Effects of Stimulus and Recording Parameters on the Air Conduction Ocular Vestibular Evoked Myogenic Potential
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Abstract

Background: Vestibular evoked myogenic potentials (VEMPs) have been recorded from the sternocleidomastoid muscle (cervical VEMP or cVEMP) and more recently from the eye muscles (ocular VEMP or oVEMP) in response to air conduction and bone conduction stimuli. Both cVEMPs and oVEMPs are mediated by the otoliths and thereby provide diagnostic information that is complementary to videonystagmography and rotational chair tests. In contrast to the air conduction cVEMP, which originates from the saccule/inferior vestibular nerve, recent evidence suggests the possibility that the air conduction oVEMP may be mediated by the utricle/superior vestibular nerve. The oVEMP, therefore, may provide complementary diagnostic information relative to the cVEMP. There are relatively few studies, however, that have quantified the effects of stimulus and recording parameters on the air conduction oVEMP, and there is a paucity of normative data.

Purpose: To evaluate the effects of several stimulus and recording parameters on the air conduction oVEMP and to establish normative data for clinical use.

Research Design: A prospective repeated measures design was utilized.

Study Sample: Forty-seven young adults with no history of neurologic disease, hearing loss, middle ear pathology, open or closed head injury, cervical injury, or audiovestibular disorder participated in the study.

Data Collection and Analysis: The effects of stimulus frequency, stimulus level, gaze elevation, and recording electrode location on the amplitude and latency of the oVEMP for monaural air conduction stimuli were assessed using repeated measures analyses of variance in an initial group of 17 participants. The optimal stimulus and recording parameters obtained in the initial group were used subsequently to obtain oVEMPs from 30 additional participants.

Results: The effects of stimulus frequency, stimulus level, gaze elevation, and electrode location on the response prevalence, amplitude, and latency of the oVEMP for monaural air conduction stimuli were significant. The maximum N1-P1 amplitude and response prevalence were obtained for contralateral oVEMPs using a 500 Hz tone burst presented at 125 dB peak SPL during upward gaze at an elevation of 30°.

Conclusions: The optimal stimulus and recording parameters quantified in this study were used to establish normative data that may be useful for the clinical application of the air conduction oVEMP.

Key Words: Ocular reflexes, ocular vestibular evoked myogenic potentials, otoliths, saccule, utricle, vestibular evoked myogenic potentials

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The peripheral vestibular system is comprised of two types of sensory organs, the semicircular canals and the otoliths, that sense angular acceleration and linear acceleration, respectively. Conventional vestibular assessment (videonystagmography) is limited to the evaluation of horizontal semicircular canal and superior vestibular nerve function. The cervical vestibular evoked myogenic potential (cVEMP) supplements the conventional vestibular test battery by providing diagnostic information about saccular and inferior vestibular nerve function. cVEPs are short-latency electromyograms (EMG) evoked by high-level acoustic stimuli recorded from surface electrodes over the tonically contracted sternocleidomastoid (SCM) muscles. The clinical utility of the cVEMP has been established for a number of peripheral audiovestibular disorders as well as brainstem disorders (for reviews see Murnane and Akin, 2009; Rosengren et al, 2010). The normal cVEMP waveform is characterized by a positive peak at z normal cVEMP waveform is characterized by a positive peak at 10–12 msec (n10 or N1) and a subsequent positive peak at 15-20 msec (p15 or P1) poststimulus onset. Similar to the cVEMP, the oVEMP is an ipsilateral inhibitory response and requires sustained contraction of the SCM muscle by either turning the head laterally while sitting or supine or raising the head from supine. The response, therefore, may be difficult to record in certain patient groups including the elderly, the cognitively impaired, the infirm, and patients with cervical disorders (Welgampola and Colebatch, 2001a; Su et al, 2004).

Short-latency vestibular evoked potentials have also been recorded in humans from surface electrodes placed frontally or near the eyes in response to imposed head movements (Rodionov et al, 1996a, 1996b; Sohmer et al, 1999) and following intraoperative electrical stimulation of the vestibular nerve (de Waele et al, 2001). Recent reports indicate that it is possible to record short-latency ocular vestibular evoked myogenic potentials (oVEPs) from surface electrodes below the eyes in response to air conduction, bone conduction, and galvanic stimuli (Rosengren et al, 2005; Iwasaki et al, 2007; Todd et al, 2007; Cheng et al, 2009; Rosengren et al, 2009). The normal oVEMP waveform is characterized by an initial negative peak at 10–12 msec (n10 or N1) and a subsequent positive peak at 15-20 msec (p15 or P1) poststimulus onset. Similar to the cVEMP, the oVEMP is a myogenic response that is present in patients with profound sensorineural hearing loss but intact vestibular function and either absent or reduced in amplitude in patients with vestibulopathy (Rosengren et al, 2005; Chihara et al, 2007; Iwasaki et al, 2007; Chihara et al, 2009a).

