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Normative data for TM electrocochleography measures

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Abstract

Objective: Establish normative data for tympanic electrocochleography (TM ECochG) parameters in normal hearing adults without Ménière's disease's (MD) symptoms. Describe TM ECochG variables that help to distinguish normal from MD ears.
Material and methods: We enrolled 100 subjects (N = 200 ears), 59 females, aged between 19 and 71 years from 09/2010 to 04/2014. Inclusion criteria: normal otomicroscopy, hearing thresholds ≤25 dB nHL from 250 to 4000 Hz, normal tympanogram, no symptoms of MD according to the AAO-HNS 1995 criteria and Gibson's score <7. We excluded subjects with dizziness, aural fullness or other symptoms of endolymphatic hydrops. The following parameters were analyzed: SP/AP amplitude ratio, SP/AP area ratio and the difference between AP latency with rarefaction and condensation stimuli.
Results: There was no significant difference between right and left ears (Intraclass correlation coefficient < 0.6). SP/AP amplitude ratio varied between 0.084 and 0.356 and SP/AP area ratio between 0.837 and 1.671 (percentiles 5 and 95). The AP latency difference to rarefaction and condensation clicks was between 0.0 and 0.333 ms.
Conclusion: Normative data for TM ECochG parameters were established in 100 normal hearing subjects without MD. These data can be used to distinguish normal from pathological findings and in follow-up of MD patients.

Keywords: Electrocochleography; Ménière disease; Hearing; Dizziness; Tinnitus

1. Introduction

Electrocochleography (ECochG) is one of the diagnostic tools used in patients with Ménière's disease (MD). The wide spectrum of symptoms and the clinical course of MD continue to make diagnosis and management challenging to clinicians. Besides the AAO HNSF criteria (1995), the criteria suggested by Gibson (2009) and The International Criteria (Lopez-Escamez et al., 2015), vestibular tests, VEMP and ECochG are useful not only for diagnosis but also to determine the evolution of the disease (Young, 2013; Ferraro, 2010; Ferraro and Durrant, 2006).

The most widespread used measure in ECochG remains the summating potential-to-action potential (SP/AP) amplitude ratio, whose sensitivity for the diagnosis of MD varies between 60% and 92% (Margolis et al., 1995; Ferraro et al., 1985; Devaiah et al., 2003). Notwithstanding, other measures have been proposed to enhance diagnostic accuracy like the SP/AP area ratio, the action potential latency difference to rarefaction and condensation clicks and the tone-burst evoked

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SP (Ferraro and Tibbils, 1999, Baba et al., 2009; Al-Momani et al., 2009, Ohashi et al., 2009; Margolis et al., 1995).

Ferraro and Tibbils (1999) proposed a method for measuring the SP and AP areas in tympanic electrocochleography (TM ECochG). They found that including both SP/AP amplitude and area ratios in the diagnostic criteria significantly increased the sensitivity to MD. As a follow up to this study, Devaiah et al. (2003) reviewed the charts of 138 patients with MD. Among 20 patients with possible MD, eight passed the exclusion criteria. The TM ECochG recordings of 8 patients and 13 controls were reviewed and SP/AP amplitude and SP/AP area curves were measured as described in the previous publication (Ferraro and Tibbils, 1999). The authors concluded that the SP/AP area curve ratio significantly improves the ECochG sensitivity in possible Ménière's disease.

A large retrospective chart review conducted by Baba et al. (2009) identified in a 15-year period 198 patients (209 ears) with Ménière's disease, diagnosed according to the Committee on Hearing and Equilibrium of AAO HNSF criteria and compared them to 16 volunteers (controls). They analyzed transtympanic (TT) ECochG records and measured the SP and AP areas as proposed by Ferraro and Tibbils (1999). An image of the waveform of the AP and SP complex was captured by an image scanner, and the outline of the captured image was then traced with the computer mouse to calculate the area using the NIH Image software. These authors concluded that the SP/AP area ratio might not necessarily have higher sensitivity in the diagnosis of endolymphatic hydrops than the SP/AP amplitude ratio in TT ECochG.

