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The vestibular evoked-potential profile of Ménière's disease

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ABSTRACT

Objective: To define the ocular and cervical vestibular evoked myogenic potential (oVEMP and cVEMP) profile in Ménière's Disease (MD), we studied air-conducted (AC) sound and bone-conducted vibration (BCV)-evoked responses in 77 patients and 35 controls.
Methods: oVEMPs were recorded from unrectified infra-orbital surface electromyography (EMG) during upward gaze. cVEMPs were recorded from rectified and unrectified sternocleidomastoid EMG during head elevation against gravity. Responses to AC clicks delivered via headphones and BC forehead taps delivered with a mini-shaker (bone-conduction vibrator) and a triggered tendon-hammer were recorded.
Results: In clinically definite unilateral MD ($n = 60$), the prevalence of unilateral VEMP abnormalities was 50.0%, 10.2% and 11.9% for click, minitap and tendon-hammer evoked oVEMPs, 40.0%, 22.8% and 10.7% for click, minitap and tendon-hammer evoked cVEMPs. The most commonly observed profile was abnormality to AC stimulation alone (33.3%), followed by abnormalities to both AC and BCV stimuli (26.7%). Isolated abnormalities to BCV stimuli were rare (5%) and limited to the minitap cVEMP. The prevalence of abnormalities for each of the AC VEMPs was significantly higher than for any one BCV VEMP. For click cVEMP, click oVEMP and minitap cVEMP, average Reflex Asymmetry Ratios (AR) were significantly higher in MD compared with controls. Test results for AC cVEMP, AC oVEMP, minitap cVEMP and caloric asymmetry were significantly correlated with hearing loss.
Conclusions: Predominance of abnormalities in oVEMP and cVEMP responses to AC sound is characteristic of MD and indicative of saccular involvement.
Significance: This pattern of VEMP abnormalities may enable separation of Ménière's disease from other peripheral vestibulopathies.

1. Introduction

Ménière's disease (MD) is characterised by fluctuating hearing loss, tinnitus, aural fullness and episodic vertigo (Hamid, 2009). Its histopathological correlate, endolymphatic hydrops, is observed most frequently in the cochlea and the saccule, followed by the utricle and the semicircular canals (Paparella, 1985; Schuknecht, 1986; Okuno and Sando, 1987). Distortion of the membranous labyrinth (Horner, 1993), labyrinthine ruptures (Fraysse et al., 1980), and complete collapse of the membranous labyrinth (Okuno and Sando, 1987) may lead to alterations in the mechanical and electrical properties of the inner ear, which in turn may explain symptoms and abnormalities in auditory and vestibular function.

The diagnosis of Ménière's disease relies upon clinical presentation and pure tone audiometry, which in the early stages of the disease shows low frequency hearing loss in a "rising configuration" and later progresses to a flat hearing loss of moderate severity (Sajjadi and Paparella, 2008). Electrocochleography (ECochG) can be used to demonstrate hydrops in the cochlea (Gibson, 2009), and vestibular function tests to quantify vestibular loss, although these tests are not incorporated into the diagnostic criteria for MD.

The bithermal caloric test, which assesses horizontal semicircular canal function is asymmetrical in 65–73.5% of affected ears in MD (Hulshof and Baarsma, 1981; Proctor, 2000; Palomar-Asenjo et al., 2006). Vestibular evoked myogenic potentials (VEMPs: Colebatch et al., 1994) which assess *otolith function* are absent or depressed in 30–54% of patients with MD when using air-conducted (AC) sound (deWaele et al., 1999; Murofushi et al., 2001; Young et al., 2003; Ribeiro et al., 2005; Osei-Lah et al., 2008). AC cervical VEMP abnormalities correlate with the degree of hearing loss (deWaele et al., 1999; Young et al., 2003), and are reportedly more common immediately following an attack of vertigo (Kuo et al., 2005). cVEMP amplitudes are abnormally large in a proportion of

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early MD (Young et al., 2002), and attenuated or abolished later on, suggesting that the VEMP, like the audiogram evolves with disease progression. The normal tuning of cVEMPs may also be altered in MD, as reflected by frequency dependent threshold shifts (Rauch et al., 2004; Lin et al., 2006). These changes can be evident even in the unaffected ear, possibly heralding the onset of bilateral disease.

The cVEMP, an *ipsilateral inhibitory surface potential* from the sternocleidomastoid muscles, assesses otolith pathways to the neck (Colebatch and Rothwell, 1993; Colebatch et al., 1994; Halmagyi and Colebatch, 1995). The oVEMP, a myogenic response from the extra-ocular muscles evoked by sound and vibration (Todd et al., 2007; Iwasaki et al., 2007), is a *contralateral excitatory* potential that is used to assess otolith *ocular* pathways. Single unit studies show predominantly saccular activation by AC sound (Murofushi and Curthoys, 1997); activation of utricular afferents by bone-conducted vibration (BCV) has been demonstrated by Curthoys et al. (2006). The use of both stimuli is likely to enable a more complete assessment of otolith function.

