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ORIGINAL ARTICLE



# Comparing the sensitivity and specificity of cervical vestibular-evoked myogenic potentials and electrocochleography in the diagnosis of Ménière's disease

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## ABSTRACT

**Objective:** To compare the sensitivity and specificity of objective cervical vestibular-evoked myogenic potential (cVEMP) tuning curves and electrocochleography (ECoChG) for the diagnosis of Ménière's disease (MD).

**Design:** Sensitivity and specificity were calculated from 95% normative ranges of 500 Hz cVEMP threshold and ECoChG SP/AP amplitude ratios.

**Measures:** Extra-tympanic ECoChG testing to 90 dB nHL clicks and cVEMP threshold tuning curves (250–1000 Hz).

**Study sample:** We tested 15 patients (30 ears) diagnosed with definite bilateral MD based on the clinical criteria proposed by the American Academy of Otolaryngology Head and Neck surgery, 1995 (assumed gold standard) and 20 controls.

**Results:** 500 Hz cVEMP threshold was the most promising parameter to differentiate MD ears from controls. cVEMP and ECoChG showed high specificity (83.3 and 100%, respectively) and low to moderate sensitivity (22.2 and 71.4%) for long term MD. ECoChG sensitivity increased to 89% during a symptomatic period, compared to 33% for cVEMP. However, ECoChG can be difficult to schedule during symptomatic periods. Sensitivity of cVEMP for the diagnosis of MD appears limited.

**Conclusions:** ECoChG has higher sensitivity than cVEMP in the diagnosis of Ménière's patients, but the ECoChG SP/AP amplitude ratio measure is not perfect for the diagnosis of MD.

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## KEYWORDS

cVEMP; ECoChG; Ménière's disease; Sensitivity; Specificity

## 1. Introduction

In 1861, Prosper Ménière described a new disease that affected the inner ear, which was characterised by episodic spells of vertigo lasting several minutes and was associated with tinnitus, ear fullness, and fluctuating hearing loss (Stapleton and Mills 2008). It is believed to be caused by an abnormal accumulation of endolymph fluid termed endolymphatic hydrops (EH) most often in the cochlear duct and the sacculus followed by the utricle and the semi-circular canals, respectively based on evidence from human temporal bones studies (Merchant, Adams, and Nadol 2005), although hydrops alone does not explain the mechanism underlying all the clinical symptoms of the disease, including the progression of hearing loss and the frequency of vertigo attacks (Rauch, Merchant, and Thedinger 1989). It has been shown that whilst all patients with Ménière's disease (MD) symptoms in life show evidence of EH in at least one ear post-mortem, there are also patients with EH without signs or symptoms of MD (Merchant, Adams, and Nadol 2005; Rauch, Merchant, and Thedinger 1989). This suggests that pre-existing hydrops is not directly responsible for the symptoms of MD, but it can merely be an epiphenomenon of the pathophysiological mechanism of the disease (Merchant, Adams, and Nadol 2005).

In 1995, the American Academy of Otolaryngology Head and Neck surgery (AAO-HNS) developed a set of criteria to help in the diagnosis of MD, which are now widely used. Based on these criteria, patients are clinically classified as having definite MD if

they have had at least two definite episodic spontaneous vertigo attacks for at least 20 min, documented hearing loss on at least one occasion, and the presence of tinnitus or ear pressure in the affected ear. The diagnosis of MD can be difficult, especially if vestibular symptoms occur in isolation, so objective tests are essential in addition to historical information for the identification of the disease.

Electrocochleography (ECoChG) has been widely used as an objective clinical tool for the diagnosis of cochlear hydrops. The ECoChG response is composed of three basic potentials: the action potential (AP), the summing potential (SP), and the cochlear microphonic (CM) (Ferraro and Durrant 2006; Wuyts et al. 1997). The AP, which is also referred to as the whole nerve or compound AP, is the summation of the APs of the spiral ganglion and auditory cochlear nerve. The CM is an alternating current voltage, which is generated predominantly by the outer hair cells in the cochlea. The SP is a constant direct current component, which is thought to reflect the displacement of the basilar membrane (BM) toward the scala tympani in response to the asymmetrical vibration of the BM at high intensities (Wuyts et al. 1997). Currently, the CM is thought to be useful in the differential diagnosis of inner ear and auditory nerve diseases. Typically the magnitude of AP is measured relative to that of SP. SP amplitude is thought to increase in ears with hydrops due to the distention of the BM towards the scala tympani. It is thought that elevation of SP amplitude compared with AP amplitude

may be a positive indicator of EHs in patients with suspected MD. For details on the history of ECochG, see Eggermont (2017).

