J Am Acad Audiol 15:198–215 (2004)

Clinical Experience with the Vestibular Evoked Myogenic Potential

David A. Zapala*
Robert H. Brey†

Abstract

The vestibular evoked myogenic potential (VEMP) is a promising test of the descending vestibulocollic system. Our aim was to determine whether the VEMP can be applied to an older patient population and can detect lesions in descending vestibulospinal pathways. We also compared VEMP clinical performance with that of the standard caloric test. VEMP test performance was retrospectively analyzed in relation to clinical diagnosis and other vestibular test performance in 62 patients (age, 30–85 years) referred for vestibular testing to Mayo Clinic, Jacksonville, Florida. The VEMP was evoked using a 250 Hz tone burst. Results suggest age-related changes in VEMP amplitude and latency in this patient population. VEMP tests were sensitive to lesions not detected by electronystagmography. VEMP and caloric sensitivity and specificity were essentially equal ($d' = 1$). Combining both tests improved sensitivity. However, VEMP false-positive rates hampered specificity. VEMP testing may be refined to improve false-positive rates and clinical utility.

Key Words: Electromyography, motor evoked potentials, saccule, sternocleidomastoid muscle, vestibular evoked myogenic potentials, vestibular function tests, vestibular nerve

Abbreviations: EMG = electromyogram; ROC = receiver operator characteristic; SCM = sternocleidomastoid; VEMP = vestibular evoked myogenic potential; VOR = vestibulo-ocular reflex

Sumario

El potencial evocado miogénico vestibular (VEMP) es una prueba promisoria para el sistema vestíbulo-colicular descendente. Nuestro propósito fue determinar si los VEMP pueden ser aplicados a una población de pacientes de mayor edad y si pueden detectar lesiones en la vía vestibuloespinal descendente. También comparamos el desempeño clínico del VEMP con el de las pruebas calóricas convencionales. Se analizó retrospectivamente el desempeño de la prueba de VEMP con relación al diagnóstico clínico y al rendimiento de otras pruebas vestibulares en 62 pacientes (edades: 30-85 años), referidos a la Clínica Mayo en Jacksonville, Florida, para evaluación vestibular. El VEMP fue evocado utilizando un burst tonal de 250 Hz. Los resultados sugieren cambios relacionados con la edad tanto en la amplitud como en la latencia del VEMP en esta población de pacientes. Las pruebas de VEMP

*Audiology Section, Department of Otolaryngology—Head and Neck Surgery, Mayo Clinic, Jacksonville, Florida; †Division of Audiology, Mayo Clinic, Rochester, Minnesota

Reprint requests: David A. Zapala, Ph.D., Audiology Section, Department of Otolaryngology—Head and Neck Surgery, Mayo Clinic, 4500 San Pablo Road, Jacksonville, FL 32224

Portions of this work were presented at the American Auditory Society 2003 Science and Technology Meeting, Scottsdale, Arizona, March 13–15, 2003.

fueron sensibles a lesiones no detectadas por electronistagmografía. La sensibilidad y la especificidad del VEMP y de las pruebas calóricas fue esencialmente igual (d´ = 1). La combinación de ambas pruebas mejoró la sensibilidad. Sin embargo, la tasa de falsos positivos con VEMP afectó la especificidad. La evaluación por VEMP puede ser refinada para mejorar la tasa de falsos positivos y su utilidad clínica.

Palabras Clave: Electromiografía, potenciales evocados motores, sáculo, músculo esternocleidomastoideo, potenciales evocados miogénicos vestibulares, pruebas de función vestibular, nervio vestibular

Abreviaturas: EMG = electromiograma; ROC = característica del receptor operador; SCM = esternocleidomastoideo; VEMP = potencial evocado miogénico vestibular; VOR = reflejo vestíbulo-ocular

There is increasing interest in the role of sound-evoked muscle contractions in the evaluation of the dizzy patient. The vestibular evoked myogenic potential (VEMP) is a change in the surface-recorded electromyogram (EMG) that can be evoked over neck and spinal muscles following a high-intensity acoustic transient. The shortest latency VEMP waveforms that can be recorded over a contracted sternocleidomastoid (SCM) muscle are thought to reflect a specialized vestibulo-spinal reflex. The VEMP is reviewed in summary articles by Colebatch (2001), Ferber-Viart et al (1999), and Halmagyi and Curthoys (1999). A careful description of the VEMP in normal subjects is given by Akin and Murnane (2001).

The VEMP is potentially important in the evaluation of the dizzy patient for three reasons. First, the VEMP is thought to reflect stimulation of the saccule, a sensory structure not currently evaluated by traditional electronystagmographic methods (Colebatch et al, 1994; Halmagyi and Colebatch, 1995). Because of its orientation in the vertical plane, the saccule is thought to be primarily responsive to vertical translations of the head that may occur during walking, running, or descending a flight of stairs. Acoustical sensitivity of the saccule has been postulated for several years (Townsend and Cody, 1971). Animal experiments have shown that mammalian otolith organs can be stimulated by loud noise (Young et al, 1977; Didier et al, 1987), and saccular nerve stimulation can provoke an ipsilateral motor response in neck muscles in cats (McCue and Guinan, 1994; Sato et al, 1994) and guinea pigs (Matsuzaki and Murofushi, 2002). In humans, the saccule rests directly beneath the stapes footplate and is therefore in an ideal position to be stimulated by loud noise (Bath et al, 1998).

There is an increasing body of evidence that the VEMP recorded from the SCM muscle (SCM VEMP) can be altered by pathologic processes affecting the vestibular end organ, particularly the saccule (Murofushi et al, 1999; Ito et al, 2001; Ochi et al, 2001). For example, abnormal VEMP responses have been recorded in cases of Meniere's disease or Meniere's syndrome (de Waele et al, 1999; Heide et al, 1999; Seo et al, 1999), acute peripheral vestibulopathy (Heide et al, 1999), vestibular neuronitis (Murofushi et al, 1996; Chen et al, 2000; Halmagyi et al, 2002), superior canal dehiscence syndrome (Brantberg et al, 1999; Watson et al, 2000; Streubel et al, 2001), idiopathic bilateral loss of vestibular function (Matsuzaki and Murofushi, 2001), ototoxicity (Perez et al, 2000), and congenital malformations of the labyrinth (Sheykholeslami and Kaga, 2002). Additionally, several researchers have demonstrated that sound-evoked muscle contractions may persist in the face of considerable sensorineural hearing loss (Bickford et al, 1964; Colebatch and Halmagyi, 1992; Sheykholeslami and Kaga, 2002).

A second reason that the VEMP might be important in the evaluation of the dizzy patient is that the neural pathway underpinning the response differs significantly

from the vestibulo-ocular reflex (VOR). The VOR reflects vestibular information processed in a pathway that is oriented rostrad from the level of the vestibular nuclei through the midbrain. Significant structures involved with the VOR include the vestibular nuclei, abducens nuclei and nerves, medial longitudinal fasciculus, ocular motor nuclei and nerves, and areas of the anterior cerebellum (Baloh and Honrubia, 1990; Shepard and Telian, 1996). Lesions that involve the cerebellopontine angle, pons, or midbrain may impair the VOR and be evident on electronystagmographic evaluation.

In contrast, the VEMP reflects a pathway organized caudally from the vestibular nuclei through cervical portions of the spinal cord (see Buttner-Ennever, 1999, for an anatomic review). It reflects activation of the medial, lateral, or reticulospinal vestibulospinal tracts as they descend through the medulla and cervical cord (Robertson and Ireland, 1995; Halmagyi and Curthoys, 1999). From there, the reflex pathway may follow one of two courses. The SCM muscle is mainly innervated by cranial nerve XI (Fitzgerald et al, 1982). Assuming the reflex is carried in this cranial nerve, interaction would occur between these descending vestibular spinal pathways and motor areas associated with the motor nucleus of cranial nerve XI (Todd et al, 2000). The motor nucleus of cranial nerve XI extends from the medulla through the anterior horn cells as far caudal as the fifth or sixth cervical segment (Ullah and Salman, 1986). Axons leaving the nucleus course back upward (rostrally) and emerge on the lateral aspect of the medulla as the spinal segment of cranial nerve XI. The spinal segment of the nerve then passes upward through the foramen magnum, exits the cranium through the jugular foramen, and courses through the SCM and then the trapezius muscles (Carpenter and Sutin, 1983; Ullah and Salman, 1986).

An alternative pathway may involve the interconnections between the lateral vestibulospinal tracts and the anterior horn cells of the various spinal motor roots. This pathway would explain how sound-evoked myogenic potentials can be recorded from spinal and lower limb muscles such as the soleus (Watson and Colebatch, 1998) or gastrocnemius muscles (Iida et al, 1998). Under this alternate hypothesis, the efferent pathway would include the ventral cervical roots (C1-C4). The cervical roots innervate the muscles along the cervical spinal cord but send branches to the SCM and trapezius muscles. However, these branches are thought to be primarily afferent fibers (Todd et al, 2000) and may not play a role in the generation of the SCM VEMP.

