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Effects of the stimulus phase on the air-conducted ocular vestibular evoked myogenic potential in healthy subjects

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HIGHLIGHTS

- Latencies of oVEMPs are sensitive to the phase of air-conducted sounds (ACS).
- Responses tend to be generated from the rarefaction to the condensation phase of the stimulus.
- ACS tends to stimulate the same type of vestibular afferent units, independent of stimulus polarity.

ABSTRACT

Objective: The study aimed to examine the effect of the stimulus phase of air-conducted sound on ocular vestibular evoked myogenic potentials (oVEMPs).
Methods: oVEMPs were recorded after air-conducted sounds (500 Hz, 4 ms duration), presented with initial condensation (positive), rarefaction (negative), and alternant polarities from 12 healthy subjects.
Results: Most responses showed a bifid n10 peak separated by ~1.9 ms. The most prominent sub-peak after condensation was shorter than the most prominent sub-peak after rarefaction; however, the first sub-peak was shorter after the rarefaction stimuli. When a third sub-peak appeared, it occurred before the most prominent sub-peak after condensation and after the most prominent sub-peak after rarefaction. The latency difference between this third sub-peak and the closest sub-peak was shorter than the difference among the others sub-peaks, in both cases; the oVEMPs after alternating stimuli was an amalgam of the responses to the different stimuli.
Conclusions: The findings suggest that the negative to positive change of the stimulus was the main event responsible for the stimulation, and that when a third sub-peak appeared it was related to the initiation or the end of the stimulus.
Significance: These findings suggested that the oVEMP response, obtained by air conducted sound, was secondary to stimulation of the same type of afferent vestibular unit, independent of the stimulus polarity.

1. Introduction

Following the study of electromyographic responses modulation after auditory stimulation as a means to evaluate the vestibular system by Colebatch and Halmagyi, 1992; Colebatch et al., 1994), clinicians started using vestibular evoked myogenic potentials (VEMPs) to assess the vestibular system.

VEMPs were soon consolidated as vestibular tests that allowed independent evaluation of the utricle/superior vestibular nerve and the saccule/inferior vestibular nerve, and also their central pathways through the ocular VEMP (oVEMP) and the cervical VEMP (cVEMP), respectively. The oVEMP is the result of the modulation of the electromyographic (EMG) activity of the inferior oblique muscle, and the cVEMP is the result of the modulation of

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the EMG activity of the sternocleidomastoid muscle (Colebatch and Rothwell, 2004; Govender et al., 2015; Rosengren et al., 2010; Venhovens et al., 2016; Weber et al., 2012).

VEMPs are short latency reflex responses produced by stimulation of the otolith organs by different types of stimuli, including air-conducted sounds (ACS), bone-conducted vibration (BCV), and electrical stimuli (Brantberg and Tribukait, 2002; Colebatch and Halmagyi, 1992; Colebatch et al., 1994; Halmagyi et al., 1995; Murofushi et al., 1999; Sheykholeslami et al., 2000; Watson and Colebatch, 1998).

It has been known for more than 80 years that loud sounds and vibration may stimulate the vestibular system in healthy humans (von Békésy, 1935). It is also already known that otolith receptors are excited at low frequencies by linear acceleration acting on otoconia, therefore deflecting the hair cells cilia. It was recently proposed, however, that after BCV or ACS at high frequencies, fluid pressure waves are established in the inner ear; which are responsible for the deflection of the cilia that ends up in phase locked action potentials in the irregular afferent units (Curthoys and Grant, 2015).

The oVEMP was introduced later than the cVEMP, and its clinical use was rapidly accepted (Chihara et al., 2009; Iwasaki et al., 2007; Rosengren et al., 2010; Todd et al., 2007; Welgampola, 2008). Knowledge of the effects of stimuli on the responses became an important consideration for understanding their generation, and these characteristics have not yet been fully determined (Cheng et al., 2012; Kantner et al., 2014; Lim et al., 2013; Rosengren et al., 2009).