The clinical utility of ECochG remains a subject of debate among researchers because 25–54% of patients who were considered to have MD based on the AAO-HNS guidelines showed normal ECochG results (Kim et al. 2005). The major debated point in the literature is the establishment of the SP/AP ratio cut-off (Mammarella et al. 2017) to indicate MD. Gibson, Prasher, and Kilkenny (1983) proposed a value of 0.29. Other authors proposed somewhat higher ratios as indicative of hydrops, between 0.40 and 0.45 (Al-Momani et al. 2009; Margolis et al. 1995; Wuyts et al. 1997). It has been speculated that the false negative rates for ECochG result from the transient nature of EHs (Kim et al. 2005). However, Ohashi and others found that an elevated SP/AP ratio of ECochG is maintained over an extended period of time and despite medical and surgical treatment (Ohashi et al. 1991). Thus, it appears that the ECochG SP/AP ratio only indicates EHs and it is not necessarily correlated with MD symptoms (Gibson 2017). This is consistent with the findings of temporal bone studies that found the presence of hydrops does not necessarily correlate with MD symptoms (Merchant, Adams, and Nadol 2005; Rauch, Merchant, and Thedinger 1989). Overall, a number of factors may contribute to the reported low sensitivity of ECochG for MD, including fluctuation of Ménière's symptoms, lack of standardisation regarding ECochG stimulus parameters, recording techniques and interpretation, and distortion of ECochG components due to deterioration of cochlear hair cells in more advanced stages of the disease (Ferraro and Durrant 2006). This has limited the clinical utility of ECochG in the diagnosis of MD (Lamounier et al. 2014).

Other measures than the SP/AP ratio have been proposed in the literature to increase the diagnostic sensitivity of ECochG in detecting cases of MD. Combination of the area under the SP/AP curve and SP/AP amplitude ratios significantly improved the sensitivity to 92% of extra-tympanic (ET) ECochG in the diagnosis of MD, while maintaining specificity as high as 84% (Al-Momani et al. 2009). Ferraro and Tibbils (1999) found that the inclusion of the SP/AP area curve measurement resulted in improving the sensitivity of ET ECochG to 90% in the diagnosis of definite cases of MD. Devaiah et al. (2003) conducted a retrospective study on 138 patients with possible MD undergoing trans-tympanic (TT) ECochG and compared the sensitivity of SP/AP amplitude ratio and SP/AP area curve ratio in the diagnosis of EH. They found sensitivities of 50% and 87.5% for amplitude ratio and area ratio, respectively. In contrast, a retrospective study on 198 patients with MD showed that the inclusion of the SP/AP area ratio measurement in addition to the conventional SP/AP amplitude ratios, as well as using SP/AP area alone, did not increase the diagnostic sensitivity of TT ECochG in identifying MD cases (Baba et al. 2009). The sensitivities for SP/AP amplitude ratio and SP/AP area ratio in patients with definite MD were 57.1 and 43.9%, respectively (Baba et al. 2009). These authors attributed the discrepancy in results between their study and previous studies on sensitivity of the SP/AP area ratio (Al-Momani et al. 2009; Ferraro and Tibbils 1999) to various methods of measurements, e.g. TT versus ET ECochG. Further research is necessary to assess the sensitivity of the inclusion area measurements with ET ECochG in the diagnosis of EH. However, measurement of the area under the SP/AP curve is not easily performed, and it requires specialist software, which is not yet commercially available (Ferraro 2010; Mammarella et al.

2017). In addition, there is still no consensus among researchers about the most practical method to establish the SP/AP area measurement (Grasel et al. 2017).

Other researchers have used 1000 Hz tone-bursts rather than broadband clicks to improve the sensitivity of ECochG in detecting EHs. For example, Conlon and Gibson (2000) showed that the diagnostic sensitivity of TT ECochG increased from 50% for clicks to 85% when using a 1000 Hz tone-burst stimuli (1 ms rise/fall and 14 ms plateau) to measure SP amplitude. A tone burst will test a more specific region of the cochlea than a click and it is possible that the 1000 Hz frequency is more specific to MD than the range of frequencies tested with a click. Sass, Densert, and Arlinger (1998) found that the sensitivity of TT ECochG obtained by using measurements of SP/AP amplitude ratio and SP amplitudes at 1000 Hz tone-burst increased from 62 to 82%, without changing specificity. As yet few other studies have explored the sensitivity of SP/AP measurements to MD using tone-burst stimuli.

The cervical vestibular-evoked myogenic potential (cVEMP) is a short-latency electromyographic (EMG) potential elicited by stimulating the ear with high-level air-conducted sound (ACS) (around 95 dBA: A-weighted sound level). It can also be elicited with bone-conducted vibration, forehead taps or electrical stimulation and this can provide diagnostic information about the vestibulocollicreflex pathway (Rosengren, Welgampola, and Colebatch 2010). For more details on cVEMP, see (Rosengren, Welgampola, and Colebatch 2010) or Obeidat and Bell (2019). cVEMP responses to AC stimulation are primarily considered to be saccular in origin and it has been proposed that cVEMP response frequency will be altered in patients with MD, hence it may be sensitive to EH in the saccule. Previous studies on healthy subjects found that cVEMP exhibits a frequency-tuning curve with best response (frequency tuning) at 500 Hz (Akin, Murnane, and Proffitt 2003; Park et al. 2010; Piker et al. 2013; Rauch et al. 2004; Timmer et al. 2006). Rauch et al. reported that subjects with MD exhibit a different cVEMP tuning pattern from healthy subjects and propose that dilatation of the saccule due to hydrops could raise its resonant frequency, and thus alters VEMP tuning curves. In their study, the affected ear in unilateral MD subjects showed a shift upward from 500 to 1000 Hz with a rise in the thresholds of all frequencies (Rauch et al. 2004; Timmer et al. 2006). The unaffected ear of MD subjects also showed alterations in cVEMP tuning and a threshold shift compared to normal subjects; however, the reason was not identified. They suggested that an altered cVEMP tuning pattern could be a marker of saccular EH and hence it is believed that altered tuning in the unaffected ear may indicate early signs of the development of bilateral MD.