The neural pathway mediating the VEMP differs from that typically assessed on standard electronystagmographic evaluation in another important way. Cranial nerve VIII has three main branches in the internal auditory canal: one auditory branch and two vestibular branches. The superior vestibular branch innervates the anterior and horizontal canal ampulla, the utricle, and parts of the saccule. The inferior branch innervates the posterior canal ampulla and the saccule (Buttner-Ennever, 1999). The VEMP appears to be sensitive to disorders affecting the inferior vestibular branch, which is the site of many vestibular schwannomas (Matsuzaki et al, 1999; Tsutsumi et al, 2000; Takeichi et al, 2001; Chen et al, 2002).

A third reason for the clinical importance of the VEMP is that it may help us to better understand pathologic processes involving the vestibulospinal system. The lateral vestibulospinal system is thought to promote tonic extensor tone to neck and antigravity muscles. The medial system is thought to help orchestrate fine eye, head, and neck movements. The prevailing view appears to be that the VEMP reflects a vestibulocollic reflex, that is, a quick reflexive change in muscle tone (flexor or extensor, depending on the muscle group) that occurs to stabilize the head following an unexpected translation (Colebatch et al, 1994; Uchino et al, 1997; Wu et al, 1999; Todd et al, 2000). Others have suggested that the VEMP is related to a withdrawal reflex or that it is an epiphenomenon unrelated to balance function (reviewed in Ferber-Viart et al, 1999 and Todd et al, 2000).

Although the exact role of the reflex is unknown, theory and increasing clinical experience suggest that the VEMP should be sensitive to lesions involving the saccule, inferior vestibular nerve, and descending vestibulospinal pathways (Shimizu et al, 2000; Takegoshi and Murofushi, 2000; Itoh et al, 2001). Conceivably, peripheral neuropathies and myopathies affecting the cervical musculature may also cause abnormal VEMP results. By correlating patient complaints,

abilities, and outcomes when the VEMP is present or absent, we may gain some insight into the role of the saccule and descending vestibulospinal system. We may also recognize treatable pathologic entities that are not currently appreciated (Akin and Murnane, 2001).

Herein we present a preliminary report of our efforts to use the VEMP for vestibular evaluation at Mayo Clinic, Jacksonville, Florida. We specifically asked three questions. First, do the characteristics of the VEMP vary with age in patients without clinical evidence of current vestibular dysfunction? Second, do VEMP characteristics change with lesions affecting the saccule, inferior nerve, and descending vestibulospinal pathways? Third, in a clinical setting, how sensitive and specific is the VEMP to vestibular deficits relative to the standard bithermal caloric test?

METHODS

Setting

Mayo Clinic uses a multidisciplinary model for the evaluation and treatment of patients. After evaluation by a staff primary care physician (usually an internal medicine specialist), patients complaining of dizziness or imbalance may be seen by specialists in otolaryngology, neurology, and physical medicine, as well as by cardiovascular, pulmonary, psychiatric, and other specialty consultants as needed. Most patients who are seen for dizziness or imbalance problems are older than 65 years, and their condition is medically complex, with multiple causes. They have often been evaluated by local physicians and have symptoms that are persistent enough to make a visit to a tertiary care center necessary.

Subjects

During a three-month period in 2002, we retrospectively reviewed the clinical records of consecutive patients who were referred for vestibular evaluation and who had a VEMP study. In addition to the VEMP, we reviewed electronystagmographic, posturographic, audiometric, and rotational test data for patient classification purposes. We also reviewed patients' charts to identify any dizziness or balance-related diagnoses. Retrospective chart reviews and study methods were approved by the Mayo Foundation Institutional Review Board before the initiation of the study. All procedures were designed to ensure patient safety and confidentiality.

Patients were classified based on their medical diagnosis at the time of review as "presumed normal" or as having a vestibular or extravestibular disorder. The vestibular group was further subclassified into "end organ," "retrolabyrinthine/central vestibular," and "bilateral vestibulopathy" subgroups. The extravestibular group was subclassified into a "central" lesion group (patients with lesions of the central nervous system) and an "unknown" lesion group.

Patients were classified as presumed normal if they met the following criteria: (1) a normal neuro-otologic examination (performed by either otolaryngology or neurology clinic staff); (2) no positional nystagmus with slow-phase velocity greater than 3° per second; (3) no abnormality on slow harmonic acceleration; (4) no caloric asymmetry greater than 15%; and (5) a diagnosis of anxiety-, panic-, or cardiovascular-based dizziness, or a diagnosis of resolved benign paroxysmal positional vertigo at the time of testing. Within the limits of clinical knowledge, these patients were considered free of vestibulopathy. However, one should keep in mind that some of these patients may have had subclinical vestibular deficits despite the absence of complaints, clinical signs, or test results at the time of data collection.

Caloric asymmetries greater than 24% (the established 95% limit for our clinic), spontaneous or positional nystagmus greater than 3° per second, or slow harmonic acceleration tests that demonstrated phase leads or low VOR gains at a minimum of two or more adjacent test frequencies were considered abnormal. Bilateral weaknesses were defined as caloric responses of less than 5° per second or abnormally low rotational VOR gains affecting all frequencies below 0.32 Hz. Patient classification, test data, and clinical diagnoses were consolidated for subsequent analysis.

Vestibular Evoked Myogenic Potential

Stimuli consisted of 250 Hz Blackman-gated tone bursts (one cycle rise and fall, no plateau), presented at a rate of 5.1 bursts per second through Etymotic ER-3A insert earphones

(Etymotic Research, Elk Grove Village, IL). This frequency was chosen on the basis of empirical evidence showing that the saccule exhibits resonance between 200 and 400 Hz (Todd et al, 2000). All patients were presented with 90 dB normal hearing level (nHL) stimuli (123 dB peak sound pressure level). In selected cases, when patient strength allowed, VEMP thresholds were obtained in 5 dB steps.

Recordings were made with an inverting lead placed on the belly of the ipsilateral SCM muscle, midway between the mastoid and the sternum. A noninverting lead was placed on the back of the patient's right hand, and a ground electrode was placed on the right wrist. Waveforms were thus displayed as positive peaks pointing downward. A large 2 x 3 inch disposable surface electrode served as the inverting lead over each SCM. The large surface area of this electrode increased the VEMP signal-to-noise ratio and decreased the amount of signal averaging required to obtain a reliable response. A normal 200 μV VEMP could be recorded within 45 to 60 epochs. The large surface area also minimized the effect of electrode placement on the response (Sheykholeslami et al, 2001). The myogenic signal was amplified by 5,000, band-pass filtered from 1 to 250 Hz, digitized at a sample rate of 5 kHz, and signal-averaged with a Nicolet Spirit evoked potential unit (Nicolet Instrument Corp., Madison, WI). Epochs consisted of a 20 msec prestimulus interval and an 80 msec poststimulus interval of EMG activity.

To obtain a VEMP, the patient was positioned supine on an examination table with the upper half of the table elevated 30° (as for a caloric test). Before each average was obtained, the patient was instructed to rotate his or her head so that the test ear was up. As averaging began, the patient was instructed to lift the head one inch off the table to achieve an isolated contraction of the ipsilateral SCM. Although the EMG amplitude was periodically observed, averaging was not stopped unless it appeared that the patient's best effort was not being put forward.

Between 40 and 130 epochs (median, approximately 60) were collected for each average with the subject so positioned. Between three and five such averages were added into a composite average to document the VEMP. For each subaverage, recording stopped when the VEMP was at least three times larger than any competing wavelet in the prestimulus period or when 130 epochs were collected. It has been shown that the amplitude of the VEMP is proportional to the degree of muscle contraction during the average (Colebatch et al, 1994; Lim et al, 1995; Akin and Murnane, 2001; Versino et al,

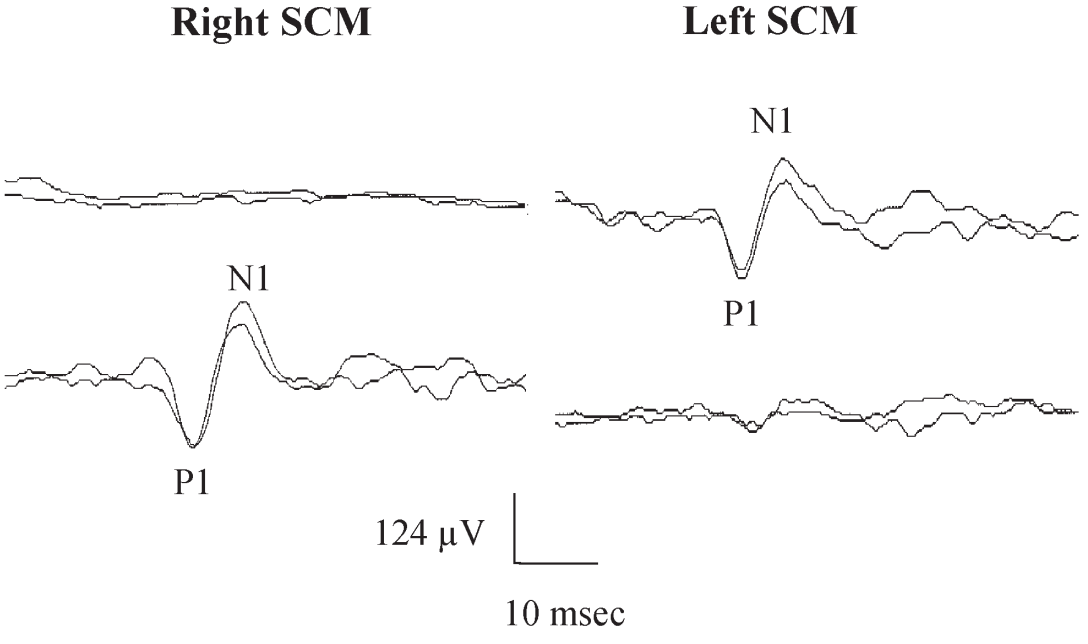

Figure 1. Example of vestibular evoked myogenic potential (VEMP) evoked by a 250 Hz tone pip presented at 90 dB nHL. Only two of four subaverages of 60 epochs shown. P1: first positive polarity peak in the composite average; N1: first negative peak after P1; SCM: sternocleidomastoid muscle.