The largest oVEPs in response to monaural air conduction stimuli are obtained from electrodes located just beneath the eye contralateral to the stimulus ear with the patient looking up (Chihara et al, 2007; Todd et al, 2007; Rosengren et al, 2008; Govender et al, 2009). The oVEMP is absent from the affected side in patients with exenteration (removal) of the eye and extraocular muscles but present in patients with exenteration of the eye but intact extraocular muscles (Todd et al, 2007; Chihara et al, 2009a). In addition, the oVEMP is present in patients with profound facial nerve palsy and is independent of the blink reflex (Chihara et al, 2009a; Smulders et al, 2009). These observations suggest that the oVEMP is likely produced by synchronous activity in the inferior oblique and/or inferior rectus muscles and mediated by a predominantly contralateral otolith-ocular pathway. In contrast to the cVEMP, which is an ipsilateral inhibitory response that requires sustained contraction of the SCM muscle, the oVEMP (n10 or N1) is an excitatory response, reflects predominantly contralateral otolith-ocular function, and requires the patient to sit quietly and fix their gaze on a stationary visual target.

When the oVEMP is elicited by delivering a bone conduction (acceleration) stimulus to the midline forehead or to the mastoid area, the n10 component originates predominantly from the utricle/superior vestibular nerve (Todd et al, 2008; Iwasaki et al, 2009; Manzari et al, 2010a). In contrast to the air conduction cVEMP, which is mediated by the saccule/inferior vestibular nerve, recent evidence suggests the possibility that the air conduction oVEMP (like the bone conduction oVEMP) may also be dependent, at least in part, on the function of the utricle/superior vestibular nerve (Manzari et al, 2010b; Murofushi et al, 2010; Curthoys et al, 2011). The air conduction oVEMP, therefore, may provide complementary diagnostic information relative to the cVEMP and can be measured in patients from whom the cVEMP cannot be recorded due to inadequate contraction of the SCM muscle.

The effects of a number of stimulus and recording parameters on the air conduction oVEMP have been examined (Todd et al, 2007, 2009; Chihara et al, 2007, 2009b; Govender et al, 2009; Wang et al, 2009; Welgampola et al, 2009; Park et al, 2010). There are, however, no quantitative investigations of the effects of stimulus level, stimulus frequency, gaze elevation, and location of the recording electrode (ipsilateral vs. contralateral eye) on the oVEMP within the same group of subjects. The purpose of this study was to evaluate the effects of these stimulus and recording parameters
on the oVEMPs produced by monaural air conduction stimuli and to establish normative data for clinical use.

**METHODS**

**Subjects**

Twenty-four participants were recruited for the initial portion of this study. From the initial population of 24, data were obtained from 17 participants (24.5 ± 4.3 yr; range = 18 to 34 yr; 11 females) to assess the effects of several stimulus and recording parameters on the air conduction oVEMP (4 of 24 participants met the audiometric exclusion criteria, and 3 failed to complete the study). Each of the participants was assigned a number at the time of their recruitment, and data were obtained from one ear for Experiments 1 and 2 (the left ear of the odd-numbered participants and the right ear of the even-numbered participants) and from both ears for Experiment 3. Data were obtained subsequently from both ears of 30 additional participants (21.6 ± 3.2 yr; range = 18 to 28 yr; 17 females) using the optimal parameters obtained in the first group (33 participants were recruited for this portion of the study; 2 participants met the audiometric exclusion criteria, and 1 was excluded due to a history of concussion). The exclusion criteria for all participants included neurologic disease, hearing loss, middle ear pathology, air-bone gap >10 dB at any frequency from 500-4000 Hz, open or closed head injury, cervical injury, abnormal/absent cVEMPs, or audiovestibular disorder (including reported symptoms of imbalance and/or dizziness). To rule out audiovestibular disorders, a comprehensive audiological evaluation, videonystagmography (VNG), sinusoidal harmonic acceleration (SHA), and cVEMP testing were performed. Normal hearing was defined as pure-tone thresholds ≤20 dB HL (American National Standards Institute, 2004) at the octave frequencies 250 through 8000 Hz. Normal VNG test results were defined as a negative Dix-Hallpike maneuver, absence of spontaneous and positional nystagmus, normal tests of saccadic, gaze, smooth pursuit, and optokinetic system integrity, and a caloric weakness <20%. Normal SHA test results were defined as slow component velocity phase, gain, and asymmetry data within normal threshold values at 0.01 through 0.64 Hz. cVEMPs were obtained using air-conduction stimuli (120 dB peak SPL 500 Hz tone burst; 2 msec rise/fall and 6 msec plateau; Blackman gating function), unilateral activation of the SCM muscle, and a 50 μV target EMG level. For a more detailed description of the methods used to record the cVEMPs see Akin and Murnane (2001). Normal cVEMPs were defined as present responses bilaterally and a P1-N1 amplitude asymmetry ratio of <40%. This study was approved by the institutional review board at East Tennessee State University/VAMC, and all participants signed an informed consent form prior to participation in the study. The study participants were given nominal payment for their time.

**Stimulus and Recording Parameters**

Two-channel oVEMP recordings were obtained with a commercially available evoked potential instrument (GN Otometrics EP200; version 6.2.1). The stimuli were alternating polarity Blackman-gated tone bursts at the octave frequencies 250–4000 Hz presented monaurally via air-conduction either at 125 dB peak SPL or in 5 dB decrements from 125 to 100 dB peak SPL via ER3A insert earphones at a repetition rate of 5 Hz. The rise-fall time was 2 msec for all frequencies except 250 Hz (4 msec rise-fall), and there was no plateau.