Oh et al. (2014) used extratympanic (ET) ECochG in 60 Ménière patients and 30 controls. They also captured an image of the waveform of the AP and SP complex, outlined the captured image with the computer mouse and calculated the area using the ImageJ software, a time consuming procedure. They found no statistically significant difference in the mean SP/AP area ratio between patients with definite, probable, or overall Ménière's disease, as compared to controls.

Contrasting with the previous studies, Al-Momani et al. (2009), comparing 178 suspected MD patients and twenty volunteer subjects with normal hearing thresholds who produced normative ECochG values for the study, found that the SP amplitude to click stimuli, the SP/AP amplitude ratio, and the SP/AP area ratio were the most sensitive and specific measures associated with a diagnosis of MD. More importantly, when the SP/AP area and amplitude ratios were included together (versus the area or amplitude ratio alone) the sensitivity value improved from approximately 60% to 92%, while specificity remained high at 84%.

Margolis et al. (1995) recorded data on rarefaction and condensation clicks in 28/53 subjects using tympanic electrode (Margolis et al., 1995). At 88 dB nHL the mean AP latency difference between rarefaction and condensation clicks was 0.15 ± 0.13. The 95th percentile was determined at 0.38 ms. The authors recommended that the AP latency difference to condensation and rarefaction clicks should be included among the indicators of endolymphatic hydrops.

There is still no consensus about the best ECochG method for evaluating MD: TT ECochG or TM ECochG or ET ECochG, nor about the type of stimulus, intensity and the most practical approach to establish the area measures. Some manufacturers have recently included software algorithm upgrades that calculate automatically the areas when the clinician determines the baseline, onset and end of AP and SP as well as AP and SP peaks. So measurements are now user-friendlier and can be performed easily within the manufacturer's software.

While the SP/AP area ratio, AP latency difference to rarefaction and condensation clicks and the tone-burst evoked summating potential are used in clinical practice for more than 10 years, there is a lack of normative data for these measures as most papers were focused on symptomatic patients (Devaiah et al., 2003; Baba et al., 2009; Ferraro and Tibbils, 1999; Al-Momani et al., 2009). The largest sample of normal controls (n = 30) was reported by Oh et al. (2014). In this study no data on the action potential latency difference to rarefaction and condensation click were reported.

The aim of this study is to establish normative data for SP/AP amplitude ratio, SP/AP area ratio and the AP latency difference to rarefaction and condensation clicks in a population of normal hearing adults without symptoms of MD, following the criteria proposed by the AAO HNS 1995 (1995) and Gibson (2009).

2. Material and methods

2.1. Study population

In this retrospective chart review from September 2010 to April 2014 we enrolled 100 subjects (N = 200 ears) aged between 19 and 71 years (mean age 43.6 ± 11.8 years), 59 females. Inclusion criteria were: normal otomicroscopy, pure tone thresholds ≤25 dB nHL from 250 to 4000 Hz, normal tympanogram. Only subjects without any symptoms of MD according to the criteria of the Committee on Hearing and Equilibrium of the American Academy of Otolaryngology − Head and Neck Surgery Guidelines AAO-HNS 1995 (1995) and with a Gibson's score <7 (Gibson, 2009) were eligible. We excluded subjects with middle or external ear abnormalities as well as patients with dizziness, aural fullness or other symptoms of possible endolymphatic hydrops not included among the AAO-HNS criteria.

2.2. Ethics

This study was approved by the Institution Ethics Committee (number 835.965/2014).

2.3. ECochG recording

After careful otomicroscopic inspection and cleansing of the external ear canal, 10% xylocaine spray was filled into the ear canal to reduce patient's discomfort. After 10 min the ear canal was irrigated with warm 0.9% saline solution and

