Effect of Stimulus Frequency on Air-Conducted Vestibular Evoked Myogenic Potentials

Wei Fu1, Junliang Han2, Feng He2, Yuanyuan Wang2, Dong Wei2, Ying Shi2, Ya Bai2, Xiaoming Wang1

1Department of Geriatrics, Xijing Hospital, Air Force Medical University, Xi’an, Shaanxi, China
2Department of Neurology, Xijing Hospital, Air Force Medical University, Xi’an, Shaanxi, China

OBJECTIVE: The aim of this study is to explore the effect of stimulus frequency on air-conducted cervical and ocular vestibular evoked myogenic potential (cVEMP and oVEMP) in healthy subjects.

METHODS: The study included 45 healthy subjects who underwent the VEMP tests. Different stimulus frequencies (250-1500 Hz) were used for air-conducted cVEMP and oVEMP.

RESULTS: In cVEMP, P1 and N1 latencies were significantly affected by different frequencies (P < .01). The amplitude at 500 Hz was significantly larger than those at other frequencies (P < .01). There was no significant main effect of frequency on asymmetry ratio (AR) (P > .05). In oVEMP, there was a tendency for the N1 and P1 latencies to decrease from 250 Hz to 1500 Hz (P < .01). The amplitudes at 500 Hz and 1000 Hz were significantly larger than the amplitudes at 250 Hz and 1500 Hz (P < .01). There was no significant main effect of frequency on AR (P > .05).

CONCLUSION: The optimal stimulus frequency of the cVEMP is 500 Hz and for the oVEMP is 500Hz or 1000Hz. Due to the absence of impact of stimulus frequency, AR is the best parameter of VEMP for clinical use.

KEYWORDS: Frequency, otolith, vestibular, vestibular evoked myogenic potentials

INTRODUCTION
Vestibular evoked myogenic potential (VEMP) is currently being utilized in the assessment of otolith function. It was first described by Colebatch and Halmagyi in 1992 and has since become a standard clinical test of otolith function.1 In clinical application, there are 2 major VEMPs: one is recorded on the neck muscle, termed the cervical vestibular evoked myogenic potential (cVEMP), the other is on the extraocular muscle, termed the ocular vestibular evoked myogenic potential (oVEMP).2 The cVEMP primarily originates from the saccule via the vestibulo-collic reflex, along the inferior vestibular nerve to the ipsilateral sternocleidomastoid muscle.3 The oVEMP primarily originates from the utricle via the superior vestibular nerve, which then crosses the midline to the contralateral medial longitudinal fasciculus and the oculomotor nucleus to the contralateral inferior oblique muscles.1

Air-conducted VEMPs may be affected by different factors such as age, type of stimulus, and stimulus phase.4,7 Furthermore, there is significant variability in individual responses to stimuli of different frequencies. Although the relation between VEMP results and different frequencies has been explored in some reports,8-10 the effect of different frequencies in Asian subjects is unclear. In order to clarify the optimal stimulus frequency of the cVEMP and oVEMP in Asian subjects, we used different frequencies to evoke air-conducted cVEMPs and oVEMPs to investigate the effect of stimulus frequency on air-conducted VEMPs.
MATERIALS AND METHODS

Participants
We recruited 45 healthy subjects in this study. Their mean age was 43.93 ± 10.43 (ranging from 19 to 59 years, 26 males and 19 females). All subjects had normal hearing and vestibular function. Subjects with audiological, vestibular, or central disorders were excluded.

VEMP Testing
VEMP Stimulus Parameter
For VEMP testing, an evoked potential instrument was used (GN Otometrics EP200; version 6.2.1). Air-conducted tone bursts at 250 Hz, 500 Hz, 1000 Hz, and 1500 Hz were presented monaurally via calibrated insert earphones at an intensity of 100dB nHL. The stimulation rate was 5/s, with a 2 ms rise time, 2 ms plateau time, and a 2 ms fall time, with the analysis time for each response of 60 ms; 100 repetitions per trial were delivered. The EMG signals were amplified and bandpass-filtered between 1 Hz and 1000 Hz. We used visual monitoring to control the EMG level (minimum 40 μV and maximum to 200 μV), and the amplitude was raw.

cVEMP Recording
In cVEMP, after the patients were laid supine, an active electrode was attached about 1 cm below the lower eyelid. The reference electrode was placed about 1-2 cm below the active electrode, and the ground electrode was attached on the forehead. The electrode impedance was kept under 5 kΩ. During recording, the subject was asked to look upwards by about 30° at a target. Four frequencies were randomized to apply in all subjects. Each subject was asked to rest for an hour between 2 frequencies of cVEMP tests. The initial positive–negative biphasic waveform comprised peaks P1 and N1.

oVEMP Recording
In oVEMP, an active electrode was attached about 1 cm below the lower eyelid. The reference electrode was attached about 1-2 cm below the active electrode, and the ground electrode was attached on the forehead. The electrode impedance was kept under 5 kΩ. During recording, the subject was asked to look upwards by about 30° at a target. Four frequencies were randomized to apply in all subjects. Each subject was asked to rest for an hour between 2 frequencies of oVEMP tests. The initial negative–positive biphasic waveform comprised peaks N1 and P1.