Studies investigating cVEMP in MD have shown variable results, although VEMP parameters investigated have varied between studies: some explored an absence of a response in MD affected ears (Akkuzu, Akkuzu, and Ozluoglu 2006; de Waele et al. 1999; Egami et al. 2013; Murofushi et al. 2001; Ribeiro et al. 2005), some explored decreased VEMP amplitude or P1 latency prolongation with MD (Akkuzu, Akkuzu, and Ozluoglu 2006; Murofushi et al. 2001; Ribeiro et al. 2005) and some explored abnormal amplitude asymmetry ratio (AR) (Akkuzu, Akkuzu, and Ozluoglu 2006; Ribeiro et al. 2005; Young, Wu, and Wu 2002). A retrospective study by Jariengprasert et al. (2017) on 67 MD patients showed that the sensitivity and specificity of cVEMPs in diagnosing unilateral definite MD in relation to the clinical diagnosis by the AAO-HNS criteria were 62.68 and 96.88%, respectively. They categorised VEMPs that were absent

or had abnormal AR as abnormal. A retrospective study by de Waele et al. (1999) on 59 patients with unilateral MD showed that AC cVEMP responses to clicks were absent in 54% of MD affected ears and their absence corresponded with low-frequency hearing loss in subjects. Egami et al. (2013) studied 114 patients with unilateral definite MD and reported that 26 patients (22.8%) had absent cVEMPs in response to clicks and short tone burst stimulation on the affected side and 8 patients (7%) had reduced cVEMP amplitude. Murofushi et al. (2001) tested 43 unilateral MD cases and reported 34.8% with absent click-cVEMP, 16% with reduced amplitude, and 2% with prolonged P1 latency on the affected side. In a study of 32 unilateral definite Ménière's cases, Jariengprasert, Tiensuwan, and Euasirattapanaisan (2013) reported that 14 MD patients (43%) had absent VEMP in response to short tone burst of 500 Hz and 5 (15%) had abnormal AR of VEMP. Kim et al. (2013) studied 41 unilateral Ménière's cases of whom 14 (34.1%) had abnormal VEMP AR on the affected side. Chen et al. (2016) studies 30 cases of MD and reported 12 of 30 (40%) had absent cVEMP in response to 500 Hz tone-burst stimuli on the affected side.

A common issue with cVEMP threshold measurements is that the waveforms are analysed subjectively. In our previous work (Obeidat and Bell, 2019), there was significant variability between experienced raters in their subjective identification of cVEMP response thresholds, which is consistent with effects seen for ABR threshold estimation (Vidler and Parker 2004). Hence, we introduce an objective analytical approach using the Hotellings  $T$  squared ( $HT^2$ ) test for the automated response detection of VEMPs (Obeidat and Bell, in press). We measured cVEMP tuning curves from 250 to 1000 Hz using  $HT^2$  estimates of threshold in Ménière's patients and healthy volunteers. We found that objective estimates of the saccular tuning curve in healthy adults showed cVEMP frequency tuning with the largest response at 500 Hz on average and in patients with MD the tuning curve was flatter, so 500 Hz appears to be the best test frequency that can be used to differentiate normal ears from MD affected ears. The current study is a continuation of the previous work in which the previously described VEMP tuning curves are compared to ECoChG measurements, which were taken from the same subjects.

The diagnostic power of the two objective tests to detect the presence or absence of the disease were measured and results were compared to 95% normative ranges of cVEMP threshold at 500 Hz tone burst and ECoChG SP/AP amplitude ratio defined from normative data.

The current study aimed to evaluate the sensitivity and specificity of cVEMP and ECoChG in the diagnosis of MD compared to a clinical diagnosis based on the 1995 AAO-HNS criteria, which is here considered a gold standard for the purpose of the calculation of sensitivity and specificity.

## 2. Methods

### 2.1 Study population

To obtain normative data of cVEMP recording, responses were recorded from 20 otologically normal subjects (20 ears), with a mean age of 30 years (range 20–45). Eleven men and nine women participated as normal subjects. In our previous study, responses were recorded from the left SCM muscles on all normal subjects.

Normative data of ECoChG were established in 20 normal healthy adults (40 ears), with a mean age of 35 years (range

18–40), of whom 9 were male and 11 were females, who were staff members of the Middle East Hearing and Balance Centre in Jordan-Amman and their associates.

All normal subjects gave informed consent to participate and had pure-tone thresholds of around or better than 20 dB HL at frequencies between 250 Hz and 8000 Hz.