2001; Al-Abdulhadi et al, 2002). This subaveraging technique, with rest periods in between, was used to minimize muscle fatigue during the course of the recording session. A representative VEMP is displayed in Figure 1.

Analysis

Following the labeling conventions of Akin and Murnane (2001), the first positive polarity peak in the composite average was labeled P1, and the following negative peak was labeled N1. From each composite average, P1 and N1 peak latencies and P1–N1 amplitude were measured. Further, amplitude and latency asymmetries between right and left sides were tabulated.

Calculation of Normal Limits

The mean and SDs for P1 latency, N1 latency, P1–N1 amplitude, and associated side asymmetries were tabulated for the presumed-normal group. Paired t-tests were used to compare peak latency differences between sides. Linear regressions were used to clarify the effect of age on the above test parameters. Specifically, to determine the effect of age on P1–N1 amplitude, the significance of the regression slope was tested by means of t-tests. P1–N1 amplitude ratios were calculated as

$$\frac{(\text{P1–N1 amplitude right side}) - (\text{P1–N1 amplitude left side})}{(\text{P1–N1 amplitude right side}) + (\text{P1–N1 amplitude left side})}$$

All statistical measurements were made using the Excel 2000 Analysis Tool Pack (9.0.4402 SR-1, Microsoft). Unless otherwise indicated, a statistical probability (P) of 0.05 or less was considered significant. Because the data set is preliminary, 2.5 SD was used to define normal limits for subsequent analysis.

Vestibular, Central, and Unknown Etiology Groups

The percentage of patients with abnormal VEMP studies was calculated for the vestibular, central, and unknown etiology groups using the limits set in the analysis of the presumed-normal group. These percentages and the type of VEMP abnormality in each group were compared with the caloric test results to determine whether VEMP deficits were more common in conditions potentially affecting the descending vestibulospinal pathways. Further, the sensitivity, specificity, and predictive value of the VEMP and the caloric test were calculated by using the limits established in this study and by using criterion-free comparisons with receiver operating characteristic (ROC) curves for each test.

RESULTS

Classification of Patients

Medical records were reviewed for a total of 64 patients. Two patients were subsequently excluded from the analysis. One patient with conductive hearing loss was excluded because significant conductive hearing loss has been shown to abolish the VEMP (Bath et al, 1999). A second patient with unilateral vestibulopathy and cervical spinal problems was excluded because he had a heavy beard that precluded optimal VEMP electrode placement. In this case, VEMPs were bilaterally absent, and we could not reliably determine if this reflected cervical impairment, electrode location, or labyrinthine involvement.

Two additional patients were not included in the group data because they presented with serious cervical spinal problems that may have affected the recorded VEMP. They are described separately in the "Discussion" below.

The remaining 60 patients were classified on the basis of the diagnosis available at the time of review. A total of 21 patients met the criteria for inclusion in the presumed-normal group (mean age, 52.3 years; SD, 15.8; range, 30–83). Thirty-nine patients did not meet these criteria and were further classified.

Twenty-seven patients were classified as having a vestibular disorder (mean age, 65.0 years; SD, 17.3; range, 27–84). Of these, 17 patients had no clear evidence of retrolabyrinthine or central nervous system involvement underpinning their dizziness complaints (mean age, 66.7 years; SD, 16.5; range, 31–84). These patients were classified as having a unilateral "end-organ" vestibular disorder. Diagnoses in this group were as follows: unilateral vestibulopathy

(vestibular neuritis, vestibular labyrinthitis, unspecified vestibulopathy, recurrent vestibulopathy, or transverse temporal bone fracture) in nine patients, Meniere's syndrome in five, and suspected migrainous vertigo with co-occurring temporal bone fibrous dysplasia in one. In one case, an 84-year-old patient with end-stage Meniere's syndrome was classified as having peripheral vestibulopathy even though cerebellar small vessel disease was also discovered. In this case, it was the opinion of the attending otologist that the patient's complaint of episodic vertigo stemmed from residual Meniere's effects.

Six patients had evidence of retrolabyrinthine or central vestibular involvement (mean age, 60.2 years; SD, 20.0; range, 27–80). Of these, three patients had a diagnosis of vestibular schwannoma, one had a diagnosis of unspecified central vestibulopathy involving the vestibular cerebellum, and one had a diagnosis of vertebral basilar artery disease causing an incomplete lateral medullary syndrome. The remaining patient had a diagnosis of posterior fossa stroke with evidence of pontine vascular disease with concomitant sudden-onset hearing loss, vertigo, and oculomotor deficits. Four elderly patients (mean age, 70.3 years; SD, 7.4; range, 61–77) had bilateral vestibulopathy of unknown origin and were placed in the bilateral group.

Twelve patients were determined to have extravestibular disorders underpinning their balance complaints. Three of these patients were classified as having central lesions from vascular disease not thought to have affected the vestibular system (mean age, 77.5 years; SD, 6.7; range, 71–84). Patient diagnoses were as follows: small vessel disease involving the pons, transient ischemic attacks involving the cerebellum, and unilateral basal ganglion disease.

Nine patients in the extravestibular group were classified as having balance disorders of unknown origin (mean age, 55.4 years; SD, 19.2; range, 32–84). In these cases, a definitive diagnosis could not be formed based on history or clinical findings. Four were thought to have anxiety-based problems. In one patient, dysautonomia was suspected. Two had loss of lower limb proprioceptive input from either peripheral neuropathy or a spinal lesion. Two had no diagnosis at the time of review. Both complained of episodes of nonspecific dizziness in the face of normal vestibular and neurotologic evaluations. All unknown-origin patients demonstrated caloric asymmetries between 16% and 22%.

VEMP Performance

Presumed-Normal Group

The average responses for P1 and N1 latency, P1–N1 amplitude, and amplitude and latency asymmetries are presented for the presumed-normal group in Table 1. No significant difference was detected between the right and left sides for P1 latency (t = 0.259, P = 0.399, α = 0.1), N1 latency (t = 1.238, P = 0.114, α = 0.1), or P1–N1 amplitude (t = 0.166, P = 0.434, α = 0.1). For subsequent analysis, values for P1, N1, and P1–N1 amplitude were pooled across sides.

There was a significant decrease in P1–N1 amplitude with age (t = –4.096, P < .001). Subjects under age 40 years easily produced a VEMP greater than 100 μV. Subjects 80 years of age seldom generated responses this large. The regression for P1–N1 amplitude by age is shown in Figure 2.

There was also an apparent increase in response latency with increasing age (Fig. 3). For P1 latency, the linear regression equation age in years x 0.0487 + 14.41 best modeled the data. The slope value (0.0487) was just significant at the 0.05 level (t = 4.12, P = 0.0002). For N1, the linear regression equation was age in years x 0.0318 + 23.42, again with a significant slope value (t = 2.32, P =

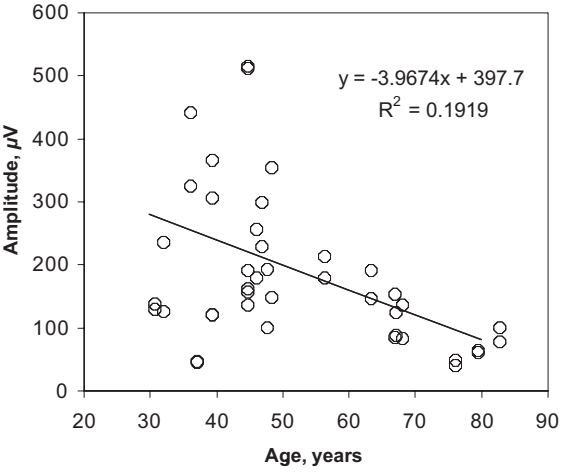

Figure 2. Influence of age on the amplitude of the VEMP evoked by a 250 Hz tone burst.