Using both cVEMP and oVEMP responses to air-conducted sound and bone-conducted vibration, we sought the typical evoked-potential profile of MD. If saccular involvement were indeed frequent in MD, a higher prevalence of abnormalities in air-conducted sound-evoked cVEMP responses with relative preservation of vibration-evoked oVEMP responses would be expected. Such dissociation could prove a useful diagnostic tool in suspected MD. To understand the patterns of end organ involvement, we also explored the relationship between VEMP abnormalities and other commonly used audio-vestibular tests.

2. Methods

2.1. Subjects

Thirty-five normal volunteers (aged 47.1 ± 12.1) and 77 patients with unilateral Ménière's disease (aged 52.2 ± 11.8) gave informed consent and were studied in accordance with the guidelines of the Helsinki Declaration.

2.2. Clinical screening of patients

Patients were classified into clinically definite, probable, or possible Ménière's disease according to AAO-HNS criteria and were further grouped into disease stage (1–4), using the 4 frequency pure-tone average (.5, 1, 2, 3 kHz) of their audiogram. The results of Subjective Visual Horizontal (SVH) and ECochG testing were documented. Bithermal caloric testing was undertaken using videonystagmography (water irrigated for 40 s at 30° and 44° C). Results were interpreted based on degree of canal paresis (CP), determined by the Jongkees formula from the slow phase velocity component of nystagmus. A CP greater than 25% was considered abnormal.

2.3. Stimuli

AC clicks (0.1 ms/140 dB peak-SPL) of alternating polarity were presented monaurally at 5/s via TDH-49 calibrated earphones. A 140 dB SPL 0.1 ms click at 5 Hz when expressed as an integrated A-weighted intensity is equivalent to an LAeq of 105 dB (Rosengren et al., 2009). Current Regional Guidelines for sound exposure specify a maximum of 140 dB Peak SPL for impulse noise and an 8-h equivalent continuous A-weighted sound pressure level of 85 dB(A) (Australian Standard AS/NZS 1269). Using this criterion, a stimulus of 105 dB LAeq could be presented for 4.8 min, equivalent to a total of 1440 stimuli for each ear (at a rate of 5 Hz). Our study used a maximum of 325 stimuli per ear, thus the level of stimulation was within regional safety guidelines. Clicks were used in preference over low frequency tone-bursts since in our laboratory's normative data, AC clicks were associated with a higher prevalence of oVEMP reflexes (than 120 dB SPL 500 Hz tone-bursts). The normal cVEMP asymmetry ratio for 500 Hz tones is also broader than that for clicks (Welgampola et al., 2003).

BCV stimuli were delivered, binaurally, by two methods: vibration–pulses (condensation polarity, 20 V amplitude) of 1 ms delivered at 5/s by a hand-held bone-vibrator (Bruel and Kjaer 4810 minishaker) at Fz. This is equivalent to an intensity of 147 dB Force Level (24 N). Calibration of the minishaker was achieved using a Bruel and Kjaer sound level meter and an artificial mastoid (Bruel and Kjaer 4930). Forehead-taps were delivered manually over Fz via a custom-made tendon-hammer with a trigger switch at 1/s.

2.4. Procedure

VEMPs were recorded and analysed using a Medelec Synergy 2000 Evoked Potential system and Synergy (version 12) software. Self-adhesive 5 mm Ag/AgCl surface EMG recording electrodes were placed according to the oVEMP and cVEMP electrode montage outlined in Fig. 1.

2.5. oVEMP recording technique

Subjects were tested supine. The active (inverting) electrodes were placed just below the lower lid margin of each eye, in line with the pupil in primary position with the reference 2 cm below this. At the commencement of testing, subjects were asked to gaze maximally upwards. Breaks were given at every 10 s to allow the participant to blink. Unrectified EMG was band-pass filtered from 3–1000 Hz and sampled at 10 kHz. Responses were averaged for 100 air-conducted stimuli and 50 bone-conduction stimuli. If the response was absent, a further 50 or 100 repetitions were averaged. The first negative peak between 8–12 ms was marked n10. The peak–peak amplitude between the first negativity and positivity was used as the parameter of interest (Fig. 1).

2.6. cVEMP recording technique

Subjects lay semi recumbent at 45° from horizontal. The active electrode was placed over the bulk of the SCM muscle belly (Fig. 1) at the junction of the middle and upper third of the muscle and referenced to the medial end of the clavicle. The ground electrode was placed over the manubrium sternii. The SCM muscles were activated, bilaterally, by lifting the head from the supine position while the stimuli were presented. Rectified and unrectified EMG activity was recorded from 20 ms pre-stimulus to 80 ms post-stimulus onset. Responses to 125 AC or 50 BCV stimuli were band-pass filtered (20–2000 Hz), sampled (10 kHz) and averaged. The raw amplitude (μV) of the cVEMP was measured between the peaks of p13 and n23 potentials. Corrected amplitudes were determined by dividing the raw amplitude by the mean rectified EMG during the 20 ms pre-stimulus recording period.

2.7. Analysis

A cVEMP and oVEMP response was defined as "abnormal" when absent for only the affected ear, or when reflex amplitudes were asymmetrical relative to control data. Additionally, a cVEMP amplitude was defined as abnormal when below the 95% amplitude range of controls. Subjects who had *increased* reflex amplitudes on the affected side with an absolute amplitude outside the normal range and reflex asymmetry outside the normal range ("Augmentors") were also considered abnormal. Amplitude asymmetry was expressed as an asymmetry ratio (AR), where