The Effects of Click and Tone-Burst Stimulus Parameters on the Vestibular Evoked Myogenic Potential (VEMP)

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Vestibular evoked myogenic potentials (VEMPs) were first described by Bickford et al (1964), and recently have been proposed as a reliable clinical test of saccular or inferior vestibular nerve function (Colebatch, 2001). VEMPs are short latency electromyograms (EMG) that are evoked by high-level acoustic stimuli and are recorded from surface electrodes over the tonically contracted sternocleidomastoid (SCM) muscle. The neurophysiological and clinical data indicate that VEMPs are mediated by a pathway that includes the saccular macula, inferior vestibular nerve, the lateral vestibular nucleus, the lateral vestibulospinal tract, and the motoneurons of the ipsilateral SCM muscle (Halmagyi and Curthoys, 2000). Currently, conventional vestibular assessment (caloric and rotational testing) is limited to the evaluation of the horizontal semicircular canal, which is one of the five peripheral vestibular organs. VEMP recordings may supplement the current test battery by providing diagnostic information about saccular or inferior vestibular nerve function.

The VEMP waveform consists of an early positive-negative component (p13-n23) and a later negative-positive (n34-p44) component. The early positive-negative component is dependent on the integrity of vestibular afferents as it is abolished after vestibular nerve section but preserved in subjects with severe-to-profound sensorineural hearing loss (Colebatch and Halmagyi, 1992). Conversely, the later negative-positive component appears to be mediated by cochlear afferents (Colebatch et al, 1994) although recent evidence suggests that the source of the later component has not been delineated (Wu and Young, 2002).

Most investigators have measured VEMPs using high-level click stimuli (Lim et al, 1995; Robertson and Ireland, 1995; Bath, 1998; Li et al, 1999; Murofushi, 1999; de Waele et al, 1999) and have found that VEMP amplitude is influenced by click level and EMG level whereas latency is independent of both variables. The few click-evoked VEMP threshold data indicate that VEMP thresholds to clicks range from 75 to 100 dB nHL (Colebatch et al, 1994; Lim et al, 1995; Ochi et al, 2001).

Data from animal studies indicate that single afferent saccular nerve fibers are most sensitive to low-frequency acoustic stimuli; therefore, low-frequency tone bursts may provide a more robust VEMP response than broadband clicks (McCue and Guinan, 1994; Murofushi et al, 1995). There are few data, however, on the characteristics of VEMPs obtained with tone-burst stimuli. Two investigators have reported that the VEMP amplitude is influenced by stimulus frequency (Murofushi et al, 1999; Todd et al, 2000), although these studies were restricted to amplitude measurements at a single stimulus, and no latency data were provided. Recently, Welgampola and Colebatch (2001) found that tone-burst-evoked responses showed no latency effect and frequency tuning with the largest amplitude at 500 and 1000 Hz.

Prior to routine clinical application of the VEMP, further study is needed to determine the effects of stimulus parameters on the response characteristics. Most previous studies were performed with bilateral activation of the SCM muscle, and/or VEMP amplitudes were normalized to control for the effects of the tonic EMG activity (Colebatch et al, 1994; Murofushi et al, 1999; Welgampola and Colebatch, 2001). The present experiments were designed to determine the effects of stimulus parameters on VEMP latency, amplitude, and threshold using a direct method to control for tonic EMG level during unilateral activation of the SCM muscles (Akin and Murnane, 2001).
METHOD

Two experiments were performed. Experiment 1 was designed to assess the effect of click level on the VEMP, whereas Experiment 2 was designed to determine the effect of tone-burst frequency and tone-burst level on the VEMP. All subjects in both experiments had normal hearing sensitivity ($\leq$ 20 dB HL, ANSI 1996) at octave intervals from 250 to 8000 Hz, negative histories of middle-ear pathology, and no history of vestibular or neurological disease.