Table 1. Normal Limits for Vestibular Evoked Myogenic Potential

Variable	Mean	SD	+2 SD limit
Right			
P1 latency, msec	16.94	1.22	19.99
N1 latency, msec	25.16	1.59	29.12
P1–N1 amplitude, μV	179.14	111.28	457.35
Threshold, dB nHL	72.67	3.72	63.37
Left			
P1 latency, msec	16.85	1.65	20.97
N1 latency, msec	25.31	1.71	29.59
P1–N1 amplitude, μV	182.29	131.67	511.47
Threshold, dB nHL	72.67	3.72	63.37
Pooled right and left			
P1 latency, msec	16.90	1.43	20.47
N1 latency, msec	25.24	1.63	29.31
P1–N1 amplitude, μV	180.71	120.42	
Side asymmetries			
P1 latency, msec	0.09	1.35	3.39
N1 latency, msec	-0.16	1.42	3.54
P1–N1 amplitude, μV	-0.02	0.19	0.47

Note: N1: first negative peak after P1; P1: first positive polarity peak in the composite average. See text for details.

0.0255). Overall, the VEMP latency increased by approximately 0.49 msec per decade, and P1–N1 amplitude decreased by 40 μV per decade.

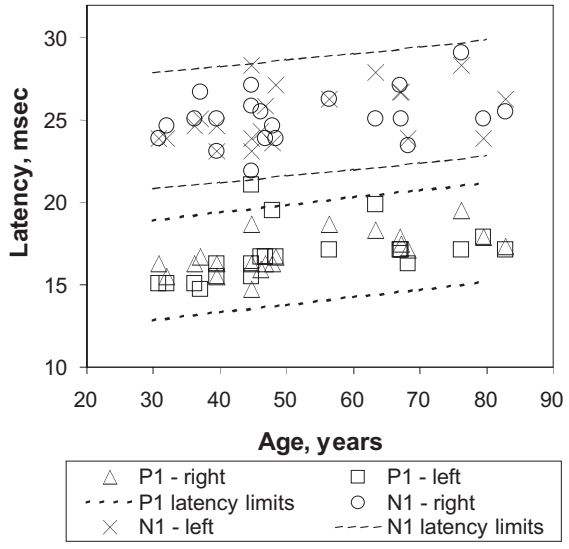

Figure 3. Influence of age on P1–N1 latency. P1: first positive polarity peak in the composite average; N1: first negative peak after P1.

This trend toward increased VEMP latency with age necessitated the development of age-specific absolute latency norms. These were developed for P1 and N1 by calculating the SDs for the absolute latency of P1 and N1 after removing the age effect in the raw latency values. The derived SDs were 1.21 msec for P1 and 1.41 msec for N1. For subsequent analysis, ±2.5 SD was arbitrarily set as the upper and lower limit of normal for P1 and N1 latency. Age-specific limits were thus determined by calculating the regression equation for peak latency described above and adding ±3.02 msec for P1 and ±3.51 msec for N1 (Fig. 3). When these values were used as the normal limits, one patient in the presumed-normal group showed a prolonged P1 latency on one side. This patient had a clinical diagnosis of resolved benign paroxysmal positional vertigo. We interpreted this as a false-positive outcome, which meant a false-positive rate of 5% in this group.

The distribution of N1 latencies was bimodal, even after removing the age effect. Specifically, in 30% of measurements (13 of

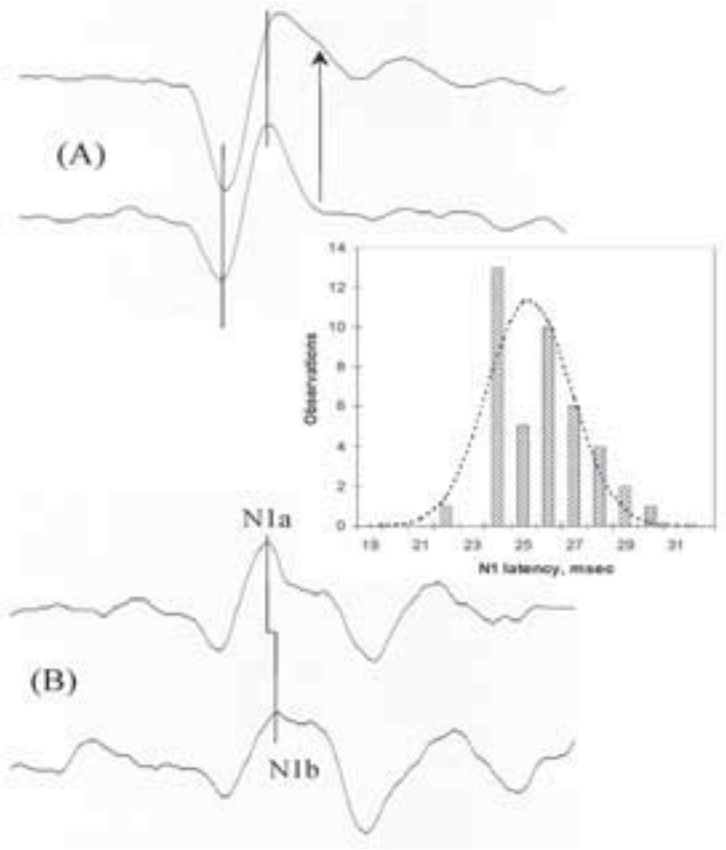

Figure 4. Effect of fatigue on VEMP morphology. (A) Superaverages of 521 epochs from the VEMP obtained from the author (D.A.Z.). The lower trace shows the VEMP from the first 512 averages. The upper trace shows the VEMP from the last 512 epochs during continuous collection of 2,056 epochs. The first negative peak (N1) becomes broader and rounder, and secondary peaks may be seen as the SCM fatigues and other muscle groups are recruited to maintain neck flexion (arrow). (B) N1a and N1b components observed in one 62-year-old patient. The larger N1a was recorded initially. However, it fatigues over the course of obtaining subaverages, and N1b was observed. It seems possible that the bimodal distribution of N1 latency reflects the influence of muscle fatigue and recruitment of other muscle groups during VEMP data collection. The inset shows the bimodal distribution of N1 latencies from the presumed-normal group.

42), N1 latency was between 23 and 24 msec, and in 38% of measurements (16 of 42), the peak was identified between 26 and 27 msec. The distribution of N1 latencies is shown in the inset of Figure 4.

VEMP thresholds were established in 5 dB steps in the 21 presumed-normal patients. Thresholds varied from 60 to 75 dB nHL (70 dB nHL or 103 dB peak sound pressure level nominally). Thresholds were not attempted when the measured VEMP at 90 dB nHL was less than 30 μV because more signal averaging was required to detect these responses, and muscle fatigue was thought to become a factor. In those subjects with VEMP responses greater than 30 μV, intra-ear threshold asymmetries did not exceed 10 dB (Table 1). Few patients in other groups completed this part of the VEMP procedure. Consequently, further analysis of threshold differences was deferred.

Patients with Vestibular, Central, or Unknown Disorders

Table 2 compares the number and type of abnormal VEMP findings among groups. In the group with extravestibular disorders of unknown etiology, one patient had an abnormal VEMP. This patient complained of lightheadedness, and orthostatic hypotension was suspected. The VEMP was abnormally small, with prolonged P1 and N1 latencies on one side. We interpreted this as a false-positive outcome, which gave a false-positive rate of 8% for this group.

In patients classified as having vestibular end-organ problems, P1–N1 amplitude asymmetries were the most common

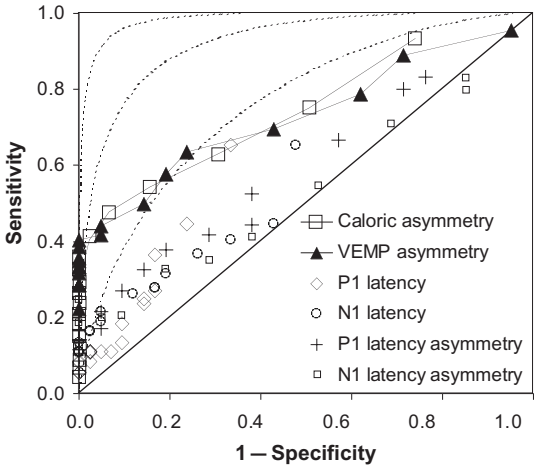

Figure 5. Receiver operating characteristics for the caloric test and each of the VEMP parameters. Sensitivity corresponds with hit rate. 1 – Specificity corresponds with false-positive rate. See text for details. P1: first positive polarity peak in the composite average; N1: first negative peak after P1.

Table 2. Numbers of Patients with Various Types of VEMP Abnormalities

Group	No.	Long P1 latency, no. (%)	Long N1 latency, no. (%)	Long P1 asymmetry, no. (%)	Long N1 asymmetry, no. (%)	Abnormal amplitude asymmetry, no. (%)
Presumed normal	21	1 (5)	0	0	0	0
Vestibular disorder	27	5 (11)	6 (15)	2 (7)	2 (7)	9 (33)
End-organ	17	1	2	1	1	6
Retrolabyrinthine/central	6	2	2	1	1	3
Bilateral	4	N/A	N/A	N/A	N/A	N/A*
Extravestibular disorder	12	0	0	0	0	2 (17)
Central	3	0	0	0	0	1
Unknown	9	0	0	0	0	1
Total cases	60					

Note: Unilaterally absent VEMP coded as an amplitude asymmetry. N/A: not applicable; N1: first negative peak after P1; P1: first positive polarity peak in the composite average; VEMP: vestibular evoked myogenic potential.
*One bilateral vestibular case demonstrated a VEMP evoked from one ear.

abnormal finding; latency prolongations were less common. Latency abnormalities and amplitude asymmetries did not always occur in the same cases, however. This may be surmised by comparing the percentages in Table 2 with those of the first column of Table 3.