The clinical test group with MD consisted of 15 patients (nine women and six men), with a mean age of 40 years (range 18–60), who had been diagnosed with bilateral definite MD according to the 1995 AAO-HNS. Both ears were tested (30 ears). Based on these guidelines, both ears ( $n = 30$ ) of the 15 patients were symptomatic, but, unexpectedly, left ears were more affected by the disease than the right ears. Testing was conducted at the Middle East Hearing and Balance Centre in Jordan-Amman. As the progression of the disease in each ear was different, left and right MD ears were sub classified into “most” and “least” affected ears respectively according to the severity of the subjective symptoms (ear fullness, tinnitus) and the stage of hearing level. In line with the AAO-HNS guidelines, AC pure tone averages at 0.5, 1, 2, and 3000 Hz frequencies were used to classify the stage of the hearing level. The worst audiometric results during the 6-month period prior to treatment were used for stage classification. Based on these guidelines, all left ears were classified as stage 3 (four tone average is 50 dB HL), while right ears were classified as stages 1 and 2 (four tone average is 10 and 35 dB HL, respectively) (see Obeidat and Bell [in press] for more details). Patients who were determined to have middle or external ear pathology, neck/back stiffness or pain, or allergy to alcohol swabs were excluded from the study. In addition, patients who underwent surgical treatment were also excluded. Ethics Committees of Jordan-Amman Hearing and Balance Centre and the University of Southampton approved the experimental protocol for this study.

### 2.2 cVEMP recording

500 Hz 1:2:1 (one cycle rise/fall and two cycles plateau) tone-bursts stimuli were presented using insert earphones (Etymotic ER-3A). The stimulus level was decreased in 3 dB steps from 106 to 85 dB LAS (A-weighted sound level with a slow time constant) (125 to 105 LLpK (peak SPL)). We also measured levels in dB LAeq (A weighted equivalent continuous sound level) which gave almost identical results. Each recording consisted of 150 repeats of an 8 ms short tone-burst. A repetition rate of 10 Hz was fixed for all measurements, so total duration for each recording was 15 s. The rate of 10 Hz was found to be the optimal trade-off between recording time and response detection for the majority of subjects in our previous study (Obeidat and Bell 2018). The order of presentation of stimulus intensities was randomised among subjects.

The equipment used in this study to deliver the stimuli for cVEMP measurement was Cambridge Electronic Device's CED 1401 data acquisition system and CED “signal” software (<http://ced.co.uk/>). A sampling rate (input and output) of 10000 Hz was used. The output from the Digital to Analogue Converters (DAC) port was routed through a headphone amplifier (OBH-21) to control the intensity of the stimulus. Amplification of the signals was performed using an isolated amplifier (CED 1902) with a 1–3000 Hz bandpass filter with 1000 times gain.

VEMPs from the SCM muscle were recorded ipsilaterally while subjects were seated upright on a chair with their chin turned over the contralateral shoulder to tense the SCM muscle. The EMG activity of the SCM muscle was recorded using surface



electrodes placed on the muscle: active on the belly of the ipsilateral SCM muscle, and reference on the upper sternum of the test side. A ground electrode was placed on lower forehead. The impedance of the electrodes was kept below 10 K $\Omega$ . The EMG activity of the SCM muscle was visually monitored on an oscilloscope and kept between 80 and 100 mV.

### 2.3 ECochG recording

The stimulus was a 100  $\mu$ s broadband click generated using the Vivosonic Integrity™ V500, and delivered at intensity of 120 dB p.e. SPL (90 dB nHL) at a rate of 11.3 times per second. 1000 responses were collected in each run with an alternating polarity (500 rarefaction and 500 condensation), so total duration for each recording was 2 min (1000 repeats/11.3 Hz). Signals were filtered with 3000 Hz low-pass and 5 Hz high-pass filters. A sampling rate of 34000 Hz was used with 50 k amplification. All subjects had bilateral recordings, and this was repeated in each ear. Of the repeats, the test run with the largest AP amplitude was chosen for analysis. Recordings were conducted in a sound-attenuated room.

ECochG was recorded using an ET electrode. After otoscopic examination, the tested ear canal was irrigated with 0.9% saline solution and dried. The ET wick electrode (Sanibel) was inserted in the external auditory meatus and placed under otomicroscopy on the tympanic membrane. The foam rubber tip of the ER-3A insert phone was placed and helped to secure the ET wick electrode in place. Recording of ECochG was performed using the ET wick electrode as reference. An active electrode was placed on the earlobe of the non-test ear, and the ground (common) electrode was placed on the lower forehead. The impedance of the electrodes was maintained below 5 K $\Omega$ .

### 2.4 Response analysis

#### 2.4.1 cVEMP

The presence of the responses was objectively detected using a cut-off  $p$ -value of 0.05 (false positive rate of 5%) obtained from a one-sample HT<sup>2</sup> test on the array of cVEMP data. For more detailed of the method see Chesnaye et al. (2018) and Obeidat and Bell (in press).

#### 2.4.2 ET ECochG

A 10 ms ECochG analysis time window was used. Two runs were performed for each ear, so the test run with the largest AP amplitude in each ear is chosen for data analysis. As shown in Figure 1, the stimulus baseline, SP, and AP peaks were visually determined, and the SP/AP amplitude ratio was analysed and reported as a percentage. The amplitudes of SP and AP were measured with reference to the stimulus baseline. The SP amplitude was calculated from the stimulus onset (defined as baseline start) to the first peak, while AP amplitude was measured from the onset of the stimulus onset to its first peak in the way described by Ferraro (2000). The AP latency measured from stimulus onset to the AP peak should be identical to the latency of wave 1 in ABR, with normal range between 1.3 and 1.7 ms (Ferraro 2000). Unfortunately the SP/AP area under the curve ratio measurement was not available on the equipment used for the study. Hence, SP/AP amplitude ratio was the primary ECochG parameter used in the analysis.