Procedures

Since VEMP amplitude increases as a function of tonic EMG amplitude (Colebatch et al, 1994; Lim et al, 1995), the VEMP and tonic EMG were recorded concurrently. VEMPs were obtained by averaging the acoustically evoked electromyogram of the SCM muscle during tonic contraction. Recording methods were similar in both experiments and reported previously (Akin and Murnane, 2001). Briefly, the subjects were seated upright and instructed to turn their heads to one side to activate unilaterally the SCM muscle. A two-channel recording of the myogenic response was obtained with noninverting electrodes placed at the midpoint of the SCM muscle, the inverting electrode sites were at the sternoclavicular junctions, and the ground electrode was placed on the forehead. Both the click and tone-burst stimuli were presented monaurally to the ear ipsilateral to the activated SCM muscle via ER3A (Etymotic Research) insert earphones at a repetition rate of 5/sec. The VEMP response was amplified (5,000) and bandpass filtered from 20–1500 Hz with a 12 dB/octave slope (Nicolet Spirit 2000). The 100 msec epochs included a 20 msec prestimulus baseline. Responses to 128 stimuli were averaged, and three responses were obtained from each side at each stimulus level.

A two-channel EMG recording from the SCM muscles was obtained concurrently with the VEMPs. An EMG stand-alone differential surface electrode (DelSys, DE-2.1) was placed on the SCM muscle midway between the mastoid process and sternoclavicular junction on each side of the neck, with a reference electrode attached to the wrist. The subjects were provided visual feedback of their EMG amplitude via the computer monitor and software (DelSys, EMGworks Signal Acquisition and Analysis Software) (Akin and Murnane, 2001). The subjects were asked to maintain head rotation during each trial to produce a rectified EMG rms amplitude of $\sim$50 mV. The 50 mV tonic EMG level was verified before and after each trial. Tonic EMG amplitude ranged from 45 to 50 mV for the right and left SCM muscles for each experimental condition, indicating that subjects were able to approximate consistently the 50 mV target level.

EXPERIMENT 1: CLICKS

Subjects and Procedures

Nineteen subjects (ten males and nine females) ranging in age from 22 to 51 years (mean = 32.1 years, SD = 10.1) were enrolled in Experiment 1. VEMPs were obtained from each side using rarefaction click stimuli presented at levels from 80 to 100 dB nHL (0 dB nHL = 35 dB peak SPL) in 5 dB increments. Peak-to-peak amplitudes (P1-N1) and absolute latencies (P1 and N1) were calculated from the mean of the three responses obtained from each subject at each click level.

Results and Discussion

Representative VEMP waveforms obtained from one subject are shown in Figure 1. For this subject, no response was obtained...
at 85 dB nHL, and a questionable response was obtained at 90 dB nHL. The VEMP threshold for this subject was 95 dB nHL with the largest amplitude response obtained at 100 dB nHL. The waveforms obtained at 100 dB nHL were characterized by a positive peak (P1) at 12 msec and a negative peak (N1) at 20 msec. These latencies are consistent with previously reported descriptions of the VEMP elicited by clicks (e.g., Colebatch et al, 1994). A second positive peak was observed at ~26 msec, but previous studies have suggested that only P1 and N1 are of vestibular origin (Colebatch and Halmagyi, 1992), and the later components may originate from cochlear afferents (Colebatch et al, 1994) or a cochleovestibular source (Wu and Young, 2002). These later components were not considered in the current study.

VEMPs were obtained with 100 dB nHL clicks in all 19 subjects (38 sides total), and most subjects (35 of 38 sides) had VEMPs at 95 dB nHL on both sides. VEMPs were recorded at 90 dB nHL in 20 of 38 sides (53 percent) and at 85 dB nHL in 10 of 38 (26 percent) sides. Below 100 dB nHL, the presence or absence of VEMPs differed between sides in some subjects. For example, at 95 dB nHL, three subjects had VEMPs on only one side.

