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ScienceDirect

Journal of Otology 12 (2017) 29-33



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Electrocochleographic recording in Asian adults: Preliminary normative data and demographic analyses

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Received 15 October 2016; revised 29 January 2017; accepted 6 February 2017

Abstract

Objective: Electrocochleography (ECochG) is valuable to diagnose Meniere's disease objectively. The aim of the present study was to provide preliminary normative data for ECochG among Asian adults. The influences of ethnicity (Malay versus Chinese) and gender on ECochG results were also studied.

Methods: Twenty-two Malay adults (10 men and 12 women) and twenty Chinese participants (10 men and 10 women) aged between 20 and 49 years participated in this study. Extratympanic ECochG (ET-ECochG) was recorded according to standard non-invasive procedure. Summating potential (SP) amplitude, action potential (AP) amplitude and SP/AP ratio were analyzed accordingly.

Results: ET-ECochG results were found to be comparable between left and right ears (p > 0.05). No notable differences in ET-ECochG results were found between Malay and Chinese groups (p > 0.05). No significant influence of gender on ET-ECochG outcomes was also noted (p > 0.05). The derived normative data for Asian adults (84 ears) are consistent with previous reports.

Conclusion: The present study provides preliminary normative data for ET-ECochG among Asian adults. The ECochG components do not appear to be influenced by either ethnicity or gender. The derived normative data can be used for clinical applications and as the reference for future studies involving Asian population.

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Keywords: Electrocochleography; Normative data; Ethnicity; Gender; Meniere's disease

1. Introduction

Electrocochleography (ECochG) is a short latency auditory evoked response (AER) that assesses the functional integrity of the cochlea and auditory nerve (Hall, 2007). It is recorded by placing the typical scalp electrode on a head and a special electrode near, on or through tympanic membrane (TM). If the electrode is placed in the ear canal or on TM, the procedure is known as extratympanic ECochG (ET-ECochG) (Hall, 2007).

Peer review under responsibility of PLA General Hospital Department of Otolaryngology Head and Neck Surgery.

On the other hand, transtympanic ECochG (TT-ECochG) is an invasive procedure in which the electrode is placed through TM and rests gently on the promontory or round window of the cochlea (Hall, 2007). Since ECochG is a near-field response, the most robust waveforms are produced by the TT-ECochG procedure (Hall, 2007). However, due its invasiveness, it may not be suitable to be carried out routinely. In this regard, the non-invasive ET-ECochG procedure is the better option. In fact, well-designed and reliable electrodes are available commercially for recording ET-ECochG (known as tiptrode and tymptrode to be placed in the ear canal and on TM, respectively). Due to closer proximity to cochlea, ET-ECochG waveforms are typically larger and more reliable when recorded with the electrode on TM (Hall, 2007). On the other hand,

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even though the waveforms are less robust, the ET-ECochG procedure with tiptrode is more comfortable and particularly useful when testing children (Anastasio et al., 2008).

If alternating clicks are used as the stimuli, two prominent components of ECochG are produced: summating potential (SP) and action potential (AP) (Fig. 1). SP is a direct current endocochlear potential in response to an acoustical stimulation (Hall, 2007). AP is the sum of synchronous action potentials generated by the distal portion of the auditory nerve (Hall, 2007). It is in fact analogous to wave I of auditory brainstem response (ABR). If rarefaction or condensation clicks are used for recording ECochG, cochlear microphonic (CM, instead of SP) is produced. CM is an alternating electrical potential generated predominantly by the outer hair cells in the cochlea (Hall, 2007).

Clinically, ECochG is typically performed to diagnose Meniere's disease objectively (Gürkov et al., 2016). The sensitivity of ECochG in detecting Meniere's disease can be as high as 92% (Ferraro et al., 1985). In fact, it can be better than gadolinium magnetic resonance (MRI) in diagnosing Meniere's disease (Hornibrook et al., 2015). In this ear disorder, due to endolymphatic hydrops, the resting position of the basilar membrane is altered leading to an increase of SP amplitude (Klis and Smoorenburg, 1994). Consequently, an elevated SP/AP ratio is observed. The SP/AP ratio that exceeds 0.3–0.4 is highly indicative of endolymphatic hydrops (Ferraro, 2010). Apart from diagnosing Meniere's disease, ECochG can also be used in other clinical applications. It is useful for verifying the presence of wave I of ABR, diagnosing auditory neuropathy and for intraoperative monitoring (McMahon et al., 2008; Krieg et al., 2014; Minaya and Atcherson, 2015).