### 2.5 Sensitivity and specificity analysis for ECochG and cVEMP

The diagnostic power of the two objective tests to detect the presence or absence of MD were calculated by comparing results from the MD group to the 95% normative ranges of cVEMP threshold to 500 Hz tone bursts and the ECochG SP/AP amplitude ratio defined from normative data.

Based on the ECochG test, patients with any SP/AP amplitude ratio for clicks exceeding the normative data values (or the 95% range of the SP/AP amplitude ratio), were classified as “positive”, while, those with SP/AP amplitude ratio within the 95% normative range were classified as “negative”. For cVEMP tests, patients were similarly classified as “positive” or “negative” based on threshold: those with cVEMP thresholds for 500 Hz tone-burst greater than the 95% normative range (mean + 1.96  $\times$  SD, or 102.9 dB LAS) and also those with no response at the highest stimulus level used were considered as “positive”. While, patients with cVEMP thresholds for 500 Hz tone burst within the 95% normative range were classified as “negative”. This was chosen because threshold appears to be the best measure to use to discriminate the groups, as reported in Obeidat and Bell (in press).

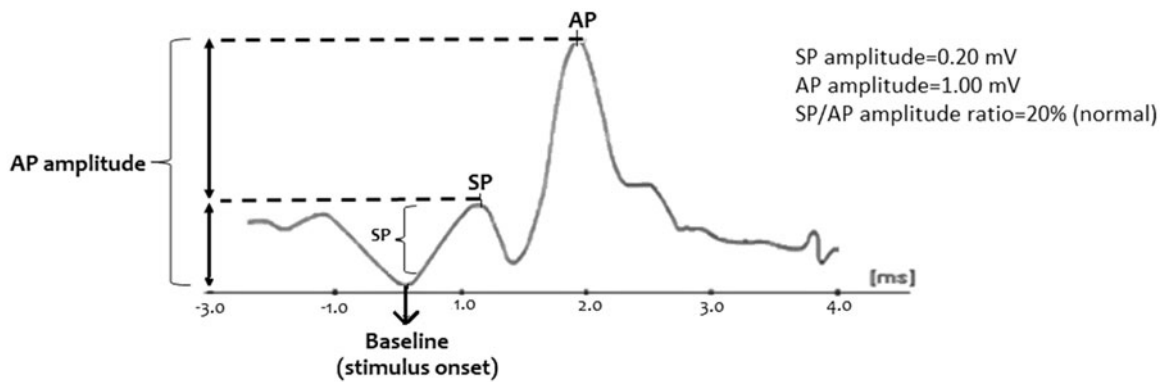
Measures taken by the three diagnostic tools were compared: AAO-HNS criteria, ECochG, and cVEMP, with the AAO-HNS criteria considered as the “gold standard” for the purpose of sensitivity and specificity analysis.

## 3. Results

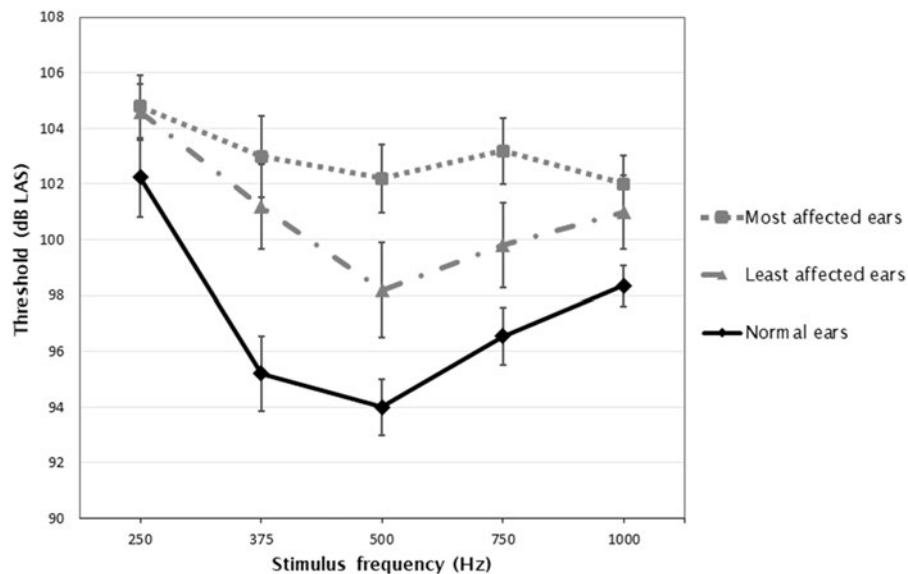
### 3.1 Objective estimate of cVEMP tuning curve