Amplitude

The individual and mean P1-N1 amplitudes are plotted as a function of click level in Figure 2 (upper panel). Mean VEMP amplitude increased as a function of click level (filled symbols). P1-N1 amplitudes for 100 dB nHL clicks ranged from 16 to 179 µV (mean = 60 µV). A 2 x 4 (side x level) repeated measures ANOVA for amplitude at 85–100 dB nHL indicated that the main effect of side was not significant (p = 0.21), but the main effect of click level was significant [F (3,18) = 21.8, p < 0.0001]. As the level of the click increased there was a corresponding increase in the level of the VEMP amplitude, a finding that has been observed in previous studies (Colebatch et al, 1994; Ochi et al, 2001). Post hoc means contrasts were significant for all nonadjacent pairs (e.g., 85 dB nHL vs. 100 dB nHL) (p < 0.01) and the 90–95 dB nHL adjacent pair [F (1,18) = 42.6, p = 0.002]. The stimulus level and side interaction was not significant (p = 0.14), indicating that the change in VEMP amplitude as a function of stimulus level was not dependent on the side (right versus left) from which the VEMP was recorded. A t-test indicated no significant difference between VEMP amplitudes to 120 dB nHL clicks in male and female subjects (p = 0.26).

Latency

The individual and mean P1 and N1 latencies are plotted as a function of click level in Figure 2 (lower panel). The mean P1 and N1 latencies were 12 msec (SD = 2.5 msec) and 19 msec (SD = 1.5 msec), respectively, for 100 dB nHL clicks. A 2 x 3 (side x click level) repeated measures ANOVA for latency on the 90, 95, and 100 dB nHL data revealed no significant main effects for side (p = 0.77) and level (p = 0.60). The 80 and 85 dB nHL latency data were not included in the ANOVA, because responses were not recorded at these levels in most subjects. A t-test indicated no significant difference between VEMP latencies to 100 dB nHL clicks in male and female subjects (P1: p = 0.89; N1: p = 0.53).

In contrast to VEMP amplitude, the VEMP latency did not vary as a function of click level in the present study or in previous studies (Colebatch et al, 1994; Lim et al, 1995). Colebatch et al suggested that this finding is consistent with the reflexive nature of the response and reflects a simple neurophysiological pathway for the VEMP.
response. The neurophysiological and clinical data suggest that VEMPs are generated by activation of vestibular afferents arising from the saccule and rapidly transmitted through the lateral vestibular nucleus to the lateral vestibulospinal tract and the motoneurons of the ipsilateral SCM muscle (Halmagyi and Curthoys, 2000).

**Threshold**

VEMP threshold was defined as the lowest stimulus level that elicited a replicated, visually detectable P1-N1 wave. Click-evoked VEMP thresholds ranged from 80 to 100 dB nHL, and the average threshold was 91 dB nHL (SD = 5.2 dB). Other studies have reported mean VEMP thresholds similar to the present study. Using a similar tonic EMG level, Colebatch et al (1994) obtained thresholds at 75–85 dB nHL. Similarly, Ochi et al (2001) calculated mean VEMP thresholds at 87.8 dB nHL, and Welgampola and Colebatch (2001) found that click-evoked VEMP thresholds ranged from 75 to 100 dB nHL (mean = 89.6). Comparisons among studies, however, are confounded by differences in tonic EMG levels, decibel reference levels, and recording methods.

VEMP thresholds in humans are consistent with animal studies that show the threshold for evoking responses in the saccular afferent is 60 to 70 dB above the auditory brainstem response threshold for click stimuli (Murofushi et al, 1995). Lower VEMP thresholds (< 75 dB nHL), however, have been reported in patients with dehiscence of the superior semicircular canal (Brantberg et al, 1999; Watson et al, 2000) and in patients with vestibular hypersensitivity to sound (Tullio phenomenon) (Bronstein et al, 1995; Colebatch et al, 1998; Watson et al, 2000).