Comparisons of VEMP and Caloric Test

Table 3 presents the overall performance of the VEMP and caloric tests in identifying abnormalities in each patient group. In the vestibular group, the VEMP and the caloric tests performed comparably, with the VEMP identifying 59% of cases (16 of 27) and the caloric test identifying 63% of cases (17 of 27). However, the two tests did not always identify the same patients. When the two tests were combined, 81% (22 of 27) of vestibular patients had at least one abnormal test result (Table 4). In one case of unilateral vestibulopathy (Meniere's syndrome), the VEMP was absent bilaterally. This was conservatively classified as an incongruent (false-positive) response because the VEMP did not detect the lesion side.

To further compare the performance of the VEMP and caloric tests, the various parameters of each were plotted on a series of receiver operating characteristic (ROC) curves (Fig. 5). The x-axis represents the probability of a false-positive detection (1 – specificity). The y-axis represents the probability of a correct identification (sensitivity). The 45° line represents the point at

Table 3. Number and Percentage of Patients with VEMP and Caloric Test Abnormalities

Group	No.	VEMP abnormal, no. (%)	Caloric asymmetry abnormal, no. (%)	Caloric or VEMP abnormal, no. (%)	Caloric and VEMP normal, no. (%)	Incongruent results, no. (%)
Presumed normal	21	1 (5)	0	1 (5)	20 (95)	1
Vestibular disorder	27	16 (59)	17 (63)	22 (82)	5 (18)	
End-organ	17	8	10	14	3	1
Retrolabyrinthine/ central	6	4	3	4	2	0
Bilateral group	4	4*	4	4	0	
Extravestibular	12	2 (17)	0	2 (17)	10 (83)	
Central	3	1	0	1	2	1
Unknown	9	1	0	1	8	1
Total cases	60					4 (7)

*One bilateral case demonstrated a VEMP on one side. This was not classified as an incongruent outcome.

Table 4. Sensitivity and Specificity for the Caloric and VEMP Tests in Patients with Vestibular Disorders

	Sensitivity	Specificity
VEMP	0.52	0.93
Caloric	0.62	0.95
VEMP + caloric	0.81	0.89

Note: Sensitivity is the proportion of subjects with disease who have a positive test result. Specificity is the proportion of subjects without disease who have a negative test result.

which a test is no better than chance. The three dashed lines plot hypothetical curves of the parameter d´, ranging from 1 to 3. According to signal detection theory (Turner and Nielsen, 1984; Gescheider, 1985), the higher the d´ value, the further toward the upper left of the chart the plot will be, and the better the test will be at detecting an abnormality accurately. By comparing the data from each of the VEMP parameters and the caloric tests with the expected d´ plots, one can gather the relative accuracy of each measure.

Figure 5 shows ROC plots for P1–N1 amplitude asymmetry, P1 and N1 latencies and asymmetries, and caloric asymmetries. To calculate these data, performance on each of these measures in the presumed-normal group was compared with performance in the remaining groups (including the unknown group). The goal was to simulate test performance in a diverse set of patients likely to present in a balance clinic. Only the caloric test and VEMP asymmetry performed better than d´ = 1. Caloric and VEMP asymmetries appeared to be equally sensitive and specific, although they may detect different conditions. Overall, neither caloric nor VEMP asymmetries appeared to be particularly sensitive when applied to a diverse set of patients with balance disorders.

Because the caloric and VEMP tests appeared to be sensitive to different conditions, combining the tests in a parallel fashion might have improved protocol sensitivity and overall performance. To test this hypothesis, estimates of test sensitivity, specificity, positive and negative predictive values were developed using the methods described by Newman et al (1988) (Table 4). Estimates were developed for each test individually and for a combined protocol.

Three assumptions were made to complete this analysis. First, we assumed the

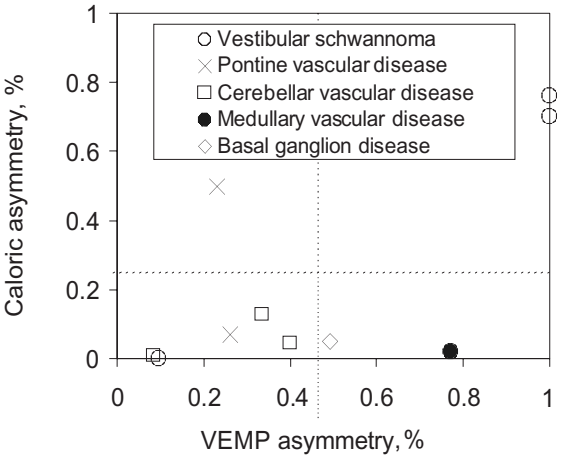

Figure 6. Distribution of P1–N1 amplitude and caloric asymmetries by central lesion. The dashed lines represent the +2.5 standard deviation limits used to establish abnormal VEMP asymmetry and the 95% limits for the caloric test. Normal performance on both tests is plotted in the lower left quadrant. Data points outside the lower left quadrant are abnormal on at least one test.

best estimate of the VEMP false-positive rate as 6.7%, which was the higher false-positive rate for the presumed normal (1 in 21) or the overall incongruent results rate (4 of 60) (Table 3). Second, we set the false-positive rate for the caloric test at 4.6%. We believed this was justified because the 24% caloric asymmetry cutoff used in this study represents the 95% limit for the test in our laboratory (Zapala, unpublished data). Finally, we assumed that the false-positive rates for each test were independent of each other. That is, the total false-positive rate for the combined protocol would be the sum of the false-positive rates for the individual tests. Thus, the false-positive rate for the combined VEMP and caloric test protocol was conservatively estimated as 11.3% (4.6% + 6.7%). This had no effect on the sensitivity, which improved with the combined protocol. However, the high false-positive rate did decrease the specificity, positive and negative predictive values, and likelihood ratios for the combined protocol.

Sensitivity of Caloric and VEMP Tests to Lesion Location

Further analyses were performed to determine whether the caloric response might be more sensitive to lesions in the ascending pathway of the VOR and whether the VEMP might be more sensitive to lesions on the

descending vestibulospinal pathways (Fig. 6). Patients with retrocochlear, central vestibular, and other central nervous system lesions were combined for this analysis. Of three vestibular schwannomas, only two were detected by the caloric and VEMP tests. One, a small intracanalicular-type tumor, was missed by both measures. Of two pontine lesions, one was detected by the caloric test but missed by the VEMP asymmetry measure. The second lesion was not detected by either test and was not thought to underpin the patients' complaints of dizziness.

Neither the VEMP nor the caloric test was abnormal in the three patients with cerebellar disease. In the sole patient with medullary disease in this group, the VEMP was abnormal on the involved side, but the caloric test was normal. Finally, in one patient with right basal ganglion disease, the VEMP was absent on the right side. Except for this case, the pattern of VEMP and caloric deficits roughly followed the expected relationship.

DISCUSSION

Procedural Effects on the VEMP

We chose our VEMP recording techniques to optimize our ability to detect responses in our clinical population. This population contained a significant number of patients over the age of 65. Some of the techniques we employed differ from methods used in other reports, and the differences are summarized as follows.

First, we selected a low-frequency tone burst on the basis of observations on saccule tuning and concerns about patient comfort. Previously, Todd et al (2000) had reported that the saccule is optimally tuned to approximately 300 Hz. That report, coupled with observations that a 250 Hz tone burst was more easily tolerated by subjects than clicks, prompted our use of this stimulus. Since then, several papers have suggested that a 500 Hz or 1000 Hz stimulus might be more effective (Welgampola and Colebatch, 2001a; Akin et al, in press). Todd et al (2000) recorded responses from 19 of 20 ears using a 200 and a 400 Hz stimulus. Akin et al (in press) reported an absent 250 Hz-evoked VEMP in one of 20 ears. Welgampola and Colebatch (2001a) recorded 250 Hz VEMPS from all 12 of their subjects. However, the responses had smaller amplitudes than those evoked by a 500 Hz tone burst. We found a 6.6% false-positive rate in patients not suspected of having vestibular disease. This is roughly in line with the false-positive rates reported in the literature. Both the Akin et al (in press) and Welgampola and Colebatch (2001a) papers suggest that a 500 or 1000 Hz stimulus generates a more robust VEMP than a 250 Hz stimulus. In retrospect, we may have been able to evoke more responses had we chosen a 500 Hz tone-burst stimulus. We are currently exploring this protocol change.