Figure 2 shows the cVEMP thresholds (in dB LAS) for normal subjects' ears ( $n=20$ ), and the “most” ( $n=15$ ) and “least” ( $n=15$ ) affected ears of bilaterally affected patients with MD, which were objectively detected by the HT<sup>2</sup> test for a significance level of  $\alpha=5\%$  (150 sweeps) as a function of stimulus frequency. The objective estimate of the saccular tuning curve in healthy adults showed cVEMP frequency tuning with the best frequency response at 500 Hz on average. Across normal subjects, there was some variation in individual thresholds and the pattern of the saccular tuning curve varied a little, but in general it was U shaped with the best frequency response between 375 and 500 Hz, on average. cVEMP tuning curves that were affected by the presence of MD showed flatter tuning than those in the control group. The largest difference between the groups was seen at 500 Hz. It appears that 500 Hz is the best frequency to differentiate normal ears from MD affected ears based on threshold alone. The 95% normative range (mean  $\pm$  1.96  $\times$  SD) of cVEMP threshold at 500 Hz tone-burst defined from normative data ranged from 85 to 102.9 (mean 94) dB LAS.

We also explored how peak-to-peak amplitude of cVEMP as a function of frequency compared between normal hearing subjects and patients with MD. Both amplitude and threshold measures show cVEMP frequency tuning with the strongest response at 500 Hz. Similarly, both measures show changes in both ears for bilateral MD patients, with more alteration in the most-affected ear. However, cVEMP amplitudes show more variance than threshold measurements, and thus threshold appears to be the best measure to use to discriminate the groups, as previously reported in Obeidat and Bell (in press).



**Figure 1.** An example of normal ET ECoG tracing at 90 dB nHL using click sound. The ECoG is analysed by comparing the amplitude of the SP to the AP. The baseline is used as a reference point for SP and AP amplitude measurements.

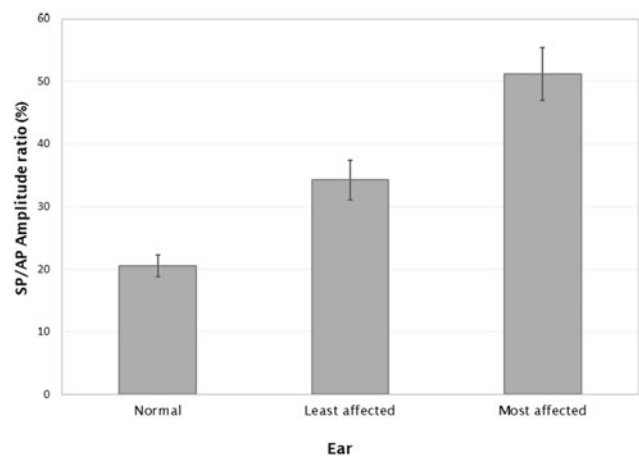


**Figure 2.** Mean cVEMP thresholds at different tone-burst stimuli for “most” and “least” affected ears of bilaterally affected patients with MD ( $n=15$ ), and for normal subjects’ ears ( $n=20$ ). The error bars represent  $\pm 1$  SE of the mean.

### 3.2 ECoG in normal subjects and study group

For the control group ( $n=20$ ), all 40 ears showed AP and SP. There was no significant difference in the SP/AP amplitude ratio between right and left ear, based on the repeated measures  $t$ -test ( $p > 0.05$ ), so data from both ears were combined. Mean SP/AP amplitude ratio was  $0.205 \pm 0.074$  (mean  $\pm$  SD) for 40 ears. In this study, the variability in the SP/AP amplitude ratio was low, and thus the 95% cut-off value (mean  $+ 1.96 \times$  SD) was 0.35. In the clinical test populations, ECoG results exceeding the 95% range of SP/AP amplitude ratio were considered abnormal. For patients with MD ( $n=30$  ears), the SP/AP amplitude ratio for MD affected ears ( $n=30$ ) was 0.43 (SD = 0.166): for “most” affected ears ( $n=15$ ) it was 0.51 (SD = 0.164) and for the “least” affected ears ( $n=15$ ) was 0.34 (SD = 0.121) (Figure 3). An increased value of SP/AP amplitude ratio is consistent with endolymphatic hydrops (MD).

As the majority of the data was normally distributed, a  $t$ -test was conducted to find out if there was a significant difference in the SP/AP amplitude ratio between normal and MD affected ears. Independent samples tests revealed that normal ears showed significantly lower SP/AP amplitude ratios than MD “most” affected ears  $t(33) = -7.246$ ,  $p < 0.001$ , and MD “least” affected



**Figure 3.** ECoG mean percentage SP/AP amplitude ratios for normal ears ( $n=40$ ), and for “least” ( $n=15$ ) and “most” ( $n=15$ ) affected ears of patients with MD. Error bars represent  $\pm 1$  SE of the mean.

ears  $t(33) = -4.061$ ,  $p < 0.001$ . A paired samples test within the MD group showed that the MD “most” affected ears had significantly higher SP/AP amplitude ratios in comparison to MD “least” affected ears  $t(14) = 3.495$ ,  $p < 0.001$ .

