMP and the contralateral superior nerve (probably mainly the urocricle) for sound-oVEMPs and vibration-oEMPs, suggesting that the reflexes can provide additional diagnostic information about the function of the otolithic organs. Future research should aim to investigate the possible contributions of the semicircular canals to the reflexes and further delineate the vestibulo-colic and vestibulo-ocular projections in humans. In addition to their clinical utility, these reflexes can also be used to investigate the vestibular system and its properties. Many of the recently published oVEMP studies shed new light on the vestibulo-ocular reflex, including the behaviour of single extraocular muscle units to vestibular stimulation with sound and vibration [8*] and the ability of the otoliths to respond to vibration of different directions, even up to quite high frequencies [60,61*,62]. Continued development of the cVEMP and oVEMP over time will likely lead to increased understanding of the vestibular system and its response to sound and vibration as well as new opportunities in the diagnosis of disorders of vestibular function.

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**Conflicts of interest**

There are no conflicts of interest.

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**REFERENCES AND RECOMMENDED READING**

Papers of particular interest, published within the annual period of review, have been highlighted as:

- of special interest
- of outstanding interest

Additional references related to this topic can also be found in the Current World Literature section in this issue (p. 107).


New evidence of the myogenic origin of the oVEMP is described in this study. Single motor unit recordings from the inferior oblique and inferior rectus muscles in humans showed that the n10 oVEMP peak originates in the inferior oblique muscle. The study shows the behaviour of single extraocular motor units to vestibular stimulation in humans for the first time.


This study examined cVEMPs and oVEMPs in patients with vestibular neuritis using a variety of stimulation methods, including air-conducted sound, impulses (i.e. controlled taps given with a minishaker) delivered to the mastoids and forehead taps. The results confirmed that sound-oVEMPs originate in the superior vestibular nerve and showed that this nerve portion is also important for vibration-cVEMPs.

24. In this study, patients with acute vestibular neuritis were recruited using well-documented clinical criteria and careful observation of spontaneous nystagmus. On the basis of these results, their head impulse test results and their sound-cVEMP reflexes, patients were classified as having SVN or IVN. The authors showed that the sound-oVEMP is abnormal in patients with SVN and normal in patients with VN.

25. Manzari L, Burgess AM, Curthoys IS. Ocular and cervical vestibular-evoked myogenic potentials to 500 Hz Fz bone-conducted vibration in superior semicircular canal dehiscence. Ear Hear 2012; 33:508–520. The data presented in this study show that vibration-oVEMPs and vibration-oVEMPs (evoked with a forehead 500 Hz stimulus) are also abnormal in patients with superior canal dehiscence, similar to sound-evoked VEMPs. These data differ from previous reports of forehead taps and mastoid vibration, which show lower rates of abnormality in superior canal dehiscence.


32. This study on frequency tuning of the vibration-oVEMP in normal individuals compared the reflex across a very wide range of frequencies. The stimulus intensities were carefully matched across frequency, either by holding the peak stimulus force or the peak initial head acceleration constant. The preferred frequency found for both methods was around 100 Hz for both forehead and mastoid stimulation.


40. This study on oVEMPs in patients with Meniere’s disease, who were staged according to formal criteria, examined reflex threshold in addition to amplitude. The results showed a high rate of oVEMP abnormality for affected ears and an intermediate rate for clinically unaffected ears compared to control ears.


44. This study highlights the direction sensitivity of the oVEMP. It explores the potential mechanisms responsible for the changes in reflex polarity and latency that occur with different directions of head vibration.

45. Jombik P, Spodnial P, Bahy V. Direction-dependent excitatory and inhibitory ocular vestibular-evoked myogenic potentials (oVEMPs) produced by oppositely directed accelerations along the midsagittal axis of the head. Exp Brain Res 2011; 211:251–263.