completely dried. The tympanic electrode (Sanibel, Eden Prairie, Mn) was placed under otomicroscopy on the postero-inferior quadrant of the tympanic membrane. The foam rubber tip of the ER-3A insert phone (Etymotic Research, Elk Grove Village, IL) helped to secure the TM electrode in place. Surface electrodes were positioned at high-forehead (Fz), low forehead (ground) and ipsilateral ear lobe (inverting). Impedance was <5 KΩ. All subjects had bilateral recordings. The stimulus was a broadband click delivered at 90 dB nHL. We collected 1000 stimuli in each run, the stimulus rate was 11.3/second using alternating polarity (500 rarefaction and 500 condensation stimuli). Each run of clicks was repeated at least twice in both ears. The filter was set between 5 and 3000 Hz. If the test did not show the expected response amplitude and morphology, the TM electrode was replaced under otomicroscopy until achieving a high quality test response (smooth baseline, well defined AP – Fig. 1). All recordings were performed in a sound-attenuated, electrically shielded room using the Otoaccess software version 1.2.1 running on the Interacoustics Eclipse (Assens, Denmark).

2.4. ECochG analysis

At least 2 runs were performed for each ear. For data analysis we chose the test run with the largest AP amplitude in each ear. As shown in Fig. 1, we determined the baseline (BL) start, BL end, SP, AP1, AP2 and AP peak and analyzed the following parameters:

1) SP/AP amplitude ratio
2) SP/AP area ratio
3) Difference between AP latency with rarefaction and condensation stimuli (Fig. 2)

Not all normal ECochG tests exhibit SP. When the SP was not present we analyzed only the AP parameter.

2.5. Statistical analysis

Mean, standard deviation, median, percentiles 5 to 95 were calculated. The ICC test was performed to compare right and left ear test results.

3. Results

All 200 ears of normal hearing subjects showed AP, 129 of them exhibited a marked SP deflection preceding AP. Mean SP/AP amplitude ratio was 0.21 ± 0.08 for the right ear and 0.21 ± 0.07 for the left ear, respectively. The mean SP/AP area ratio was 1.22 ± 0.20 for the right ear and 1.23 ± 0.21 for the left ear. The mean AP latency differences to rarefaction and condensation clicks were 0.15 ± 0.1 ms for the right ear and

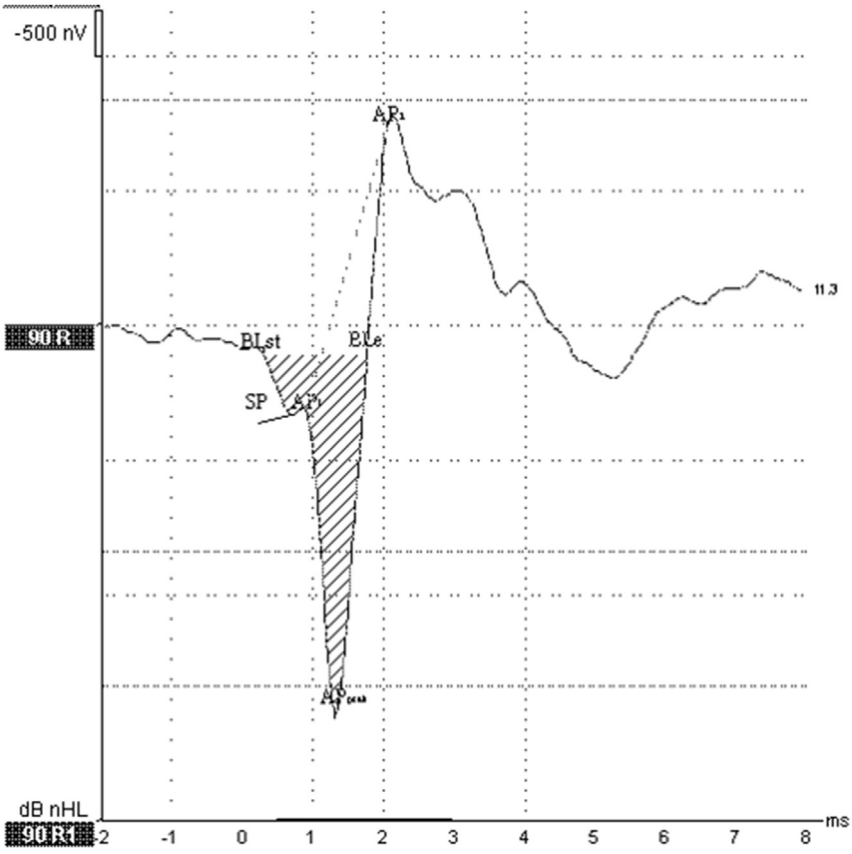

Fig. 1. Smooth baseline and well-defined AP.