Having an ECochG is advantageous when assessing otological patients, particularly those with Meniere's disease. Nevertheless, specific normative data might be required prior to its clinical applications. In an Asian country like Malaysia, according to Population Distribution and Basic Demographic

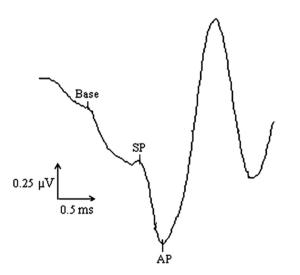


Fig. 1. Typical electrocochleography (ECochG) response from a normal subject.

Characteristic Report (2010), the majority of residents are Malay (67.4%) and followed by Chinese (24.6%). Until now, the normative data for ECochG among this particular population are not yet available. The present study, therefore, was carried out to provide preliminary normative data for ET-ECochG among Asian adults. In addition, in order to produce valid normative data, the influence of demographic factors (ethnicity and gender) on ECochG should be determined. Due to limited literature, little is known regarding the influence of ethnicity on ECochG components. It is also unclear whether ECochG outcomes are different between sexes due to discrepancies between previous studies. While the gender influence on ECochG components was reported to be negligible in some studies (Padilla La Rosa and De Vinatea, 1999; Franco and Chiong, 2002), other studies revealed greater SP and AP amplitudes in females than in males (Chatrian et al., 1985; Coats, 1986). In the present study, ET-ECochG outcomes between two ethnic groups (Malay and Chinese), as well between sexes were studied.

2. Materials and methods

2.1. Participants

Twenty-two Malay adults (10 men and 12 women) and twenty Chinese participants (10 men and 10 women) aged between 20 and 49 years (mean = 29.8 ± 8.3 years) were enrolled in the present comparative study. They were selected randomly among staff members of University Hospital. All of them were healthy, right-handed and reported no history of otological, audiological and neurological problems. This study was approved by the institutional ethics committee, which is in accordance with the 1975 Declaration of Helsinki and its later amendments. Prior to the data collection, all subjects gave a written consent to participate voluntarily in the study. They were explained regarding the purpose, importance and benefits of the study.

For ensuring the eligibility of the participants, otoscopy, tympanometry and pure tone audiometry (PTA) were carried out. Otoscopy was performed to assess the patency of the ear canal and normality of the tympanic membrane (TM). Cerumen removal might be necessary to visualize the TM and ensure a clear pathway along the ear canal for the ease of electrode placement. Tympanometry was conducted to determine the middle ear function. Hearing thresholds were determined with PTA. All participants were found to have normal hearing (hearing thresholds $\leq 20~{\rm dBHL}$ between 0.25 and 8 kHz) and type A tympanogram (suggestive of normal middle ear function) in both ears.

2.2. Recording procedure for electrocochleography

ET-ECochG was recorded using a two-channel Biologic Navigator Pro AEP system (Natus Medical Inc., Mundelein, USA). Table 1 reveals the detailed test parameters used in the present study for recording ECochG. Before the measurement began, adequate instructions were given to each participant.

Table 1 Test parameters for recording electrocochleography (ECochG) in the present study.

| Parameter | Selection | | | |
|---------------------------|---------------------------|--|--|--|
| Electrode placement | | | | |
| Non-inverting (tymptrode) | On tympanic membrane | | | |
| Inverting | Contralateral mastoid | | | |
| Ground | Fpz (low forehead) | | | |
| Transducer | Insert earphones (ER-3A) | | | |
| Stimulus | 0.1 ms alternating clicks | | | |
| Stimulus rate | 7.1/s | | | |
| Intensity | 95 dBnHL | | | |
| Presentation | Monaural | | | |
| Filter setting | 10-1500 Hz | | | |
| Amplification | 50,000 | | | |
| Analysis time | -1.0-5 ms | | | |
| Sweeps | 1000 | | | |

The ET-ECochG was performed according to the standard non-invasive procedure. After cleaning the skin gently with the conductive paste, two Ag-AgCl scalp electrodes were placed on the subject's head: inverting electrode on the contralateral mastoid and ground electrode on the low forehead (Fpz). For non-inverting placement, a TM electrode, known as tymptrode was placed on TM. Before the insertion, conductive gel was applied on the tip of the tymptrode. By using headlight, the tymptrode was then gently inserted into the ear canal until it made direct contact with TM. All the tymptrode placements were carried out by experienced clinicians. Throughout the testing, the electrode impedances were kept below 5 k Ω and 40 k Ω for scalp electrode and tymptrode, respectively.

For each ear, 0.1 ms alternating clicks were presented repetitively at a rate of 7.1/s through ER-3A insert earphones. The intensity level was set at 95 dBnHL. A time window of 5 ms (including 1 ms pre-stimulus time) and filter setting of 10–1500 were used. For ensuring good quality of the responses, the stimuli were presented with 1000 sweeps. For adequate visualization, the acquired responses were amplified 50,000 times. To ensure good reproducibility of the response, two replicate waveforms were obtained from each participant. During the testing, the participants lied comfortably on the provided bed. All measurements were performed in a sound proof room within the Audiology Clinic, University Hospital.