Surface electrodes were placed 1 cm below (noninverting electrode) and 3 cm below (inverting electrode) the center of each lower eyelid, and the ground electrode was at Fpz. The EMG was amplified (100,000×), bandpass filtered (1–1000 Hz), and sampled at 12 kHz. The 50 msec recording epoch included a 20 msec prestimulus baseline. Each oVEMP waveform consisted of responses to 500 stimuli, and a minimum of two response waveforms were obtained from each subject at each frequency, level, and vertical gaze elevation. Peak-to-peak amplitudes (N1-P1) and absolute latencies (N1 and P1) were calculated from the mean value of the replicate waveforms for each condition. The oVEMP threshold was defined as the lowest stimulus level at which a replicated waveform (N1-P1) was visually detected. The asymmetry ratio (AR) (interaural N1-P1 amplitude difference) was calculated according to the following formula:

\[
AR = \frac{|\text{Left N1-P1 amplitude} - \text{Right N1-P1 amplitude}|}{|\text{Left N1-P1 amplitude} + \text{Right N1-P1 amplitude}|} \times 100.
\]

(1)

**Procedures**

Three experiments were conducted to determine the effects of several stimulus and recording parameters on oVEMP amplitude and latency in the initial group of 17 participants. Experiment 1 examined the effect of stimulus frequency. The subjects were positioned supine on an examination table in a dimly lit sound treated booth and instructed to direct their gaze at a visual target projected on the ceiling at a distance of 1 m at a neutral (0°) angle. A weighted plumb line was suspended from the neutral target on the ceiling, and each subject’s head location was adjusted to ensure that the target was at 0° and at midline. The subjects were instructed to direct their gaze at a visual target at a vertical elevation of 30°, and oVEMPs were obtained from one ear of each subject (8 right ears and 9 left ears) in response to
monaural, 125 dB\textsubscript{peak} SPL, air conduction tone bursts at the octave frequencies 250–4000 Hz. The selection of a visual target at a gaze elevation of 30° for Experiment 1 was based on pilot data that indicated the maximum oVEMP amplitude was obtained at 30° for visual targets at vertical elevations that ranged from 0 to 30°.

In Experiment 2, the effect of vertical gaze elevation was assessed, and oVEMPS were obtained from one ear of each subject (8 right ears and 9 left ears) at gaze elevations of 0, 15, and 30°. As the results of the first experiment indicated that the largest mean amplitude was obtained at 500 Hz, the stimulus frequency was fixed at 500 Hz and presented monaurally at 125 dB\textsubscript{peak} SPL. In Experiment 3, the effects of stimulus level and electrode location (ipsilateral vs. contralateral eye) were determined for each ear (34 ears) at 500 Hz. The stimuli were presented monaurally in 5 dB decrements from 125 to 100 dB\textsubscript{peak} SPL. As the results of the second experiment indicated that the largest mean amplitude was obtained at 30°, the vertical gaze elevation was fixed at 30°. The effect of electrode location was assessed using the data obtained from each ear at 125 dB\textsubscript{peak} SPL. The average amount of time for participants to complete all three experiments was 2.5 hr. The optimal stimulus and recording parameters (contralateral oVEMP using a 500 Hz tone burst presented at 125 dB\textsubscript{peak} SPL during upward gaze at an elevation of 30°) obtained from the 17 participants in the three experiments were used subsequently to obtain oVEMPs from 30 additional participants.

Data Analysis

The following repeated measures analyses of variance (RMANOVAs) were conducted separately for oVEMP N1-P1 amplitude, N1 latency, and P1 latency using SPSS statistical software (Version 14.0, SPSS Inc., Chicago, IL): (1) frequency, (2) gaze elevation, (3) stimulus level × ear, and (4) electrode location (ipsilateral vs. contralateral eye) × ear. The RMANOVAs for frequency, gaze elevation, and stimulus level included only the contralateral response data; the RMANOVAs for electrode location included both the contralateral and ipsilateral data. Absent responses were assigned an amplitude value of 0 µV; absent responses were not included in the latency analyses. The degrees of freedom for main effects were corrected using Greenhouse-Geisser estimates of sphericity whenever Mauchly’s test indicated that the assumption of sphericity had been violated. We considered p-values <.05 as statistically significant. Post hoc tests consisted of paired comparisons, and the p-values were adjusted using the Bonferroni procedure to correct for experiment-wise error. Prior to combining the data from the two groups of participants, Levene’s test was used to assess the equality of variances between the two groups, and independent samples t-tests (using a Bonferroni-adjusted p-value of .007) were used to determine group differences in mean amplitude, latency, and asymmetry ratio.

RESULTS

Experiment 1

Figure 1 shows the individual (left column) and mean (right column) contralateral oVEMP waveforms in response to 125 dB\textsubscript{peak} SPL tone bursts at the octave frequencies 250–4000 Hz. Note the differences in the amplitude scale for the individual waveforms at 500 and 1000 Hz relative to the other frequencies. The vertical gaze elevation was 30°, and the vertical dashed line at 0 msec indicates stimulus onset. Stimulus frequency

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{figure1}
\caption{The effect of stimulus frequency on the contralateral oVEMP. The individual oVEMP waveforms are in the left column, and the corresponding grand average waveforms are in the right column. Note the differences in the amplitude scale for the individual waveforms at 500 and 1000 Hz relative to the other frequencies. The vertical dashed line at 0 msec indicates stimulus onset. Stimulus level was 125 dB\textsubscript{peak} SPL, and the vertical gaze elevation was 30°. Stimulus frequency and the number of subjects with present responses at each frequency (total number of subjects tested = 17) are indicated in the middle of the figure.}
\end{figure}
and the number of subjects with present responses at each frequency (total number of subjects tested = 17) are indicated in the middle of the figure. The largest average N1-P1 amplitude and highest response prevalence were obtained at 500 Hz; both amplitude and response prevalence decreased at frequencies above and below 500 Hz.