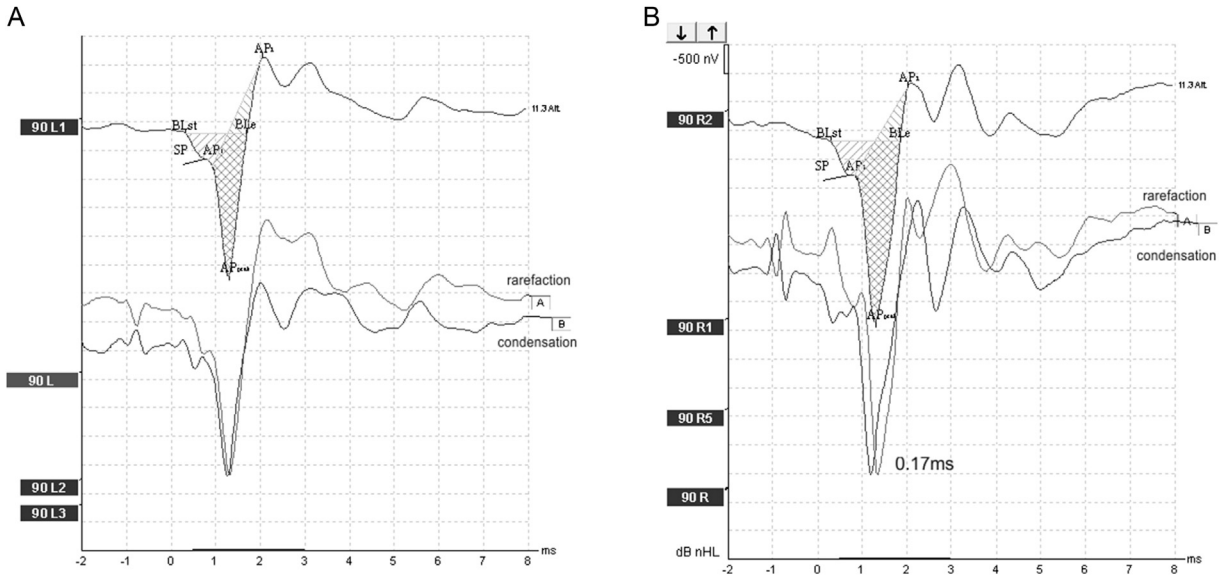

Fig. 2. Differences between AP latencies with rarefaction and condensation stimuli. A. No AP latency difference between rarefaction and condensation polarities. B. AP latency difference of 0.17 ms, in the normal range. In this example, the rarefaction AP latency was longer.

Table 1
SP/AP area ratio, SP/AP amplitude ratio and latency difference to rarefaction and condensation clicks for right and left ears (mean and SD).

	Ear	Mean	SD	N
SP/AP area ratio	Left	1.23	0.21	56
	Right	1.22	0.20	73
SP/AP amplitude ratio	Left	0.21	0.07	56
	Right	0.21	0.08	73
APrar/cond latency difference	Left	0.13	0.09	100
	Right	0.15	0.10	100

0.13 ± 0.09 ms for the left ear (Table 1). There was no significant difference between right and left ears (Intraclass correlation coefficient < 0.6). As shown in Table 2, the SP/AP amplitude ratio varied between 0.084 and 0.356 and the SP/AP area ratio between 0.837 and 1.671 (percentile 95, upper limit of normal values). The AP latency difference to rarefaction and condensation clicks was between 0.0 and 0.333. The distribution of SP/AP amplitude ratio and SP/AP area ratio are depicted in Figs. 3 and 4.

4. Discussion

This paper shows data for normal hearing subjects obtained by high-quality TM ECochG recordings in a routine clinical setting. The sample of 100 subjects is among the largest in the literature evaluating normative ECochG parameters and, to our knowledge, the only one in English language in the last 10 years reporting data exclusively from normal hearing subjects without MD.