2.3. Statistical analyses

Base, SP and AP components of ET-ECochG were identified and plotted by two experienced audiologists. AP amplitudes,

SP amplitudes and SP/AP ratios were analyzed. Mean, standard deviation (SD) and standard error of the mean (SEM) were expressed as applicable. Since the data were found to be normally distributed by Kolmogorov Smirnov test (p > 0.05), parametric statistics were then used for data analyses. Paired t test was used to compare the ECochG results between left and right ears of participants. Two-way analysis of variance (ANOVA) (with ethnicity and gender as the factors) was utilized to compare the ECochG results between Malay and Chinese subjects, as well as between sexes. P values of less than 0.05 were considered statistically significant. All data analyses were conducted with the SPSS software version 20 (SPSS Inc, Chicago, IL).

3. Results

All participants completed the ET-ECochG testing successfully. The paired t test revealed no significant differences in all ECochG components between left and right ears (p > 0.05). Hence, the left and right data were pooled for subsequent analyses.

Table 2 shows the mean and standard deviation of ET-ECochG results for Malay (n = 44) and Chinese (n = 40) participants. As revealed, no interaction effect (between ethnicity and gender) was seen for all ECochG components (p > 0.05). Hence, the main effects could be analyzed independently. As shown in Table 2, in terms of ethnicity, no significant differences were found between Malay and Chinese participants for all ECochG results (p > 0.05). Similarly, all ECochG results were found to be not statistically different between men and women for both ethnic groups (p > 0.05).

Due to insignificant influences of ethnicity and gender, the ET-ECochG data for Malay and Chinese subjects were pooled for producing the required normative data (n = 84). Table 3 reveals the mean, SD, SEM and 90% range (5th and 95th percentiles) for SP amplitude, AP amplitude and SP/AP ratio of ET-ECochG for Asian adults.

Table 3 Mean, standard deviation (SD), standard error of mean (SEM) and 90% range (5th and 95th percentiles) for SP amplitude, AP amplitude and SP/AP ratio (n=84).

| Statistics | SP (µV) | AP (μV) | SP/AP |
|------------------------------|-------------|-------------|-------------|
| Mean | 0.20 | 0.65 | 0.32 |
| Standard deviation (SD) | 0.08 | 0.25 | 0.06 |
| Standard error of mean (SEM) | 0.01 | 0.03 | 0.01 |
| 90% range | 0.08 - 0.36 | 0.31 - 1.12 | 0.21 - 0.40 |

Table 2 Descriptive and inferential statistical analyses of electrocochleography (ECochG) results by ethnicity and gender.

| ECochG component | Mean ± SD | | | | p Value | | |
|------------------|--------------------------------|------------------------------------|--------------------------------|------------------------------------|----------------|----------------|--------------------|
| | Malay (n = 44) | | Chinese (n = 40) | | | | |
| | Men (n = 20) | Women (n = 24) | Men (n = 20) | Women (n = 20) | Ethnicity | Gender | Ethnicity × Gender |
| SP (μV) | 0.19 ± 0.10 | 0.21 ± 0.07 | 0.20 ± 0.08 | 0.21 ± 0.06 | 0.702 | 0.415 | 0.762 |
| AP (μV) SP/AP | 0.64 ± 0.36 0.31 + 0.06 | 0.66 ± 0.23 0.32 ± 0.05 | 0.64 ± 0.24 0.32 + 0.07 | 0.66 ± 0.16 0.32 ± 0.07 | 0.992 0.502 | 0.650 0.777 | 0.971 0.750 |

^{*}Significant at p < 0.05 by 2-way ANOVA.

4. Discussion

In the field of auditory electrophysiology, the influence of demographic factor such as ethnicity on evoked responses is not well studied. To the best of our knowledge, no study has been conducted to directly compare the ECochG results between different ethnic groups. The rationale to study the effect of ethnicity is that different ethnic groups might produce different study outcomes. For example, differences in physiological functions of middle ear have been reported between Caucasian and Asian adults (Shahnaz and Davies, 2006; Shahnaz and Bork, 2008). That is, due to the difference in body size, lower ear canal volume, wider tympanometric width and lower static admittance values were observed in Chinese adults than in Caucasian participants (Shahnaz and Davies, 2006; Shahnaz and Bork, 2008).