Studies in different animal species have shown that after stimulation of the otolith organs, the stimulus phase (condensation or rarefaction) is responsible for the responses of different primary afferent units separated by approximately 180°. It was also shown that the afferent units have a tuning curve after ACS and BCV with maximal responses between 500 and 1000 Hz (Curthoys et al., 2006, 2016; McCue and Guinan, 1994; Murofushi and Curthoys, 1997; Young et al., 1977). Although it was demonstrated that the responses also show tuning curves (Chihara et al., 2009; Park et al., 2010; Rauch et al., 2004; Taylor et al., 2012; Todd et al., 2000, 2009; Welgampola and Colebatch, 2001; Zhang et al., 2011) and the responses tend to occur spaced by 2 ms after stimulation with 500 Hz tone bursts (Lim et al., 2013), the effect of the stimulus phase in humans, however, is not as clear. Until this study was written, Govender et al. (2016a) were the only authors to the best of our knowledge who formally described the effect of ACS stimulus polarity in humans and, contrary to what would be expected from the animal studies, they did not find significant differences in latencies or amplitude of the responses.

We believe that understanding the reason for this unexpected finding would be important additional knowledge of the determinants of the responses to ACS in humans, and consequently in their use as diagnostic tools. With this objective in mind, the present study aimed to examine the effects of the stimulus phase using 500-Hz AC stimuli for oVEMPs in normal subjects.

2. Material and methods

Twelve healthy volunteers (7 males) ranging in age from 28 to 61 years old (mean ± sd; 34 ± 10.4) were recruited for the study. All subjects had no history of trauma, vestibular affections, and infectious or inflammatory processes at the external or middle ear, and they presented no abnormalities in Rinne and Weber tests.

All subjects provided informed consent; the study was approved by the UNIFESP Institutional Review Board.

The VEMP recordings were initiated by the application of self-adhesive electrodes after a slight abrasion of the skin with alcohol-embedded gauze. Pairs of recording electrodes, separated by approximately 2 cm, were applied below the right eye slightly lateral to a line passing through the pupil (with the centers of the electrodes aligned with a line passing through the lateral border of the cornea); this montage is close to the one recently proposed by Govender et al. (2016b). A ground electrode was similarly applied to the forehead. The choice to examine the right eye was arbitrary, and it was assumed that examination of the left eye would probably not provide additional information.

After application of the recording electrodes, subjects were asked to sit in an armchair and look upward to a target which resulted in a gaze angle of approximately 35° during the stimuli presentation.

The stimulus consisted of 500 Hz tone bursts (ascending-plateau-descending phases with 0.1–4–0.1 ms) with an intensity of 135 dB SPL, presented to the left ear through a headphone at 5.1 Hz. Responses were collected after condensation, rarefaction, and alternating stimuli; the order of presentation was pseudo-randomized. A short rest was allowed between groups of about 30 stimuli each, until two averages of 100 stimuli for each stimulus phase was obtained; for some of the figures, the average was shown together with the two replications obtained for each stimulus phase.

Stimulation and recording were obtained through Nihon Khoden model Sigma equipment. For each ear stimulation, two channels were recorded simultaneously (one raw and one rectified). Signals were amplified (20 μV/div.), band-pass filtered (5-3000 Hz), and averaged.

Responses were analyzed for their presence and, when present, n10 latencies and absolute amplitudes, as well as n10-p15 peak-peak amplitudes, were measured. Given the relatively small sample size and evidence of non-normal distribution of some variables (particularly amplitudes), comparisons were performed using the Wilcoxon test and Friedman analysis of variance when appropriate; observed differences were considered significant for $\alpha \leqslant 0.05$.

3. Results

All subjects showed the n10 response after the three stimuli. Most subjects showed an n10 response with two sub-peaks, although one was always larger; one single peak was observed less frequently, as well as responses with three sub-peaks. Representative curves showing the more frequent configuration of the peaks in one subject, and the responses of all subjects superimposed, are shown in Fig. 1.

Latencies and amplitudes of the peaks and sub-peaks of the n10 response after each stimulus are shown in Tables 1 and 2.

3.1. Condensation

After condensation stimuli, eight subjects (67%) presented a bifid n10 response, and in all of them the first sub-peak had higher amplitude than the second ($p < 0.02$); in two individuals an extra early small sub-peak (referred as e1) was identified, but the relationship between the main peaks remained, with the first being more prominent (with the larger amplitude). The last two individuals showed only one peak (Table 1, Fig. 2). In all subjects, the first main sub-peak was always larger than the second ($p < 0.01$).

When two main sub-peaks were present, the difference in latency between them was 1.9 ± 0.3 ms; when an e1 sub-peak was present, the latency difference between it and the next sub-peak was between 1.2 and 1.6 ms (mean 1.4 ms), and in both these subjects the difference between the two main sub-peaks was 1.8 ms. The two individuals that showed only one peak had latencies closest to the more prominent sub-peak of the other subjects (Table 1).