Two other modifications involved the use of a large surface electrode over the SCM and the use of a subaveraging technique. VEMPs require active muscle contraction, which can be difficult for older patients. In general, impedances were lower with the larger electrodes, and more of the surface area over the SCM was covered. This resulted in larger VEMP signal-to-noise ratios for signal averaging purposes. Because subaverages were recorded, each patient had to contract their SCM for only 12 to 14 seconds per epoch. This greatly diminished muscle fatigue.

A final modification involved the location of our noninverting electrodes. Most studies refer the SCM VEMP to an electrode positioned at the base of the SCM; typically, a sternal reference is used. Li et al (1999) demonstrated that sternal or mastoid references were not electrically silent and could affect the shape of the VEMP. They advocated a linked wrist reference to avoid local field potential effects surrounding the SCM. Although we believe that we avoided local field effects, there was a risk that the dorsum of the hand was not electrically silent during VEMP recording. We did monitor hand activity during testing and did not identify any instance of overt muscle contractions during testing. However, it is possible that EMG field potentials from muscles in the hand could have contaminated some of our data.

The fact that we used larger surface-area recording electrodes, collected between three and five short-duration subaverages to minimize patient fatigue, and used a lower-frequency stimulus likely contributed to our success in obtaining responses, particularly in older or deconditioned patients. It may also explain some of the age-related differences that we found.

The ability to measure a VEMP in a shorter amount of time allowed us to observe the effects of muscle fatigue changes in the response (Fig. 4). The N1 peak appeared particularly vulnerable to fatigue effects. The bimodal distribution of N1 scores appeared to relate to informal observations that N1 consisted of two subcomponents. The first component, labeled N1a in Figure 4, is a robust potential that is relatively large and early (mean latency = 23 msec). N1a is prominent in healthy patients under 60 years of age but may disappear with muscle fatigue. The second component, designated N1b, occurs later in time (mean latency 27 msec), is smaller in amplitude than N1a, and is often masked by the earlier component. However, in some cases, if the SCM muscle is allowed to fatigue, N1a diminishes in amplitude, and the slower N1 component becomes more apparent. The observation that the N1a is less apparent in older patients and diminishes with muscle fatigue argues that the latter component may reflect recruitment of other muscle groups during sustained SCM muscle contraction. Our use of a large surface-area recording electrode may have biased our study in the direction of observing distant muscle recruitment. Alternative possibilities may include differences in the activation of SCM motor endplate units in subgroups of patients (for example, the sternomastoid and cleidomastoid elements of the SCM muscle), or perhaps different motoneuron pools in the pathways underpinning the VEMP. Further study will be needed to resolve these issues.

Age Effects on the VEMP

Our first question was whether VEMP peak amplitude, latency, and side asymmetry measurements vary significantly with patient age. In our clinical setting, this is important because many of our patients are older and often present with multiple deficits. If the VEMP cannot be reliably recorded in this patient group, or if there are significant differences in the VEMP associated with age-related changes in test performance, our ability to obtain useful information from the test might be limited.

We were able to measure the VEMP routinely in patients as old as 80 years of age. In general, our findings appear to show that, when a 250 Hz stimulus is employed, there are age-related changes in VEMP response amplitude and latency. Specifically, there were systematic decreases in P1–N1 amplitude and increases in VEMP latency measures with increasing age. Amplitude and latency-based asymmetry values did not vary by age. Because of these observations, we generated age-specific normal values for VEMP absolute latencies.

Age-related amplitude effects have been reported. Welgampola and Colebatch (2001b) found a systematic decrease in the click-evoked P1–N1 amplitude with age, beginning after the sixth decade. This occurred even when corrections for the level of EMG muscle activity were made; thus, differences in muscle strength seem to have been controlled in this study. Age-related amplitude changes for galvanic-induced VEMPs were demonstrated in the seventh decade. Because the galvanic-induced VEMP is thought to stimulate vestibular nerve afferents directly, Welgampola and Colebatch (2001b) suggested that this was evidence that end-organ degeneration precedes nerve degeneration.

Our results appear consistent with those of Welgampola and Colebatch (2001b) in showing an age-related decrease in P1–N1 amplitudes. However, in our study, the age-related decrease in amplitude did not show a sharp change in the sixth decade. The method used by Welgampola and Colebatch (2001b) might have selected against observing the N1a component, and this may account for the difference between studies. Alternatively, we might not have controlled neck muscle activation as well as they did. Thus, our amplitude changes may reflect both vestibular end-organ and muscle activation changes with age.

An effect of age on peak latency has not been previously reported and deserves consideration. It is possible that the group of patients used to generate normal limits (presumed normal group) had undetected vestibular deficits. This would mean that the age-related normal limits we generated would be biased toward missing potentially significant VEMP latency delays in older patients.

However, the age effect may not be an uncontrolled bias. Welgampola and Colebatch (2001b) noted a slight increase in the click-evoked VEMP N1 with increasing patient age. However, this did not reach statistical significance. Akin et al (in press) and Welgampola and Colebatch (2001a) clearly demonstrated latency changes with tone-

burst rise and fall times. It may be that the age-related changes reported here reflect differences in evoking stimuli or recording technique. Specifically, low-frequency (slow rise time) evoked VEMPs may be more sensitive to the effects of age than VEMPs evoked by high-frequency (faster rise time) tone bursts or clicks. The current data cannot resolve this issue. Consequently, the effect of age on VEMP latency should be considered a preliminary finding and requires validation in a group of elderly patients without complaints of dizziness or imbalance.

Effects of Site of Lesion on the VEMP

Our second question concerned the type of information that might be gleaned from the VEMP. The VEMP is thought to reflect a descending pathway starting from the saccule, involving the descending vestibulospinal system, and ending at the SCM. We questioned whether the VEMP was affected by peripheral and central vestibular lesions in a manner that might be predicted by knowledge of the anatomic pathways underpinning the response. The data set described in this report was too small to definitively resolve this question. In general, the types of disorders identified by the VEMP appear to follow the functional pathway subserving the response, including possible cervical level deficits. When there was evidence for a total vestibular end-organ collapse, the VEMP was absent. When the vestibular end organ was suspected to have residual function, the VEMP was variably present. Since there was no way to correlate VEMP presence or absence with residual saccular function, one cannot be sure of the sensitivity of the VEMP to subtotal vestibular lesions involving the saccule.

We did note two cases of sudden cochlear hearing loss and vertigo with evidence of ipsilesional horizontal canal paresis and persistent VEMPs. Considering the anatomic relationship between these structures, it was difficult to conceive of a lesion that would involve the horizontal canal and cochlea but spare the saccule. It was also difficult to relate this deficit pattern to nerve swelling or impaired vascular function. We believe this pattern likely suggests that the saccule was involved in these patients and that the VEMP persisted in the face of subtotal loss of saccular function. The overall low sensitivity of the VEMP (discussed below) is consistent with this hypothesis.

An alternative explanation would be that the saccule is somehow protected from disorders that may impair cochlear and horizontal canal function. This seems unlikely, although a mechanism for the relative vulnerability of the superior vestibular nerve has recently been proposed (Goebel and Gianoli, 2002). We have since identified cases of sudden-onset high-frequency hearing loss and dizziness with ipsilateral loss of the VEMP and persistent horizontal canal VOR function. These cases argue against protected saccular status and suggest diversity in deficit patterns observable within the vestibular sensorineural structure.

VEMP sensitivity to central lesions appears more straightforward. Although the number of cases was limited, we found that caloric deficits were sensitive to vestibulocochlear nerve and pontine level lesions and that the VEMP was sensitive to vestibulocochlear nerve and medullary lesions (Fig. 6). This is consistent with the presumed anatomic pathways underpinning both responses and with published reports. For example, Murofushi et al (2001) reported that VEMPs were absent or decreased in 77% of tests in patients with acoustic neuroma (48 patients) and in 25% of tests in patients with multiple sclerosis (three of 12 sides of six patients). They also noted that 8% of patients with acoustic neuroma (four of 48) showed a prolonged p13 (the first positive peak), and all patients with multiple sclerosis showed prolonged p13. The authors concluded that the VEMP was particularly sensitive to lesions of the descending vestibulospinal tracts. Similarly, Itoh et al (2001) compared the performance of the VEMP with the auditory brainstem response in a set of patients with posterior fossa lesions. They found the VEMP to be sensitive to both midlevel pontine and medullary lesions.

In our series, none of the cerebellar lesions were detected by caloric or VEMP asymmetries. Takegoshi and Murofushi (2000) studied the VEMP in cases of spinocerebellar degeneration. Whereas all of their patients with olivopontocerebellar ataxia and cortical cerebellar atrophy showed essentially normal VEMP responses, two of their three patients with Machado-Joseph disease showed abnormal VEMPs and reduced or absent caloric responses. It would appear

that VEMPs are relatively insensitive to cerebellar deficits, with the exception of those in Machado-Joseph disease.