The individual and mean amplitude and latency data are plotted as a function of stimulus frequency in Figure 2. The individual data were jittered in the frequency domain so that overlapping data points were not obscured. The data in the upper panel show the same effect of frequency on amplitude and response prevalence as illustrated in Figure 1 (maximum mean response prevalence and amplitude at 500 Hz). The results of the RMANOVA indicated a significant main effect of frequency on amplitude ($F(1.27, 20.38) = 10.8, p = .002$), and post hoc paired comparisons revealed that the amplitude at 500 Hz was significantly larger ($p < .04$) than the amplitude at all frequencies except 1000 Hz.

The latency data in the lower panel of Figure 2 show that the mean absolute latency of both N1 and P1 remained constant as a function of frequency except for an increase in latency observed at 250 Hz. It should be noted, however, that due to software limitations the rise-fall time at 250 Hz (4 msec) was double the rise-fall time at the other frequencies and likely produced the increased latency at 250 Hz. The latency data at 250 Hz, therefore, were not included in the statistical analysis; the latency data at 4000 Hz were also not included in the analysis as responses were absent in all but two subjects. The results of the RMANOVA at 500, 1000, and 2000 Hz indicated no significant main effect of frequency on N1 latency or P1 latency.

**Experiment 2**

oVEMP waveforms recorded at three vertical gaze elevations are shown in Figure 3. The individual contralateral waveforms are in the left column, and the corresponding grand average waveforms are in the right column. Note the difference in the amplitude scale between the individual and grand average waveforms. The stimulus was a 500 Hz tone burst presented at 125 dB$_{peak}$ SPL. The vertical gaze elevation and the number of subjects with present responses at each gaze elevation are indicated in the middle of the figure. The vertical dashed line at 0 msec indicates stimulus onset. Response amplitude and response prevalence increased as gaze elevation increased from 0 to 30°.

The individual and mean amplitude and latency data are plotted as a function of vertical gaze elevation in Figure 4. The individual data were jittered so that overlapping data points were not obscured. The data in the upper panel show an increase in both the mean N1-P1 amplitude and the variability of amplitude as a function of gaze elevation. The results of the RMANOVA indicated a significant main effect of gaze elevation on N1-P1 amplitude ($F(1.28, 20.48) = 22.61, p < .0001$). Post hoc paired comparisons revealed that the 30° gaze elevation produced significantly larger amplitudes than the 15 and 0° gaze elevations ($p < .0001$) and that the 15° gaze elevation produced significantly larger amplitudes than the 0° gaze elevation ($p < .05$).

The latency data in the lower panel of Figure 4 show that the mean absolute latency of both N1 and P1 decreased as a function of gaze elevation; however, the results of the RMANOVA indicated that the effect of gaze elevation on N1 latency was not significant. In contrast, the effect of gaze elevation on P1 latency was significant ($F(2, 12) = 18.06, p < .0001$). Post hoc paired comparisons revealed that the 0° gaze elevation produced significantly longer P1 latencies than the 15 and 30° gaze elevations ($p < .03$); there was no significant difference in P1 latency between the 15 and 30° gaze elevations.
Experiment 3

oVEMP waveforms recorded at four different stimulus levels are shown in Figure 5. The stimulus frequency was 500 Hz and the vertical gaze elevation was 30°. The response amplitude and response prevalence increased as a function of stimulus level, and the maximum response prevalence was obtained at the maximum level (125 dB peak SPL). Contralateral oVEMP thresholds ranged from 105 to 125 dB peak SPL in each ear with mean thresholds of 118.5 dB peak SPL (±6.1) and 119.4 dB peak SPL (±5.6) in the left and right ears, respectively.

The individual and mean amplitude and latency data are plotted as a function of stimulus level in Figure 6. The individual data were jittered so that overlapping data points were not obscured. The data in the upper panel show an increase in the mean oVEMP amplitude as a function of stimulus level for levels >110 dB peak SPL as well as an increase in the variability of oVEMP amplitude at 120 and 125 dB peak SPL. The amplitude data at 100 and 105 dB peak SPL were not included in the statistical analysis as responses were absent in all but 2 of 34 ears. The results of the RMANOVA indicated a significant main effect of stimulus level on amplitude ($F(1.08, 17.28) = 20.62, p < .0001$). Post hoc paired comparisons revealed significant differences in amplitude between all possible pairs of stimulus levels from 110 dB to 125 dB peak SPL ($p < .02$). There was no significant main effect for ear or for the interaction of level and ear. There was no significant main effect of stimulus level or ear on P1 latency, and the interaction of level and ear was also not significant.

Figure 3. The effect of vertical gaze elevation on the contralateral oVEMP. The individual oVEMP waveforms are shown in the left column, and the corresponding grand average waveforms are in the right column. The vertical dashed line at 0 msec indicates stimulus onset. The stimulus was a 500 Hz tone burst at 125 dB peak SPL. The vertical gaze elevation and the number of subjects with present responses at each gaze elevation are indicated in the middle of the figure (total number of subjects tested = 17).