### 3.3 Sensitivity and specificity of ECochG and cVEMP

Table 1 shows the sensitivity and specificity for the presence and absence of MD in the “most” and “least” affected ears for ECochG (SP/AP amplitude ratio) and cVEMP threshold at 500 Hz. For both tests and both ears, the results indicated that the ability of the two objective tests to identify healthy cases was high, with specificity of 83.3% for cVEMP and 100% for ECochG. However, the ability of the two diagnostic tests in both ears to identify MD cases varied from low to moderate, with sensitivity of 22.2 and 71.4%, respectively.

The agreement between the two diagnostic tests (regarding whether the MD “most” and “least” affected ears were normal or abnormal) was measured by the kappa coefficient. In the Cohen’s kappa (k) test, the agreement of both tests was equal to 0.69 in the MD “most” and 0.58 in the “least” affected ears, indicating a low and moderate agreement between the two tests’ outcomes, based on the guidelines proposed by Landis and Koch (1977).

### 3.4 Sensitivity analysis for patients with acute symptoms on the day of testing

The symptomatic status of MD patients was examined and compared to the ECochG and cVEMP test results on the day of recording. Symptoms included vertigo, tinnitus, hearing loss, or ear pressure, and all combinations of these four. At the time of testing, the nine “most” affected and four “least” affected out of 30 Ménière’s ears were symptomatic; symptoms included combinations of ear fullness, hearing loss, and tinnitus. Of the nine MD “most” affected ears, eight ears showed elevated SP/AP amplitude ratio and three ears showed absent cVEMP (at 500 Hz), giving sensitivity values of 89 and 33% for ECochG and cVEMP, respectively. Of the four “least” MD affected ears, one ear showed abnormal ECochG and cVEMP, giving a sensitivity of 25%. However, the sample of least affected ears is small, so the result for least affected ears should be treated with caution.

## 4. Discussion

The aim of this work was to measure the diagnostic power of two objective tests (cVEMP and ECochG) in the diagnosis of MD and compare it to a diagnosis based on the AAO-HNS criteria.

The ECochG testing used in this study was ET, which, based on the literature (Lamounier et al. 2014), is an effective and non-invasive measure used to identify cochlear hydrops. In this research, the only parameter considered was the SP/AP amplitude ratio, because of the simplicity of applying it to the types of equipment that were available. Normative data for the SP/AP amplitude ratio were established in 20 normal hearing subjects (40 ears) who had no hearing or balance problems. We note that there is a difference between the mean age of the control group

(30) and the clinical group (40), although effects of age of VEMP tend to be more prominent in older adults, such as over age 60 (Janky and Shepard 2009). The variability in the SP/AP amplitude ratio was low among the healthy subjects; thus, the 95% cut-off value of the ET electrode was 0.35. This finding was consistent with the data reported in Grasel et al. (2017) and Pou et al. (1996). Other previous studies found somewhat higher ratios, between 0.40 and 0.45 (Margolis et al. 1995; Al-Momani et al. 2009). This difference in SP/AP ratio cut-off values between studies probably results from differences in the method to determine baseline, as well as the AP and SP peaks in ECochG data. Roland and Roth (1997) compared the SP/AP amplitude ratios calculated from the same ECochG tracings by 10 audiologists. The inter-interpreter difference between SP/AP amplitude ratios was found to be significant. Thus, ECochG is vulnerable to subjective bias, which cannot be completely avoided, although an area for future research may be to apply objective (statistical) measures to ECochG.

Patients with MD showed a significant increase in the SP/AP amplitude ratio compared with the control subjects, and the increases were highest in the MD most affected ears. It is widely accepted that the elevation in SP amplitude relative to AP amplitude is a positive indicator of EH in patients with suspected MD, consistent with the notion that SP is enlarged in ears with hydrops due to the distention of the BM toward the scala tympani (Ferraro and Tibbils 1999).

In the identified MD cases, both cVEMP and ECochG showed high specificity of 83.3 and 100%, respectively, and low to moderate sensitivity at 22.2 and 71.4%, respectively. This result is consistent with previous findings in the literature, indicating a good ability for cVEMP and ECochG to correctly rule out the disease (Lamounier et al. 2017). The sensitivity of cVEMP in the most and least affected ears was 29 and 22.2%, respectively. This was lower than that found in previous studies, which ranged between 40 and 63.6% (de Waele et al. 1999; Lamounier et al. 2017; Young, Huang, and Cheng 2003), although they did not use objective methods to define thresholds. The sensitivity of ECochG was 71.4% in the most affected ears and 33% in the least affected ears. Previous findings ranged between 57 and 71% (Lamounier et al. 2017), so we are in the upper range that has been reported previously. The threshold of SP/AP amplitude ratio used to define abnormality varies in the literature, which leads to variation in the sensitivity and specificity of the ECochG test in the diagnosis of MD. When the cut-off value of the abnormal SP/AP ratio is increased, the specificity of ECochG in identifying EH is improved at the cost of sensitivity. When the SP/AP ratios are decreased, the reverse occurs (Kim et al. 2005). In this work, the cut-off limit for a defined MD was a little lower than in other studies. In this study, 4 of 15 Ménière’s ears (the “most” affected) in patients who were considered to have definite MD based on the AAO-HNS criteria showed normal SP/AP amplitude ratios in the ECochG test (28.6% false negative rate), resulting in a sensitivity of 71.4%.