Finally, a comment must be made concerning the two patients with cervical spinal problems who were excluded from the analysis. In each case, the VEMP was absent on the side where clinical symptoms of cervical nerve involvement were evidenced (paresthesias or upper extremity limb weakness). Cervical cord compression was identified on computed tomography and magnetic resonance imaging in both cases; in one case the deficit was low, between C5 and C7. In this patient, there appeared to be enough EMG activity produced through muscle contraction to expect a VEMP. However, this was an informal observation, and EMG evidence of muscle activation level was not directly measured or controlled. It was not possible to determine whether cord or nerve compression effects were responsible for the abnormal VEMPs, or whether pain or limited neck range-of-motion issues impeded SCM muscle contraction in these patients. Because of these concerns, we could not be sure that the VEMP was actually reflecting labyrinthine function or impairment of the final common pathway to the SCM muscle. The influence of final common pathway problems on the VEMP will require more study, first, to define the final common pathway and, second, to establish whether impairments in the pathway may affect the ability to record a VEMP.

Thus, our data support the view that the VEMP is sensitive to lesions involving the saccule, inferior vestibular nerve, vestibular nuclei, and descending vestibulospinal tracts. Moreover, when compared with the standard caloric test, the VEMP appears to be sensitive to different conditions, suggesting that the test may offer unique information about vestibular function as part of the vestibular battery.

Relative Performance of the VEMP and the Caloric Response

As shown in Table 4, sensitivity and specificity for the detection of vestibular lesions in an unselected cohort of patients were slightly lower for the VEMP than for the caloric response, but neither test was impressively sensitive. The ROC analysis confirms this impression. VEMP and caloric test performance on the ROC curves were essentially equivalent, and neither test performed much better than $d' = 1$. This is only marginal performance for a diagnostic test.

The two tests appear to detect different types of conditions, and combining them might improve the ability to detect vestibular lesions. In our data set, combining the caloric and VEMP tests increased sensitivity for the detection of vestibular lesions from 0.52 for the VEMP and 0.62 for the caloric test to 0.81 for the combined test protocol—a considerable improvement. However, the specificity dropped somewhat from 0.93 for the VEMP and 0.95 for the caloric response to 0.89 in the combined protocol. The decrease in specificity results directly from the VEMP false-positive rate. If this could be improved, the combined protocol would look more favorable.

The modest performance of the caloric and VEMP tests does not necessarily mean that these tests should be dropped from diagnostic batteries. Patients experience dizziness and imbalance for multiple reasons. Only a few causes may result in an abnormal test result at any given time. For example, some conditions are unstable (for example, Meniere's disease), and symptoms or deficits may not be evident at the time of testing. In other cases, the cause of dizziness may be multifactorial, and the concurrent presence or absence of vestibular function may be important for selecting a management strategy (long-standing dizziness following cerebrovascular accident, for example). In an unselected group of patients with dizziness, neither test is likely to be positive in all cases.

This report offers preliminary evidence that the VEMP provides unique, clinically meaningful information and that the combination of the caloric test and the VEMP represents a reasonably sensitive and specific battery. However, we must point out several weaknesses in our work. First, we did not have a true control group in this study. Rather, we used patients who were found to have problems with balance or dizziness from nonvestibular sources as controls. While we believe they were representative of subjects without dizziness or balance disorders, we cannot be sure. Future study should focus on how VEMP tests work in subjects older than 65 years without a history of dizziness or balance complaints.

Second, as a retrospective study, we classified patients on the basis of their diagnosis at the time of review. Physicians who arrived at these diagnoses for our patients were not blinded to VEMP or caloric test results and in fact considered them in the course of their evaluations. Consequently, erroneous test results could have biased diagnostic judgment, and true test error rates may be underestimated. Until a "gold standard" for vestibular function can be developed, such biases are likely to persist. We believe we used conservative estimates of test error rates to report estimated test and protocol sensitivity and specificity. However, better estimates may be developed from a blinded prospective protocol.

A related issue is the use of a 250 Hz tone burst as a stimulus. Recent reports suggest this results in a higher false-positive rate than a 500 or 750 Hz stimulus. Since completing this work, we have moved to a 500 Hz stimulus and found that the false-positive rate decreased slightly. Finally, using a larger patient pool may further clarify the effects of various lesions on the VEMP.

CONCLUSIONS

On the basis of our experience, we reached the following conclusions: (1) When a 250 Hz tone pip is used to evoke the VEMP, there appears to be a systematic increase in VEMP latency and a decrease in P1–N1 amplitude with increasing age in our patient group. If this can be substantiated in subjects without complaints of dizziness or imbalance, age-specific normal values may be needed to improve test accuracy, particularly in patients over the age of 60 years. Further testing is needed to determine whether this applies to tone-burst-evoked VEMPs elicited at other frequencies. (2) In older or deconditioned patients, the VEMP characteristics may change as a result of muscle fatigue and recruitment of other muscle groups to the response. Using larger recording electrodes and combining multiple subaverages are effective ways of minimizing muscle fatigue effects in this age group. (3) There is preliminary evidence that cervical level lesions may directly or indirectly influence the VEMP. Further study is needed to determine whether such lesions affect the VEMP because of neural pathway involvement, reduced muscle contraction from pain, or limited neck range-of-motion issues. (4) The VEMP appears to be selectively sensitive to lesions involving the saccule, inferior nerve, vestibular nuclei, and descending vestibulospinal pathways. However, both the VEMP and the bithermal caloric test appeared to be only modestly sensitive to lesions commonly encountered in a balance clinic ($d' = 1$). This likely reflects both test performance issues and the multiple types of deficits that can provoke complaints of dizziness or imbalance. VEMPs may be spared in patients in whom saccular or inferior nerve involvement is likely (lesions that impair horizontal canal and cochlear function). Consequently, the VEMP may turn out to be a crude measure of saccular output and may persist in the face of subtotal saccular damage. (5) Because the caloric test and the VEMP are sensitive to different types of lesions, the combination of the VEMP and the caloric test proved valuable (sensitivity = 0.81, specificity = 0.89). Methods to improve the VEMP false-positive rate (possibly the use of a 500 or 1000 Hz stimulus) would be helpful in improving test performance.

Acknowledgment. The authors gratefully acknowledge the Section of Scientific Publications, Mayo Foundation, and three anonymous reviewers for their assistance in preparing this paper.

REFERENCES

Akin FW, Murnane OD. (2001) Vestibular evoked myogenic potentials: preliminary report. *J Am Acad Audiol* 12:445–452.

Akin FW, Murnane OD, Medley TM. (In press) Effects of click and tone burst stimulus parameters on the vestibular evoked myogenic potential (VEMP). *J Am Acad Audiol.*

Al-Abdulhadi K, Zeitouni AG, Al-Sebeih K, Katsarkas A. (2002) Evaluation of vestibular evoked myogenic potentials. *J Otolaryngol* 31:93–96.

Baloh RW, Honrubia V. (1990). *Clinical neurophysiology of the vestibular system.* 2nd ed. Philadelphia: FA Davis Company.

Bath AP, Harris N, McEwan J, Yardley MP. (1999) Effect of conductive hearing loss on the vestibulocollic reflex. *Clin Otolaryngol* 24:181–183.

Bath AP, Harris N, Yardley MP. (1998) The vestibulocollic reflex. *Clin Otolaryngol* 23:462–466.

Bickford RG, Jacobson JL, Cody TR. (1964) Nature of average evoked potentials to sound and other stimuli in man. *Ann N Y Acad Sci* 112:204–223.

Brantberg K, Bergenius J, Tribukait A. (1999) Vestibular-evoked myogenic potentials in patients with dehiscence of the superior semicircular canal. *Acta Otolaryngol* 119:633–640.

Buttner-Ennever JA. (1999) A review of otolith pathways to brainstem and cerebellum. *Ann N Y Acad Sci* 871:51–64.

Carpenter MB, Sutin JS. (1983) *Human Neuroanatomy*. 8th ed. Baltimore: Williams and Wilkins.

Chen CW, Young YH, Tseng HM. (2002) Preoperative versus postoperative role of vestibular-evoked myogenic potentials in cerebellopontine angle tumor. *Laryngoscope* 112:267–271.

Chen CW, Young YH, Wu CH. (2000) Vestibular neuritis: three-dimensional videonystagmography and vestibular evoked myogenic potential results. *Acta Otolaryngol* 120:845–848.

Colebatch JG. (2001) Vestibular evoked potentials. *Curr Opin Neurol* 14:21–26.

Colebatch JG, Halmagyi GM. (1992) Vestibular evoked potentials in human neck muscles before and after unilateral vestibular deafferentation. *Neurology* 42:1635–1636.

Colebatch JG, Halmagyi GM, Skuse NF. (1994) Myogenic potentials generated by a click-evoked vestibulocollic reflex. *J Neurol Neurosurg Psychiatry* 57:190–197.

de Waele C, Tran Ba Huy P, Diard JP, Freyss G, Vidal PP. (1999) Saccular dysfunction in Meniere's patients: a vestibular-evoked myogenic potential study. *Ann N Y Acad Sci* 871:392–397.

Didier A, Cazals Y, Aurousseau C. (1987) Brainstem connections of the anterior and posterior parts of the saccule in the guinea pig. *Acta Otolaryngol* 104:385–391.

Ferber-Viart C, Dubreuil C, Duclaux R. (1999) Vestibular evoked myogenic potentials in humans: a review. *Acta Otolaryngol* 119:6–15.