Figure 4. The effect of vertical gaze elevation on contralateral oVEMP amplitude and latency. N1-P1 amplitude is plotted in the upper panel, and N1 (squares) and P1 (circles) latencies are plotted in the lower panel. The individual data are represented by the open symbols and the mean data by the solid symbols. The stimulus was a 500 Hz tone burst at 125 dB peak SPL. The numbers in parentheses above the x-axis in the lower panel indicate the number of subjects with present responses at each gaze elevation (total number of subjects tested = 17).
The individual and grand average ipsilateral and contralateral oVEMP waveforms are illustrated in Figure 7. The oVEMP waveforms recorded from the eye ipsilateral to the stimulus ear are in the left column, and the oVEMP waveforms recorded from the eye contralateral to the stimulus ear are in the right column. The stimulus frequency was 500 Hz (125 dB peak SPL), and the vertical gaze elevation was 30°. The stimulus level and the number of ears with present responses at each level are indicated in the middle of the figure (total number of ears tested = 34).

The individual and grand average ipsilateral and contralateral oVEMP waveforms are illustrated in Figure 7. The oVEMP waveforms recorded from the eye ipsilateral to the stimulus ear are in the left column, and the oVEMP waveforms recorded from the eye contralateral to the stimulus ear are in the right column. The stimulus frequency was 500 Hz (125 dB peak SPL), and the vertical gaze elevation was 30°. The number of ears with present responses is indicated below the individual waveforms (total number of ears tested = 34). oVEMP amplitude and response prevalence are substantially greater for the contralateral oVEMPs compared to the ipsilateral oVEMPs. In contrast to the contralateral responses, we observed either a small increase or no increase in the ipsilateral N1-P1 amplitude as a function of stimulus level or gaze elevation (not shown).

The results of the RMANOVA for amplitude indicated a significant main effect of electrode location on N1-P1 amplitude (F(1, 16) = 27.00, p < .0001) with a mean ipsilateral N1-P1 amplitude of 1.2 μV and a mean contralateral N1-P1 amplitude of 5.8 μV. The main effect of ear and the interaction effect of electrode location and ear were not significant. The results of the RMANOVA for N1 latency indicated a significant main effect of electrode location (F(1, 5) = 7.16, p < .05) with a mean contralateral N1 latency of 10.3 msec and a mean ipsilateral N1 latency of 12.1 msec. The main effect of ear was not significant, and there was no significant interaction effect of electrode location and ear. The results of the RMANOVA for P1 latency also indicated a significant main effect of electrode location (F(1, 5) = 18.74, p = .008) with a mean contralateral P1 latency of 15.5 msec and a mean ipsilateral P1 latency of 16.8 msec. The main effect of ear was not significant, and there was no significant interaction effect of electrode location and ear.

The optimal stimulus and recording parameters determined in the three experiments (contralateral response, 500 Hz, 125 dB peak SPL, vertical gaze elevation of 30°) for the initial group of 17 participants were used subsequently to obtain oVEMPs from 30 additional

Figure 5. The effect of stimulus level on the contralateral oVEMP. The individual oVEMP waveforms for both ears are shown in the left column and the corresponding grand average waveforms are in the right column. The vertical dashed line at 0 msec indicates stimulus onset. The stimulus was a 500 Hz tone burst and the gaze elevation was 30°. The numbers in parentheses above the x-axis in the lower panel indicate the number of ears with present responses at each level (total number of ears tested = 34).

Figure 6. The effect of stimulus level on contralateral oVEMP amplitude and latency. N1-P1 amplitude is plotted in the upper panel, and N1 (squares) and P1 (circles) latency is plotted in the lower panel. The individual data are represented by the open symbols and the mean data by the solid symbols. The stimulus was a 500 Hz tone burst, and the gaze elevation was 30°. The numbers in parentheses above the x-axis in the lower panel indicate the number of ears with present responses at each level (total number of ears tested = 34).
The results of Levene’s test indicated no significant differences in the variances between the two groups ($F_{14,1} = 1.14, p = .21$). The results of independent samples t-tests (using a Bonferroni-adjusted p-value of .007) revealed no significant group differences between the means for N1-P1 amplitude, N1 latency, P1 latency, and asymmetry ratio ($t_{22} = .04, p = .15$). The data for the two groups, therefore, were combined, and the descriptive statistics for all 47 participants are listed in Table 1. The response prevalence for the second group of 30 participants was $100\%$, and the vertical dashed line at 0 msec indicates stimulus onset.

Figure 7. The effect of electrode location on the oVEMP. The individual and corresponding grand average waveforms recorded from the eye ipsilateral to the stimulus ear are in the left column, and the individual and grand average waveforms recorded from the eye contralateral to the stimulus ear are in the right column. The stimulus was a monaural 500 Hz tone burst (125 dB peak SPL), and the vertical gaze elevation was 30°. The number of ears with present responses is indicated below the individual waveforms (total number of ears tested = 34), and the vertical dashed line at 0 msec indicates stimulus onset.

We measured a significant effect of frequency on oVEMP amplitude with the largest average N1-P1 amplitudes obtained at 500 and 1000 Hz. Both amplitude and response prevalence decreased at frequencies above and below 500 and 1000 Hz; the maximum response prevalence was obtained at 500 Hz. These results are consistent with previous studies that have shown broad frequency tuning with maximum amplitudes and maximum response prevalence between 500 and 1000 Hz and indicate that stimulus frequencies within this range are optimal for the clinical application of the air conduction oVEMP (Chihara et al, 2009b; Todd et al, 2009; Park et al, 2010; Lewis et al, 2010).