Peak-to-peak amplitudes, N1 latency, P1 latency, and asymmetry ratio (AR) were measured. The AR = |(Left amplitude–Right amplitude)/(Left amplitude+Right amplitude)|×100.

Statistical Analysis
Air-conducted cVEMP and oVEMP parameters are described in the study as mean±standard deviation. ANOVA was used to assess the effect of frequency on amplitudes, N1 latency, P1 latency, and AR. Post hoc paired t-tests and the Bonferroni correction were applied for multiple comparisons. All analyses were implemented in IBM SPSS statistical software (SPSS, Inc., Chicago, IL, USA). P < .05 was considered to indicate statistically significant differences.

RESULTS
Table 1 shows the parameter results of air-conducted cVEMP for different frequencies in healthy subjects. There was a tendency for the N1 and P1 latencies to decrease from 250 Hz to 1500 Hz (P < .01, Figure 1). The amplitude at 500 Hz was significantly larger than those at other frequencies (P < .01, Figure 2). However, there was no significant effect of frequency on AR (P > .05).

Table 2 shows the parameter results of air-conducted oVEMP for different frequencies in healthy subjects. There was a tendency for the N1 and P1 latencies to decrease from 250 Hz to 1500 Hz (P < .01, Figure 3). The amplitudes at 500 Hz and 1000 Hz were significantly larger than the amplitudes at 250 Hz and 1500 Hz (P < .01, Figure 4). However, there was no significant difference between 500 Hz and 1000 Hz (P > .05), and there was no significant effect of frequency on AR (P > .05).

DISCUSSION
The aim of the present study was to determine the effect of stimulus frequency on air-conducted VEMPs in healthy subjects. We compared the parameters of VEMPs in different frequencies. We found that there was a tendency for the N1 and P1 latencies to decrease from 250 Hz to 1500 Hz. Besides, the 500Hz air-conducted cVEMP demonstrated...
the largest amplitudes. After testing with air-conducted cVEMP in 10 normal volunteers at different stimulus frequencies (50-1200 Hz), Govender et al.9 showed that N1 and P1 latencies gradually increased as frequency increased, with mean latencies being earliest at 50 Hz and latest at 500-800 Hz, which then became earlier again; they also found that the mean amplitude was largest at 500 Hz. This is consistent with the result obtained in this study. Park et al.11 reported that sound stimulation at 500 Hz showed higher amplitudes in cVEMP. However, the AR of cVEMP did not differ significantly. It was similar to our result.

In addition, we also used different stimulus frequencies on air-conducted oVEMP. We found that the prevalence of air-conducted oVEMP responses was 100% at frequencies of 500 Hz, 1000 Hz, and 1500 Hz in healthy subjects. However, the prevalence of air-conducted oVEMP responses at 250 Hz was 89%. Chihara et al. reported that the air-conducted oVEMP response prevalence was lowest at 250 Hz. In contrast, when bone-conducted vibration was delivered, the oVEMP prevalence was improved at 250 Hz. The reason may be the different stimulus types. The air-conducted stimulus contains much less energy than the bone-conducted vibration stimulus. Besides, it may be related to the activated semicircular canal irregularly discharging afferent neurons. Dlugaczyk et al.13 reported that high-frequency bone-conducted vibration (BCV) is a largely selective otolithic stimulus, while low-frequency BCV can activate both otolith and SCC afferents. This finding probably explained our result. Our study also showed that N1 and P1 latencies gradually shortened from 250 Hz to 1500 Hz. The largest oVEMP amplitude was obtained at 500 Hz and 1000 Hz. Murnane et al.,14 testing at similar frequencies (250-2000 Hz), found that 500Hz and 1000Hz resulted in the highest response prevalence and the largest amplitude, and the longest N1 and P1 latencies are seen at 250 Hz. It is similar to our result. Previously, Piker et al.10 demonstrated that age can have a significant effect on the tuning of VEMP, and middle-aged individuals have a shift in their best frequencies for VEMP. On similar grounds, Singh et al.15 have also reported that there is significant interaction between age and frequency tuning for oVEMP. In our study, we recruited participants aged between 19 and 59 years. Although the best frequency was 1000 Hz in some middle-aged individuals, most participants still showed the best frequency at 500 Hz.

The effect of stimulus frequency on air-conducted VEMPs might be attributed to frequency resonance of the otolith organs. It will depend on the anatomical structures of the otolith organs. Some studies suggested that the mass of the otocoria and the stiffness of sensory hair cells can affect the frequency properties of VEMPs,11,16-18 and the
stiffness and mass influence each other and differ in their properties across frequencies. This would result in resonance at a frequency at which the energy will be intensified. The parameters of VEMPs would be further changed.

LIMITATION
There are some limitations in this study. First, the number of subjects was insufficient. Second, we did not include any patients in this study. Finally, we performed the VEMP using only the GN Otometrics EP200 system. It remains unknown whether our results could be generalized to other similar recording systems.

Ethics Committee Approval: The study was approved by the Institutional Review Board of Xijing Hospital, Air Force Medical University, where the subjects were enrolled.

Informed Consent: All subjects provided written informed consent to participate in this study.

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