Fitzgerald MJ, Comerford PT, Tuffery AR. (1982) Sources of innervation of the neuromuscular spindles in sternomastoid and trapezius. *J Anat* 134:471–490.

Gescheider GA. (1985) *Psychophysics, Methods, Theory, and Application.* 2nd ed. Hillsdale, NJ: L Erlbaum Associates.

Goebel JA, Gianoli J. (2002) Neural entrapment theory of BVP following vestibular neuritis (abstract). Paper presented at the XXII International Congress of the Barany Society, Seattle. http://www.baranysociety.com/abstract_list.htm (accessed January 30, 2003).

Halmagyi GM, Aw ST, Karlberg M, Curthoys IS, Todd MJ. (2002) Inferior vestibular neuritis. *Ann N Y Acad Sci* 956:306–313.

Halmagyi GM, Colebatch JG. (1995) Vestibular evoked myogenic potentials in the sternomastoid muscle are not of lateral canal origin. *Acta Otolaryngol Suppl* 520:1–13.

Halmagyi GM, Curthoys IS. (1999) Clinical testing of otolith function. *Ann N Y Acad Sci* 871:195–204.

Heide G, Freitag S, Wollenberg I, Iro H, Schimrigk K, Dillmann U. (1999) Click evoked myogenic potentials in the differential diagnosis of acute vertigo. *J Neurol Neurosurg Psychiatry* 66:787–790.

Iida M, Aihara H, Takahashi H, Hitouji K, Nomura K. (1998) EMG potentials elicited by forehead taps in the sternocleidomastoid muscles and lower leg muscles—a study on patients with vestibular lesions. *Tokai J Exp Clin Med* 23:225–230.

Ito K, Ishimoto S, Murofushi T. (2001) Narrow internal auditory meatus: an idiopathic case confirming the origin and pathway of vestibular evoked myogenic potentials in humans. *Arch Otolaryngol Head Neck Surg* 127:275–278.

Itoh A, Kim YS, Yoshioka K, Kanaya M, Enomoto H, Hiraiwa F, Mizuno M. (2001) Clinical study of vestibular-evoked myogenic potentials and auditory brainstem responses in patients with brainstem lesions. *Acta Otolaryngol Suppl* 545:116–119.

Li MW, Houlden D, Tomlinson RD. (1999) Click evoked EMG responses in sternocleidomastoid muscles: characteristics in normal subjects. *J Vestib Res* 9:327–334.

Lim CL, Clouston P, Sheean G, Yiannikas C. (1995) The influence of voluntary EMG activity and click intensity on the vestibular click evoked myogenic potential. *Muscle Nerve* 18:1210–1213.

Matsuzaki M, Murofushi T. (2001) Vestibular evoked myogenic potentials in patients with idiopathic bilateral vestibulopathy: report of three cases. *ORL J Otorhinolaryngol Relat Spec* 63:349–352.

Matsuzaki M, Murofushi T. (2002) Click-evoked potentials on the neck of the guinea pig. *Hear Res* 165:152–155.

Matsuzaki M, Murofushi T, Mizuno M. (1999) Vestibular evoked myogenic potentials in acoustic tumor patients with normal auditory brainstem responses. *Eur Arch Otorhinolaryngol* 256:1–4.

McCue MP, Guinan JJ, Jr. (1994) Acoustically responsive fibers in the vestibular nerve of the cat. *J Neurosci* 14:6058–6070.

Murofushi T, Halmagyi GM, Yavor RA, Colebatch JG. (1996) Absent vestibular evoked myogenic potentials in vestibular neurolabyrinthitis: an indicator of inferior vestibular nerve involvement? *Arch Otolaryngol Head Neck Surg* 122:845–848.

Murofushi T, Matsuzaki M, Wu CH. (1999) Short tone burst-evoked myogenic potentials on the sternocleidomastoid muscle: are these potentials also of vestibular origin? *Arch Otolaryngol Head Neck Surg* 125:660–664.

Murofushi T, Shimizu K, Takegoshi H, Cheng PW. (2001) Diagnostic value of prolonged latencies in the vestibular evoked myogenic potential. *Arch Otolaryngol Head Neck Surg* 127:1069–1072.

Newman TB, Browner WS, Cummings SR, Hulley SB. (1988) Designing a new study: II. Cross-sectional and case control studies. In: Hulley SB, Cummings SR, eds. *Designing Clinical Research: An Epidemiologic Approach.* Baltimore: Williams and Wilkins, 75–86.

Ochi K, Ohashi T, Nishino H. (2001) Variance of vestibular-evoked myogenic potentials. *Laryngoscope* 111:522–527.

Perez R, Freeman S, Sohmer H, Sichel JY. (2000) Vestibular and cochlear ototoxicity of topical antiseptics assessed by evoked potentials. *Laryngoscope* 110:1522–1527.

Robertson DD, Ireland DJ. (1995) Vestibular evoked myogenic potentials. *J Otolaryngol* 24:3–8.

Sato H, Imagawa M, Sasaki M, Ikegami H, Uchino Y. (1994) Connections between the saccular nerve and neck extensor and flexor motoneurons in the decerebrate cat (abstract). *Abstracts Soc Neurosci* 20:1192.

Seo T, Yoshida K, Shibano A, Sakagami M. (1999) A possible case of saccular endolymphatic hydrops. *ORL J Otorhinolaryngol Relat Spec* 61:215–218.

Shepard NT, Telian SA. (1996) *Practical Management of the Balance Disorder Patient.* San Diego: Singular Publishing Group.

Sheykholeslami K, Kaga K. (2002) The otolithic organ as a receptor of vestibular hearing revealed by vestibular-evoked myogenic potentials in patients with inner ear anomalies. *Hear Res* 165:62–67.

Sheykholeslami K, Murofushi T, Kaga K. (2001) The effect of sternocleidomastoid electrode location on vestibular evoked myogenic potential. *Auris Nasus Larynx* 28:41–43.

Shimizu K, Murofushi T, Sakurai M, Halmagyi M. (2000) Vestibular evoked myogenic potentials in multiple sclerosis (letter). *J Neurol Neurosurg Psychiatry* 69:276–277.

Streubel SO, Cremer PD, Carey JP, Weg N, Minor LB. (2001) Vestibular-evoked myogenic potentials in the diagnosis of superior canal dehiscence syndrome. *Acta Otolaryngol Suppl* 545:41–49.

Takegoshi H, Murofushi T. (2000) Vestibular evoked myogenic potentials in patients with spinocerebellar degeneration. *Acta Otolaryngol* 120:821–824.

Takeichi N, Sakamoto T, Fukuda S, Inuyama Y. (2001) Vestibular evoked myogenic potential (VEMP) in patients with acoustic neuromas. *Auris Nasus Larynx* 28 (suppl.):S39–S41.

Todd NP, Cody FW, Banks JR. (2000) A saccular origin of frequency tuning in myogenic vestibular evoked potentials? implications for human responses to loud sounds. *Hear Res* 141:180–188.

Townsend GL, Cody DT. (1971) The average inion response evoked by acoustic stimulation: its relation to the saccule. *Ann Otol Rhinol Laryngol* 80:121–131.

Tsutsumi T, Tsunoda A, Noguchi Y, Komatsuzaki A. (2000) Prediction of the nerves of origin of vestibular schwannomas with vestibular evoked myogenic potentials. *Am J Otol* 21:712–715.

Turner RG, Nielsen DW. (1984) Application of clinical decision analysis to audiological tests. *Ear Hear* 5:125–133.

Uchino Y, Sato H, Sasaki M, Imagawa M, Ikegami H, Isu N, Graf W. (1997) Sacculocollic reflex arcs in cats. *J Neurophysiol* 77:3003–3012.

Ullah M, Salman SS. (1986) Localisation of the spinal nucleus of the accessory nerve in the rabbit. *J Anat* 145:97–107.

Versino M, Colnaghi S, Callieco R, Cosi V. (2001) Vestibular evoked myogenic potentials: test-retest reliability. *Funct Neurol* 16:299–309.

Watson SR, Colebatch JG. (1998) Vestibular-evoked electromyographic responses in soleus: a comparison between click and galvanic stimulation. *Exp Brain Res* 119:504–510.

Watson SR, Halmagyi GM, Colebatch JG. (2000) Vestibular hypersensitivity to sound (Tullio phenomenon): structural and functional assessment. *Neurology* 54:722–728.

Welgampola MS, Colebatch JG. (2001a) Characteristics of tone burst-evoked myogenic potentials in the sternocleidomastoid muscles. *Otol Neurotol* 22:796–802.

Welgampola MS, Colebatch JG. (2001b) Vestibulocollic reflexes: normal values and the effect of age. *Clin Neurophysiol* 112:1971–1979.

Wu CH, Young YH, Murofushi T. (1999) Tone burst-evoked myogenic potentials in human neck flexor and extensor. *Acta Otolaryngol* 119:741–744.

Young ED, Fernandez C, Goldberg JM. (1977) Responses of squirrel monkey vestibular neurons to audio-frequency sound and head vibration. *Acta Otolaryngol* 84:352–360.