A comparison of the frequency tuning characteristics of the oVEMP and cVEMP may also provide insight concerning the peripheral origin of the two responses. For example, Todd et al (2009) compared the frequency response properties of the oVEMP and cVEMP using air conduction stimuli and transmastoid bone conduction stimuli. The results revealed a band-pass tuning for air conduction oVEMPs and cVEMPs with a best frequency between 400 and 800 Hz and a low-pass response for bone conduction oVEMPs and cVEMPs with a best frequency of 100 Hz. Since the central pathways of the two responses are different (vestibulocuclar vs. vestibulo-collic), the authors interpreted these findings as indicating that the tuning was determined at or distal to the vestibular nucleus with the greatest contribution at the level of the otolith organs. Specifically, they suggested that bone conduction activates preferentially the utricle, whereas air conduction stimuli are selective for the saccule, and that the findings are consistent with anatomical and structural differences between the two end-organs that produce a lower mechanical resonance for the utricle compared to the saccule (Rosenhall, 1972; Wright et al, 1979; Uzun-Coruhlu, et al, 2007). More recent evidence obtained in the guinea pig, however, indicates that both utricular and saccular irregular afferents respond to both air conduction and bone conduction stimuli (Curthoys and Vulovic, 2011). Curthoys et al (2011) have proposed, therefore, that the observed differences in the best frequency for VEMPs elicited by air conduction versus bone conduction stimuli are related to differences in the transmission pathway for each stimulus rather than the preferential activation of the saccule and utricle by air conduction and bone conduction stimuli, respectively. Specifically, Curthoys and colleagues have suggested that the best frequency for activation of the otolith receptors by bone conduction stimuli is dependent on the direction of the stimulus as well as the size, mass, and resonance of the skull. In contrast, air conduction stimuli initiate a pressure wave in the labyrinth via stapes motion, and therefore the best frequency is determined predominantly by the middle ear transfer function.

**DISCUSSION**

Prior to clinical use, we have measured the effects of several stimulus and recording parameters on the air conduction oVEMP. Specifically, we have quantified the relatively large effects of stimulus frequency, stimulus level, gaze elevation, and electrode location on the response prevalence, amplitude, and latency of the oVEMP for monaural air conduction stimuli. The maximum response prevalence was obtained for contralateral oVEMPs using a 500 Hz tone burst presented at 125 dB peak SPL during upward gaze at an elevation of 30°.

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In the present study, oVEMP amplitude and response prevalence increased as gaze elevation increased from 0 to 30°, and the largest average N1-P1 amplitude was observed at a gaze elevation of 30°. The 30° gaze elevation produced significantly larger amplitudes than the 15 and 0° gaze elevations, and the 15° gaze elevation produced significantly larger amplitudes than the 0° gaze elevation. Overall, these results are consistent with those of previous studies that have examined the effect of gaze elevation on the air conduction oVEMP (Chihara et al, 2007; Govender et al, 2009; Welgampola et al, 2009). We obtained almost a fivefold increase in average contralateral N1-P1 amplitude (1.3 to 6.2 μV) from 0 to 30°, whereas Govender et al (2009) and Welgampola et al (2009) showed a two- to threefold increase in average oVEMP amplitude from 0 to 20°. Govender et al (2009) observed an 83% response rate for the contralateral oVEMP during neutral gaze (0°) compared to a 41% response rate obtained in the present study. The discrepancy is likely related to differences in stimulus level as Govender et al (2009) used either a 136 dB or 142 dBpeak SPL 500 Hz tone burst compared to a 125 dBpeak SPL 500 Hz tone burst in the present study. These results indicate that a gaze elevation of 20 to 30° may be optimal for the clinical application of the air conduction oVEMP and that gaze elevation should be controlled due to its significant effect on oVEMP amplitude. It should be noted that Govender et al (2009) obtained an increase in oVEMP amplitude of >50% in five subjects when gaze elevation was increased from 20° to maximum (i.e., for maximum gaze the subjects were instructed to direct their gaze maximally upward) and suggested that a maximum gaze elevation should be attempted in patients with absent oVEMP s in order to determine the presence of any residual otolith function.

The observed increase in contralateral oVEMP amplitude as a function of gaze elevation is consistent with the inferior oblique (IO) muscle as a likely source since the IO muscle produces extorsion and elevation of the eye (Leigh and Zee, 1999), and air conduction stimuli have been shown to produce extorsion of the contralateral eye (Todd et al, 2007). In addition, the IO muscle is located superficially and transverse to the recording electrodes and is brought closer to the surface of the skin with superior gaze, which may enhance its contribution to the oVEMP (Porter et al, 2003). Air conduction stimuli, however, also produce upward and downward eye movements, so it is difficult to rule out the inferior rectus muscle as a possible additional source of the contralateral oVEMP (Zhou et al, 2004; Welgampola et al, 2009).