In the present study, we found no notable influence of ethnicity on ECochG results. That is, SP amplitude, AP amplitude and SP/AP ratio were comparable between Malay and Chinese groups. These results are sensible as both ethnic groups are from Asia origin and they share many similar anatomical features (Ngeow and Aljunid, 2009). These findings are in line with the results from a recent study by Zakaria et al. (2016a). In their study, no significant differences in speech-ABR results were found between Malay and Chinese subjects. They concluded that the insignificant outcomes were possibly due to the anatomical similarities between the two ethnic groups. In addition, by employing one-sample t test analysis, they also compared their speech-ABR findings with the corresponding Caucasian data from a study by Krizman et al. (2012). Significant differences in most speech-ABR results were reported between Asian and Caucasian adults. These findings further support the notion that the auditory evoked responses can be influenced by the body size. On the other hand, since ECochG is a near-field response, the present study had no intention to compare our ECochG results with the findings from the previous ECochG studies on other ethnic group (e.g. Caucasian). This is because the indirect comparison (by using one sample t test) might be hindered by methodological differences including type of ECochG, difference in electrode design and recording parameters.

Significant gender disparities have been reported in many types of auditory evoked responses. Specifically, more robust responses are found in women than in men (Sato et al., 1991; Don et al., 1993; Tremere et al., 2009; Krizman et al., 2012). Anatomical and hormonal differences have been suggested as the contributing factors for the gender disparities. Due to smaller head size, less brain volume and shorter cochlear length, peaks with earlier latencies and larger amplitudes were seen in women (Sato et al., 1991; Don et al., 1993; Hall, 2007; Krizman et al., 2012). Moreover, the effects of hormone (estrogen) on auditory evoked responses have been discussed elsewhere (Hultcrantz et al., 2006; Tremere et al., 2009; Zakaria et al., 2016b, 2016c). In particular, having higher levels of estrogen would increase synaptic transmission and neural conduction resulting in more robust waveforms in women (Don et al., 1993; Tremere et al., 2009).

In the present study, no such gender effect was found for SP amplitude, AP amplitude and SP/AP ratio. Recall that the ECochG data for the left and right ears were pooled as an effort to increase the statistical power when testing for gender difference. Yet, no significant differences in ECochG results were found between the genders. The findings from the present study, nevertheless, are consistent with the results from the previous reports (Padilla La Rosa and De Vinatea, 1999; Franco and Chiong, 2002). In a study by Padilla La Rosa and De Vinatea (1999), ECochG was recorded from 98 healthy subjects (50 males and 48 females) and no notable influence of gender on ECochG components was found. In contrast, larger SP and AP amplitudes in women were reported in the studies by Chatrian et al. (1985) and Coats (1986). The reason for this disagreement is unknown. The difference in sample size may not be the main reason as more subjects were recruited in the study by Padilla La Rosa and De Vinatea (n = 98) relative to the studies by Chatrian et al. (n = 60) and Coats (n = 48). Further research is warranted to verify this issue.

Nevertheless, in line with the present study, both studies by Chatrian et al. (1985) and Coats (1986) found no significant gender influence on the SP/AP ratio. Furthermore, in ABR studies, the gender effect is more pronounced for later waves (Aoyagi et al., 1990; López-Escámez et al., 1999). That is, the wave I of ABR is minimally affected by gender, which is consistent with the analysis of AP amplitude in the present study.

The normative data for ET-ECochG among Asian adults are presented in Table 3. The mean amplitudes of SP and AP, as well as mean SP/AP ratio are comparable with the published Caucasian data (Park and Ferraro, 1999; Wilson and Bowker, 2002). On the other hand, larger mean AP amplitudes were reported in a study by Minaya and Atcherson (2015). This discrepancy is possibly due to the difference in electrode design. While the present study used the commercially available tymptrode, Minaya and Atcherson (2015) recorded ET-ECochG with a custom made TM electrode.

As expected, the mean amplitudes of SP and AP in the present study are lower than that of TT-ECochG studies (Ferraro, 2010; Sass et al., 1998) and higher than the reported ET-ECochG results obtained with ear canal electrodes (Chatrian et al., 1985; Padilla La Rosa and De Vinatea, 1999). For SP/AP ratio, the upper limit of 90% range value (0.40) agrees well with the findings from the previous studies (Margolis et al., 1995; Kim et al., 2005). In this regard, an SP/AP ratio of 0.40 and greater would suggest the presence of endolymphatic hydrops.

The present study, nevertheless, has several limitations. Firstly, since an old version of AEP device was used, SP/AP area ratios could not be measured. Secondly, the normative data for ECochG would be more favorable if more subjects could be recruited. Finally, the current data only represent Malay and Chinese adults with a limited range of ages (20–49 years). In this regard, further research is warranted to study ECochG outcomes in other age and ethnic groups.

5. Conclusions

The present study provides preliminary normative data for ET-ECochG among Asian adults. In addition, the ECochG components do not appear to be influenced by either ethnicity or gender. These normative data can be valuable for clinical applications involving Asian population. Nevertheless, future large-scale studies are encouraged to further support the outcomes obtained from the present study.

Funding

Short Term Grant (304/PPSK/61313023), Universiti Sains Malaysia.

Conflict of interest

None.

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