Table 2
Percentiles 5 to 95 for ECochG parameters in normal hearing subjects.

	P5	P10	P25	P50	P75	P90	P95
SP/AP area ratio	0.837	0.929	1.083	1.254	1.425	1.579	1.671
SP/AP amplitude ratio	0.084	0.114	0.164	0.220	0.276	0.326	0.356
APrar/cond latency difference	0.000	0.000	0.061	0.140	0.219	0.290	0.333

P = percentiles.

Under the proposed test conditions, the SP/AP amplitude ratio cut-off was 0.356, which is in line with the data of Pou et al. (1996). Other researchers found higher values between 0.40 and 0.45 (Al-Momani et al., 2009, Margolis et al., 1995). Our mean SP/AP amplitude ratio and variability were low for both ears (0.21 ± 0.08), explaining the rather low cut-off of 0.356. We accepted only smooth baseline recordings what may have contributed to this finding.

Both rarefaction and condensation APs contribute to the composed SP/AP area. When the AP latency difference between rarefaction and condensation is larger, the area is expected to be larger as well. We found a small mean (0.13 for the right ear and 0.15 for the left ear) and median (0.14 for both ears) AP latency difference between rarefaction and condensation clicks, in line with Margolis et al. (1995). This finding could explain in part why our P95 SP/AP area ratio of 1.67 is lower than that proposed by Al-Momani et al. (2009). In addition, these researchers used other equipment and measured the SP area differently.

It has been shown previously (Ferraro and Tibbils, 1999; Al-Momani et al., 2009) that a TT recording with a traditional broadband click in 90 dB nHL produces a high AP amplitude response. The recording shows a smooth baseline that permits precise definition of the ECochG components (Fig. 1). As amplitude may vary according to the electrode position on the tympanic membrane, we chose the best recording with the largest AP amplitude for analysis. Reliable and reproducible normative data of normal hearing subjects without symptoms of endolymphatic hydrops/MD are essential to correctly interpret test results of patients with cochleo-

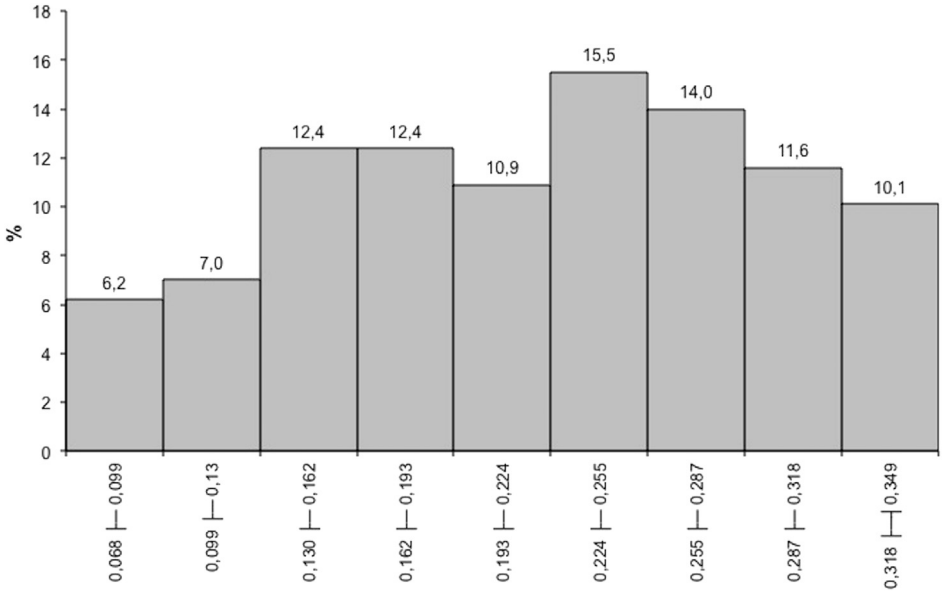

Fig. 3. SP/AP amplitude ratio.