We obtained a significant effect of stimulus level on oVEMP amplitude at 500 Hz, and significant differences in amplitude between all possible pairs of stimulus levels from 110 dB to 125 dBpeak SPL were observed. The average oVEMP threshold at 500 Hz was 118.9 dBpeak SPL (n = 34 ears). Previous studies have reported average oVEMP thresholds at 500 Hz of 129 dB SPL, 110 dB peak SPL, and 83 dB nHL (Chihara et al, 2007; Wang et al, 2009; Park et al, 2010). Our average oVEMP threshold is most comparable to the average threshold (110 dB peak SPL) obtained by Wang et al (2009) as their stimulus duration (4 msec), gaze elevation (30–35°), and the metric used to calibrate stimulus level (peak SPL) were the same as in the present study. The clinical utility of the air conduction oVEMP threshold is relevant in the assessment of patients suspicious of superior semicircular canal dehiscence (SSCD). Analogous to cVEMP threshold, the air conduction oVEMP threshold is abnormally low in patients with SSCD (Welgampola et al, 2008). oVEMP amplitude obtained at a suprathreshold level, however, has been shown to better distinguish between SSCD patients and normals than oVEMP threshold (Rosengren et al, 2008).

There was a significant effect of electrode location (ipsilateral vs. contralateral eye) on oVEMP amplitude, latency, and response prevalence. Both oVEMP amplitude and response prevalence were significantly greater for the contralateral oVEMP compared to the ipsilateral oVEMP, and contralateral latencies were significantly shorter than ipsilateral latencies. These results are

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Table 1. Mean ±SD (and range) for the Contralateral Air Conduction oVEMP at 500 Hz

<table>
<thead>
<tr>
<th></th>
<th>Left ear</th>
<th>Right ear</th>
</tr>
</thead>
<tbody>
<tr>
<td>Response prevalence (%)</td>
<td>83</td>
<td>85</td>
</tr>
<tr>
<td>N1-P1 amplitude (μV)</td>
<td>5.6 ± 4.4 (0.8–19.8)</td>
<td>5.3 ± 4.4 (1.2–25.7)</td>
</tr>
<tr>
<td>Asymmetry ratio (%)</td>
<td>18.6 ± 11.6 (2.1–41.7)</td>
<td></td>
</tr>
<tr>
<td>Threshold (dBpeak SPL)</td>
<td>118.5 ± 6.1 (105–125)</td>
<td>119.4 ± 5.6 (105–125)</td>
</tr>
<tr>
<td>N1 latency (msec)</td>
<td>10.6 ± 0.9 (9.7–13.6)</td>
<td>10.6 ± 1.1 (9.2–14.3)</td>
</tr>
<tr>
<td>P1 latency (msec)</td>
<td>15.9 ± 1.0 (14.2–18.2)</td>
<td>15.9 ± 1.1 (14.3–19.3)</td>
</tr>
</tbody>
</table>

Note: All values in the table (with the exception of threshold) were obtained at a vertical gaze elevation of 30° at 125 dBpeak SPL.

*Total number of subjects tested = 47 (94 ears).

1n = 39 left ears and 40 right ears.

2n = 37 subjects.

3n = 17 subjects.
consistent with those of previous studies (Chihara et al., 2007; Wang et al., 2009; Govender et al., 2009). In contrast to the contralateral N1-P1 amplitude, we observed little or no increase in the ipsilateral N1-P1 amplitude as a function of gaze elevation. It has been suggested that the relatively low ipsilateral response rate and the lack of a modulatory effect of gaze elevation on the ipsilateral N1-P1 amplitude make it unlikely that the ipsilateral oVEMP is mediated by the same extraocular muscle (inferior oblique) as the contralateral oVEMP (Govender et al., 2009). In addition to gaze elevation, we observed a reduced modulatory effect of stimulus level on the ipsilateral N1-P1 amplitude.

The optimal stimulus and recording parameters determined in the present study for the initial group of 17 participants were used subsequently to obtain oVEMPs from 30 additional participants. The descriptive statistics for all participants are listed in Table 1. In addition, a summary of the literature concerning the normal response characteristics of the air conduction oVEMP is provided in Table 2. As noted in the results section, the overall response prevalence in the present study was 84%. Previous studies have reported response prevalence rates for the monaural air conduction oVEMP in young normal adults that range from 80 to 100% (Chihara et al., 2007; Cheng et al., 2009; Wang et al., 2009; Welgampola et al., 2009; Park et al., 2010). The variability in oVEMP prevalence rates observed across studies may be related to the use of different vertical gaze elevations and/or stimulus levels as both factors have a significant effect on N1-P1 amplitude. For example, Govender et al. (2009) showed an approximate doubling of the average N1-P1 amplitude between a gaze elevation of 0° and 20° in 10 normal subjects (see their Figure 1). In the present study, we observed absent oVEMPs in 15 of 94 ears at the maximum gaze elevation (30°) and at the maximum stimulus level (125 dB peak SPL). When we increased the stimulus level to 130 dB peak SPL, however, the number of ears with absent responses decreased from 15 to 10. In addition to gaze elevation and stimulus level, it is also possible that stimulus duration affects oVEMP response prevalence. As noted in Table 2, the two studies with prevalence rates of 100% used stimulus durations of 8 msec whereas the studies with prevalence rates <100% used stimulus durations ≤5 msec. Although the effects of stimulus duration on the oVEMP have not been evaluated, air conduction cVEMP amplitude increases with an increase in the stimulus duration from 1 to 7 msec (Welgampola and Colebatch, 2001b). It seems likely, therefore, that the absent air conduction oVEMPs observed in some young normal adults may be related to the use of an inadequate gaze elevation, stimulus level, stimulus duration, or some combination thereof.