In previous work, different ECochG and cVEMP sensitivities have been reported based on the stage of the disease. For ECochG, an elevated SP/AP ratio has been found to be maintained for a long time and even in the asymptomatic period (i.e. the time between attacks) and despite successful treatment (Kim et al. 2005; Ohashi et al. 1991). For cVEMP, the measurements vary based on the stage of MD. Although responses may disappear or remain altered during the 24 h of a Ménière’s attack, they may return to normal after 48 h or with medical intervention, if the hair cells of the saccule remain undamaged

**Table 1.** cVEMP (based on 95% normative ranges of cVEMP threshold at 500 Hz tone-burst) and ECochG (based on 95% range for normative SP/AP ratio) sensitivity and specificity (%) in MD “most” and “least” affected ears.

	Most affected ears		Least affected ears	
	ECochG	cVEMP	ECochG	cVEMP
Sensitivity	71.4	28.6	33.3	22.2
Specificity	100	100	100	83.3

(Kuo et al. 2005). In the present study, none of the patients was tested during the first 24 h of a Ménière's attack, but some patients were in the symptomatic period, experiencing vertigo, tinnitus, ear pressure, hearing loss, or combinations of these four symptoms. This finding could explain the low sensitivity of cVEMP in the diagnosis of MD, even in the most affected ears, in contrast to ECoChG, which had the higher sensitivity of 71% in the most affected ears. In general, this finding is consistent with the concept that cVEMP testing has increased sensitivity to MD in the acute phase of the disease. Compared to the least affected ears, the sensitivity of ECoChG in the most affected ears was higher, consistent with a longer duration of the disease. This is also consistent with Kim et al. (2005), who found that ears with longer disease duration and/or more severe symptoms showed a more elevated SP/AP ratio.

Although cVEMP has lower sensitivity than ECoChG for MD, especially in the most affected ears, it has the significant advantage that the saccule is not affected by cochlear dysfunction, and hence can be performed in patients with significant hearing loss. For ECoChG, a hearing loss greater than 40–50 dB HL reduces the amplitude of SP and AP due to cochlear hair cell damage and/or fewer cochlear hair cells and nerve fibres, resulting in distortion of the SP/AP amplitude ratio (Ferraro 2010). Thus, ECoChG is best performed in the primary stage of the disease before the hearing loss has progressed. In this study, no patients had severe deterioration in hearing function. Although the ears that were the most affected by MD were classified as stage 3 (41–70 dB HL), there was no distortion in SP and AP components. Thus, the amplitude ratio could still be measured precisely. The potential disadvantages of VEMP testing include high test levels in patients with tinnitus (the stimulus levels used in this study were limited compared to other studies due to safety concerns) and a long test duration.

The relationship between cVEMP and ECoChG test results and the symptomatic status of patients with MD at the time of testing were examined. The sensitivity of ECoChG was as high as 89% in the most affected ears during a symptomatic period, which was higher than the percentage shown in the cVEMP test (33%). Thus, when patients are symptomatic, ECoChG is more sensitive to MD. However, it could be difficult to schedule patients for ECoChG testing during the symptomatic period, as patients typically feel sick, fatigued and have poor concentration during this period. From our data, the clinical utility of cVEMP for the diagnosis of MD appears limited. The sensitivity of ECoChG was increased in patients who had symptoms of MD on the day of testing, including a combination of ear fullness, hearing loss, and tinnitus. This finding was consistent with that of Ferraro, Arenberg, Hassanein (1985), who found abnormal ECoChG results in over 90% of patients who were suffering ear pressure and hearing loss on the day of recording. These authors considered the presence of the clinical symptoms of ear pressure and hearing loss as the strongest predictor of positive ECoChG outcomes (Ferraro, Arenberg, Hassanein 1985).

The agreement between the two diagnostic tests, which was measured by Cohen's kappa, was moderate for the "most" affected ear and low for the "least" affected ear, based on the guidelines proposed by Landis and Koch (1977). Although due to the low number of least affected ears in the MD group, this result should be treated with some caution. The agreement between the two tests was not expected to be perfect, because they evaluated different vestibular structures in the inner ear, which was suggested by Lamounier et al. (2017).

This study has some limitations. First, the generalisability of the results would be improved if a greater number of patients with the same duration of the disease were recruited. Second, SP/AP area ratio could not be measured because it was not available in the equipment used for the ET ECoChG recording. Thus, further research should be conducted to assess the sensitivity of the inclusion area ratio of SP/AP and the tone-burst elicited SP in MD with ET ECoChG and to compare them with the objective VEMP tuning curve over a prolonged period in patients with definite MD.

## 5. Conclusions

The measurement of VEMP tuning curves using objective analytic measures to define threshold is not very sensitive to MD in patients with long-term disease. VEMP sensitivity may increase in the acute phase, but even then does not appear high. Furthermore, noise exposure and test duration are concerns in VEMP testing. The ECoChG SP/AP amplitude ratio measures gives high, but not perfect, sensitivity for the diagnosis of MD. Both ECoChG and VEMP testing show fair specificity for MD.

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## Disclosure statement

No potential conflict of interest was reported by the authors.

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