**EXPERIMENT 2: TONE BURSTS**

**Subjects and Procedures**

Ten subjects (one male and nine females) ranging in age from 22 to 23 years were
enrolled in Experiment 2. VEMP responses were obtained from each side using tone bursts at 250, 500, 750, 1000, 1500, and 2000 Hz (rarefaction onset phase, Blackman gating function, 2-cycle rise/fall time with no plateau) presented at five levels from 100 to 120 dB peakSPL in 5 dB increments. In six subjects, no response was obtained with 120 dB peakSPL tone bursts at 250, 1500, or 2000 Hz, and the stimulus level was increased to 125 dB peakSPL. To determine if the VEMP latency was influenced by the rise/fall time of the tone burst, the VEMPs also were recorded using 120 dB peakSPL tone bursts with rise/fall time held constant (4 msec) across frequency. Peak-to-peak amplitudes (P1-N1) and absolute latencies (P1 and N1) were calculated from the mean of the three responses obtained from each subject at each stimulus level and frequency.

Results and Discussion

Representative waveforms obtained from one subject at each frequency and level are shown in Figure 3. The largest amplitudes and lowest thresholds were obtained at 500 and 750 Hz with the smallest amplitudes and highest thresholds recorded with 1500 and 2000 Hz tone bursts.

Amplitude

In Figure 4, the mean P1-N1 VEMP amplitude for each frequency is plotted as a function of stimulus level. For each frequency, mean VEMP amplitude increased as a function of stimulus level. At the higher levels, the 500 and 750 Hz tone bursts evoked the largest VEMP amplitudes, and the 2000 Hz tone burst produced the smallest amplitudes. A 2 x 5 x 6 (side x level x frequency) repeated measures ANOVA for amplitude was performed. VEMP amplitude was significantly different depending on stimulus level [F (4,9) = 30.2; p = 0.0002] and stimulus frequency [F (5,9) = 14.8; p = 0.0015]. Post hoc means contrasts indicated that only the 120–115 dB peakSPL adjacent pair was significantly different (p = 0.01), whereas all nonadjacent pairs (e.g., 100 vs. 115 dB peakSPL) were significantly different (p < 0.01). Post hoc means contrasts revealed that the following pairwise comparisons for frequency were significant (p ≤ 0.008): 250 Hz vs. 500 Hz, 500 Hz vs. 1500 Hz, 500 Hz vs. 2000 Hz, 750 Hz vs. 1500 Hz, 750 Hz vs. 2000 Hz, and 1000 Hz vs. 2000 Hz. The ANOVA showed no significant effect of side on amplitude.

The frequency and stimulus level interaction was significant [F (20,9) = 11.9, p < 0.0001), indicating that the change in VEMP amplitude (averaged across the 2 sides) as a function of stimulus level was dependent on stimulus frequency. All other interactions were not significant. The increase in VEMP amplitude as a function of stimulus level is consistent with the click results from Experiment 1 and previous studies using click stimuli (Colebatch et al, 1994; Lim et al, 1995; Ochi et al, 2001). Input-output functions for tone-burst-evoked VEMPs have not previously been reported.
The mean VEMP amplitude and standard deviations are plotted as a function of stimulus frequency at 120 dB peakSPL in Figure 5. The number of sides with VEMPs present is indicated for each frequency. All subjects had VEMPs on both sides for 500, 750, and 1000 Hz tone bursts (n = 20). VEMPs were recorded from 19 of 20 sides for 250 Hz, 17 of 20 sides for 1500 Hz, and only 10 of 20 sides for 2000 Hz. The largest P1-N1 mean amplitudes were obtained with 500 and 750 Hz tone bursts (112 mV and 110 µV, respectively), and a mean of 66 µV was obtained at 250 Hz, 95 µV at 1000 Hz, 68 µV at 1500 Hz, and 49 µV at 2000 Hz.