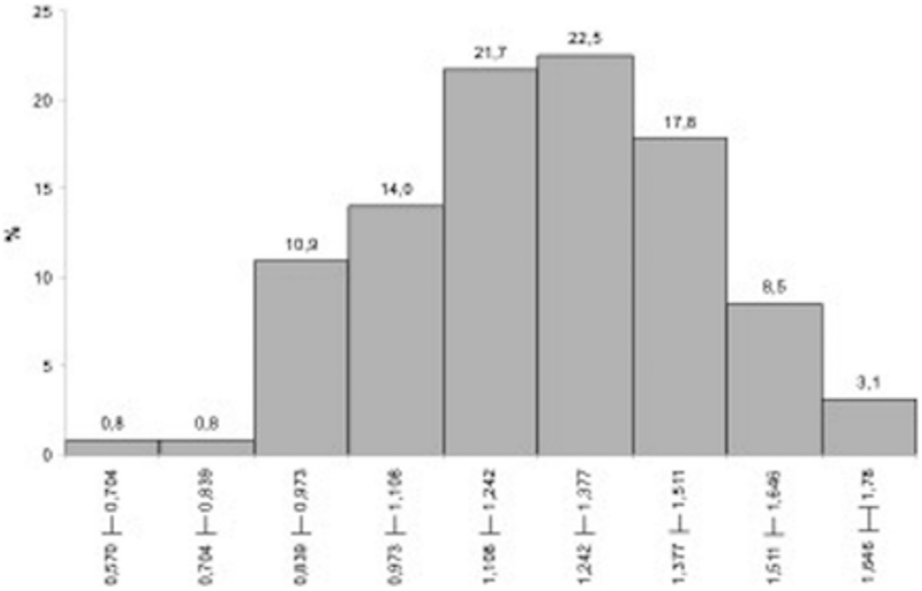

Fig. 4. SP/AP area ratio.

vestibular diseases as well as pure sensorineural, conductive or mixed hearing loss. As most researchers focused on patients with MD, this study has the purpose of filling a gap in the literature.

We cannot rule out that any of our subjects could develop an endolymphatic hydrops some time later in life. Our subjects were referred for audiologic evaluation due to symptoms like tinnitus, balance problems without vertigo or ear fullness although none of them fulfilled the AAO HNS criteria for possible or definite MD and Gibson's criteria >7. We could speculate that the normal values obtained in this study maybe even higher than those obtained among normal hearing volunteers without any hearing or balance complaints. This is a patient-based study with the aim to provide clinicians with data they may obtain from normal hearing patients in a clinical setting. On the other hand, the inclusion of patients instead of volunteers may be a limitation of this study. A prospective study of a large number of normal hearing volunteers in the same age range of MD patients could help to elucidate this question.

So, considering the proposed normative data of this study, test results exceeding the 95 percentile for SP/AP amplitude ratio, SP/AP area ratio and rarefaction and condensation latency difference can be considered abnormal in clinical practice when the proposed stimulation and recording parameters are followed. When testing patients for MD, clinicians should keep in mind that a hearing loss with PTA of 50 dB nHL or worse may reduce both SP and AP amplitudes

due to hair cell damage and/or fewer cochlear hair cell and nerve fibers contributing to the response amplitude. These conditions may result in possible distortion of SP/AP amplitude and area ratios. So, ECochG for diagnosis or evolution for MD is best used in the initial phase of the disease, close to a typical vertigo episode or aural fullness before definite hearing loss is installed (Ferraro, 2010). Data for patients with sensorineural hearing loss $\leq$50 dB nHL and no MD are currently being collected in our clinic to help to clarify this question.

Tympanic Electrocochleography permits collection of high quality recordings in a clinical setting. We propose normative data for three ECochG measures already available using most auditory evoked potential recording units that may enhance diagnostic accuracy when used altogether. Using these measures, the diagnostic protocol for suspected MD may be shortened reducing test time, costs and patient discomfort (Al-Momani et al., 2009).

5. Conclusion

Normative data for SP/AP amplitude ratio, SP/AP area ratio and the AP latency difference to rarefaction and condensation clicks were established in 100 normal hearing subjects (200 ears) without MD. These data can be used in clinical practice to improve diagnosis and follow-up of patients with MD.

Disclosure

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper. This research did not receive any specific grant from funding agencies in the public, commercial or not-for-profit sectors.

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