Table 2. Summary of Literature Review for the Monaural Air Conduction oVEMP in Normal Adult Participants Using a 500 Hz Tone Burst

<table>
<thead>
<tr>
<th>Study</th>
<th>Ears (n)</th>
<th>Age range (yr)</th>
<th>Rise-plateau-fall Level (msec)</th>
<th>Vertical gaze elevation (˚)</th>
<th>N1 latency* (msec)</th>
<th>P1 latency* (msec)</th>
<th>Prevalence (%)</th>
<th>N1-P1* (µV)</th>
<th>Asymmetry ratio* (%)</th>
<th>Threshold † (dB SPL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chihara et al., 2007</td>
<td>20</td>
<td>23–59</td>
<td>1-2-1</td>
<td>125 dB SPL</td>
<td>90</td>
<td>7.0 ± 4.0</td>
<td>80</td>
<td>6.3 ± 2.9</td>
<td>19.3 ± 6.0</td>
<td>103 ± 14</td>
</tr>
<tr>
<td>Wang et al., 2009</td>
<td>40</td>
<td>22–33</td>
<td>1-2-1</td>
<td>117 dB peak SPL</td>
<td>90</td>
<td>6.5 ± 4.0</td>
<td>85</td>
<td>6.3 ± 2.9</td>
<td>11.9 ± 6.0</td>
<td>96 ± 9</td>
</tr>
<tr>
<td>Govender et al., 2009</td>
<td>10</td>
<td>27–32</td>
<td>1-2-1</td>
<td>125 dB peak SPL</td>
<td>100</td>
<td>6.3 ± 2.9</td>
<td>90</td>
<td>4.4 ± 1.5</td>
<td>10.6 ± 3.1</td>
<td>95 ± 9</td>
</tr>
<tr>
<td>Cheng et al., 2009</td>
<td>30</td>
<td>24–31</td>
<td>1-2-1</td>
<td>127 dB peak SPL</td>
<td>100</td>
<td>6.4 ± 4.0</td>
<td>80</td>
<td>15 ± 3.1</td>
<td>11.9 ± 6.0</td>
<td>96 ± 9</td>
</tr>
<tr>
<td>Park et al., 2010</td>
<td>40</td>
<td>24–34</td>
<td>2-4-2</td>
<td>95 dB nHL</td>
<td>100</td>
<td>5.7 ± 2.8</td>
<td>80</td>
<td>31.0 ± 6.0</td>
<td>13.3 ± 4.6</td>
<td>100 ± 10</td>
</tr>
<tr>
<td>Current study</td>
<td>94</td>
<td>18–34</td>
<td>2-0-2</td>
<td>125 dB peak SPL</td>
<td>119 dB peak SPL</td>
<td>5.5 ± 2.4</td>
<td>84</td>
<td>16 ± 4.4</td>
<td>19.6 ± 9.1</td>
<td>106 ± 10</td>
</tr>
</tbody>
</table>

*Mean ± SD. †Mean thresholds. See Equation (1) for calculation of the AR.
In patients with unilateral superior vestibular neuritis (SVN), the oVEMP recorded beneath the contralateral eye is reduced or absent in response to 500 Hz tone bursts presented via bone conduction to the midline forehead (Fz) in the presence of normal air conduction cVEMPs (Iwasaki et al, 2009; Manzari et al, 2010a). These findings indicate that the bone conduction oVEMP is mediated predominantly by the utricular afferents. Recently, two case reports have shown a dissociation between the presence/absence of air conduction oVEMPs and air conduction cVEMPs (Manzari et al, 2010b; Murofushi et al, 2010), and Curthoys et al (2011) have demonstrated a reduction or absence of both the air conduction and bone conduction oVEMP in patients with SVN and normal cVEMPs. These findings have been interpreted to suggest that, in addition to the bone conduction oVEMP, the air conduction oVEMP is also mediated predominantly by the utricle/superior vestibular nerve. It seems important to note, however, that the two bone conduction oVEMP studies comprised a total of 145 SVN patients whereas the sole air conduction oVEMP study included 10 SVN patients. Using both cVEMP and oVEMP responses to air conduction and bone conduction stimuli, Taylor et al (in press) found that the prevalence of unilateral VEMP abnormalities was greatest for air conduction oVEMPs (50%) and air conduction cVEMPs (40%) in a group of 60 patients with a diagnosis of clinically definite Ménière’s disease. Given that endolymphatic hydrops is observed more frequently in the saccule than the utricle (Paparella, 1985; Schuknecht, 1986; Okuno and Sando, 1987), the similarity in the prevalence of cVEMP and oVEMP abnormalities using air conduction stimuli suggests the possibility that the air conduction oVEMP may be mediated, in part, by the saccule. The origin of the air conduction oVEMP and the specific transmission pathway/mechanism by which different stimuli (air conduction and bone conduction) activate the saccular and utricular receptors is the subject of much debate and continued research in both animals and humans (Colebatch, 2010; Curthoys, 2010a, 2010b; Halmagyi and Carey, 2010; Todd, 2010; Welgampola and Carey, 2010).

**CONCLUSIONS**

We have quantified the large effects of stimulus frequency, stimulus level, gaze elevation, and electrode location on the response prevalence, amplitude, and latency of the air conduction oVEMP. The maximum N1-P1 amplitude and maximum response prevalence were obtained for the contralateral oVEMP using a 500 Hz tone burst presented at 125 dB peak SPL during upward gaze at an elevation of 30°. These stimuli and recording parameters were used to establish normative data that may be useful for the clinical application of the air conduction oVEMP.

### REFERENCES