Previous studies have reported similar effects of stimulus frequency on the response amplitude. For example, Murofushi et al (1999) observed larger VEMP amplitudes with 500 Hz tone bursts than with 1000 and 2000 Hz tone bursts, and Welgampola and Colebatch (2001) reported largest VEMP amplitudes at 500 and 1000 Hz. Todd et al (2000) recorded VEMPs with frequencies ranging from 100 to 3200 Hz and demonstrated that the VEMP has well-defined frequency tuning with a maximum in response amplitude ranging from 200 to 400 Hz, although stimulus frequencies between 400 and 800 Hz were not used. The VEMP frequency response in humans is consistent with neurophysiological findings in cats that show the acoustically responsive afferent fibers in the inferior vestibular nerve have broad, V-shaped tuning curves with best frequencies between 500 and 1000 Hz (McCue and Guinan, 1995).

Tone-evoked VEMP amplitudes were larger than click-evoked amplitudes when comparisons were made at equal peak SPLs. For example, the mean click-evoked amplitude at 85 dB nHL (120 dB peak SPL) was 24 µV whereas the mean amplitude for a 120 dB peak SPL 500 Hz tone burst was 88 µV. The magnitude of the amplitude differences between tone-evoked and click-evoked VEMPs increased as tone-burst frequency decreased. The observed amplitude differences, however, may be due to differences in stimulus spectrum level. When comparisons are made at equal peak SPLs, the click has a lower spectrum level than the tone bursts due to its wider bandwidth. In clinical situations in which there are peak output limitations of earphones, a low frequency tone burst may be the stimulus of choice. A statistical comparison of tone-evoked and click-evoked amplitudes was not performed because a different subject group participated in each experiment.

**Threshold**

In Figure 6, the mean VEMP threshold and standard deviations are plotted as a function of stimulus frequency. VEMP thresholds ranged from 100 to 121 dB peakSPL with the lowest thresholds obtained at 500 (mean = 108.8 dB peakSPL, SD = 4.6) and 750 Hz (mean = 108.8 dB peakSPL, SD = 4.8) and the highest thresholds obtained at 2000 Hz (mean = 121 dB peakSPL, SD = 3.8). To compare the thresholds of the VEMP obtained in humans with the thresholds of acoustically
responsive vestibular afferents of the inferior vestibular nerve in cats, data from the current study were plotted with data from McCue and Guinan (1995) in Figure 7. McCue and Guinan found that the inferior vestibular nerve fibers were responsive to sound with best frequencies between 500 and 1000 Hz and thresholds ranging from 90 to 115 dB SPL. The data in Figure 7 show that the best thresholds and frequencies for the VEMP in humans were similar to those obtained from the single unit recordings from the inferior vestibular nerve in cats.

Latency

The individual and mean VEMP latencies are plotted as a function of stimulus frequency in Figure 8. The data obtained with 2-cycle rise/fall time (upper panel) show that VEMP latency decreases as the stimulus frequency increases. Mean latencies for 2000 Hz tone bursts were 13.6 msec and 18.7 msec for P1 and N1, respectively. In contrast, mean latencies for 250 Hz tone bursts were 19.1 msec for P1 and 26.6 msec for N1. A 2 x 5 (side x frequency) repeated measures ANOVA indicated a significant effect of frequency on response latency [F (4,7) = 151.1; p < 0.0001]. (Data obtained at 2000 Hz were excluded from the ANOVA, owing to the small number of subjects having VEMPs at that frequency.) Post hoc means contrasts indicated all pairwise comparisons for frequency were significant (p ≤ 0.01). The ANOVA showed no significant effect of side on VEMP latency (p = 0.78).

The effect of frequency on latency was an unexpected finding because substantial evidence exists that the VEMP is not a cochlear response (Colebatch et al, 1994). The 2-cycle rise/fall time, however, resulted in variable rise/fall times across stimulus frequency. For example, the 250 Hz tone bursts had rise/fall times of 8 msec for a total duration of 16 msec, whereas the 1500 Hz tone bursts had rise/fall times of 1.3 msec for a total duration of 2.7 msec. To determine if the latency shifts were caused by differences in rise/fall times, VEMPs also were recorded with rise/fall times held constant (4 msec) across frequency. The individual and mean VEMP latency data for constant 4 msec rise/fall times, which are illustrated in the lower panel of Figure 8, show little or no change as a function of frequency. A 2 x 5 (side x frequency) repeated measures ANOVA indicated a significant effect of frequency on latency with constant rise/fall time stimuli [F (4,8) = 6.6; p = 0.005]; however, the slopes of the latency/frequency functions for the constant rise/fall time stimuli (lower panel) approach unity whereas the functions for variable rise/fall time stimuli (upper panel) show an inverse relationship between latency and frequency (Figure 8). Furthermore, post hoc means contrasts were only significant for three comparisons, all involving 1500 Hz (250 Hz vs. 1500 Hz, 500 Hz vs. 1500 Hz, and 750 Hz vs. 1500 Hz), and the mean differences were ≤ 0.8 msec. Consistent with the reflexive nature of the response, the effects of stimulus frequency on response latencies were largely reduced. In a similar study using tone-burst stimuli with 2.5 msec rise/fall time and no plateau, Welgampola and Colebatch (2001) also reported no significant effect of stimulus
frequency on VEMP latency.

As the tone-burst stimuli did not include a plateau, it is difficult to separate the effects of rise/fall time from those of duration. For a 1000 Hz tone burst, Welgampola and Colebatch (2001) demonstrated that VEMP latency and amplitude increased with an increase in duration from 1 to 7 msec; however, the stimulus rise/fall time was not clearly defined. Similar effects of rise/fall time on VEMP latency and amplitude were found with 500 Hz tone bursts (Cheng and Murofushi, 2001). Further experiments are ongoing in our laboratory to determine the contribution of stimulus rise/fall time versus stimulus duration on the VEMP response characteristics.

CONCLUSIONS

The present experiments examined the effects of click level and tone-burst frequency and level on the VEMP latency, amplitude, and threshold in subjects with normal audiovestibular function. At the highest stimulus levels, VEMPs were recorded from both sides of all subjects enrolled in the study. Most subjects had VEMPs present at 500, 750, and 1000 Hz, and few subjects had VEMPs present at 2000 Hz. The response amplitude of the VEMP increased as a function of click and tone-burst level. The largest tone-burst-evoked VEMPs were obtained at 500 and 750 Hz. To control for the effect of tonic EMG rms amplitude on VEMP amplitude, subjects maintained tonic EMG rms at 50 mV during unilateral contraction of the SCM m. Thus, the changes in VEMP amplitude observed in the present experiments are presumably due to stimulus level and frequency effects rather than changes in the tonic EMG rms. It is noteworthy that the stimulus frequency effects of the present study are consistent with those of Welgampola and Colebatch (2001). In contrast to the present study, Welgampola and Colebatch did not attempt to control the EMG level directly but chose to normalize the amplitude of the P1-N1 to the amplitude of the prestimulus baseline. In addition, they recorded the VEMP during bilateral activation of the SCM m. versus the unilateral activation utilized in the present study.

The study demonstrated that some stimulus frequencies evoke VEMPs more reliably than others. By utilizing more optimal stimulus frequencies, valid estimates of saccular function may be obtained. Although 500 and 750 Hz tone bursts produced more robust responses than click stimuli, future studies are necessary to compare responses to clicks and tone bursts with the same spectrum level. In addition, the effect of stimulus rise/fall time versus duration on VEMP latency and amplitude needs to be determined.

Typically, clinical assessment does not include tests of otolith function. Rather, ENG and rotational tests assess the horizontal semicircular canal (one of five vestibular sensory organs). VEMPs may prove to be a useful clinical test to assess saccular or inferior vestibular nerve function, and the identification of saccular involvement may have implications in the management of patients with balance disorders. Vestibular rehabilitation therapy (VRT) exercises are typically based on principles of vestibular adaptation of semicircular canal input. If otolith organ involvement is identified, then VRT exercises designed to stimulate otolithic adaptation may be more effective for managing a patient's symptoms.

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