Action Potential Latency in Individuals with Endolymphatic Hydrops

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Abstract

Meniere's disease has one of the highest prevalence among those that affect the peripheral vestibular system. Various tests have been employed for the diagnosis of Endolymphatic hydrops. These include Glycerol test, OAE, VEMP, CHAMP, and ECochG in addition to the conventional routine audiological evaluations. However, the reports in the literature are suggestive of inaccurate and inadequate performance of these tests in the diagnosis of Meniere's disease. The present study aimed at checking the utility of latency difference between condensation and rarefaction polarities of AP and ABR in the diagnosis of Meniere's disease. The study also aimed at comparing these two techniques with the more established SP/AP amplitude ratio. In the present study, the conventional ABR and extratympanic ECochG were recorded from 21 ears of individuals with Meniere's disease with pure tone average less than 55 dB, 25 ears of individuals with sensorineural hearing loss other than sloping configuration and pure tone average less than 55 dB, and also 48 ears of healthy individuals. The latency of AP and wave I of ABR for rarefaction and condensation, and SP/AP ratio were measured for all the group of participants. There was a significant correlation for the latency difference between AP polarities and wave I of ABR. There was no correlation between SP/AP ratio and latency difference between AP polarities and also between SP/AP ratio and wave I of ABR. The AP latency difference and wave I latency difference produced higher positive results in Meniere's disease than the SP/AP ratio. A combination of the AP latency difference and SP/AP ratio could identify Meniere's disease in 85% of individuals and hence the combination would be a better choice.

Keywords: *ECochG, SP/AP amplitude ratio, Meniere's disease.*

Introduction

Electrocochleography (ECochG) is a technique of recording stimulus related responses or the electrical potentials of the inner ear and auditory nerve. It is employed to evaluate cochlear function in patients with Meniere's disease. The underlying pathologic finding in Meniere's disease is widely suspected to be endolymphatic hydrops, which has been shown in animal studies to systematically alter cochlear potentials (Kimura, 1982; Aran, Rarey & Hawkins, 1984).

The cochlear potentials of interest in clinical ECochG are eighth nerve compound action potential (AP), summating potential (SP) and cochlear microphonics (CM). The AP results from simultaneous, stimulus-locked discharge of a population of spiral ganglion neurons (Kiang, Watanabe & Thomas, 1965; Cullen, Ellis & Berlin, 1972). The SP is a stimulus-locked direct current potential that can be observed as a baseline shift in the CM, and is also generated by cochlear hair cells (Dallos, 1973). The CM is an electrical response that mimics the acoustic waveform of the stimulus and is generated by the cochlear hair cells (Dallos, 1973).

A variety of electrode locations have been employed to record these potentials in animal and human investigations. In animal studies, electrodes are commonly placed in the cochlea (Van Deelen & Smoorenburg, 1986), on the round window (Prijs, 1985) or directly on the auditory nerve (Kiang, 1965). In humans, three electrode sites have been employed. Transtympanic ECochG is performed by placing a needle electrode through the tympanic membrane and onto the promontory (Moffat, Gibson, Ramsden, Morrison & Booth, 1977). Tympanic ECochG employs an electrode that is placed on the tympanic membrane (Margolis, Rieks, Fournier & Levine, 1995). Extratympanic ECochG is performed with an electrode placement in contact with the ear canal wall (Mori, Asai, & Matsunaga, 1987). These electrode sites tend to impact the morphology of the thus recorded ECochG waveform. In general, response amplitudes diminish with increasing distance from the cochlea (Eggermont, Odenthal, Schmidt, & Spoor, 1974).

ECochG has been used for the diagnosis of several auditory pathologies. These include auditory dys-synchrony (Roland, Yellin, Meyerhoff & Frank, 1995; Santarelli & Arslan, 2002; Anastasio, Alvarenga, & Filho, 2008) and also Meniere's disease (Aso, Watanabe & Mizukoshi, 1991; Mori, Asai, Suizu, Ohta & Matsunaga, 1985; Mori, Asai & Matsunaga, 1987; Ferraro & Tibbils, 1999; Saas, Densert, Magnusson & Whitaker 1998) among others.

The inadequacy of various tests in the diagnosis of Meniere's disease calls for further studies that could aid its diagnosis. So, the present study was conducted with the aim of evaluating the utility of latency difference between rarefaction and condensation polarities of AP and also ABR wave I in the diagnosis of Meniere's disease. The study also aimed at comparing the above techniques to identify the better of the three techniques in the diagnosis of Meniere's disease.

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Table 1: Protocol for recording ECochG and ABR

Stimulus parameter	ECochG	ABR	Acquisition parameter	ECochG	ABR
Stimulus intensity	90 dB nHL	90 dB nHL	Analysis time	5ms	10 ms
Stimulus rate	11.1/s	11.1/s	Pre-stimulus time	2ms	0 ms
Stimulus polarity	Rarefaction and condensation	Rarefaction and condensation	Amplification	50000 times	100000 times
Stimulus polarity	Clicks	Clicks	Filter settings	10 Hz -3000	100 Hz- 3000 Hz
			Sweeps	1000	1000

Method

The present study was conducted to evaluate the efficacy of latency difference of action potential between rarefaction and condensation polarities in the diagnosis of Meniere's disease. This was aimed at specifically using extratympanic recording technique of ECochG for the same.

Participants

The study incorporated three sets of participants who were divided into three groups; a Meniere's disease group, a sensorineural hearing loss group and a group of healthy individuals. Group I consisted of 21 ears of participants in the age range of 18 to 55 years (9 males & 12 females) who were diagnosed with endolymphatic hydrops based on the questionnaire of American Academy of Otolaryngology Head and Neck Surgery (1995). Each of the participants within this group had pure tone average threshold of less than 55 dB HL. Their unaffected ears served as a separate group for a number of analyses. The group II consisted of 25 ears of 16 participants (7 males & 9 females) with sensorineural hearing loss (other than Meniere's disease) in the same age range as group I. The other subject selection criteria for this group included exclusion of individuals with pure-tone average threshold exceeding 55 dBHL and sloping audiometric configuration. The existence of neural pathology was screened out using ABR. Forty eight ears of healthy individuals (age & gender matched to group I) with normal audio-vestibular system served as the participants in group III.

Instrumentation

A calibrated diagnostic audiometer GSI-61 with TDH-39 supra-aural headphones housed in MX-41/AR ear-cushions and Radioear B-71 bone vibrator was used for estimating air conduction and bone conduction thresholds. The same set of equipments in AC mode alone was used for speech audiometry.

A calibrated diagnostic immittance meter GSI-Tympstar was used to obtain Tympanogram. Same equipment was also used for obtaining ipsilateral and contralateral acoustic reflex thresholds (ARTs).

An Intelligent Hearing System Smart EP version 4.0 with ER-3A insert earphones connected with TIPtrode was used to acquire extratympanic ECochG. The same instrument without TIPtrode was used to acquire ABR.

Test Procedure

The routine audiological evaluation involved pure tone audiometry, speech audiometry, and immittance evaluation. Pure tone audiometry was done using the Carhart and Jerger (1959) modified Hughson and Westlake method for the octave frequencies of 250 through 8000 Hz for air conducted stimuli using TDH-39 headphones. Bone conduction thresholds were obtained for the octave frequencies of 250 through 4000 Hz. The word recognition score were obtained at the most comfortable level using the standardized word lists in the client's native language. Immittance evaluation was done to rule out any middle ear pathologies. It involved obtaining tympanogram and acoustic reflex thresholds (both ipsilateral and contralateral). Tympanograms were obtained using a 226 Hz probe tone frequency whereas the ARTs were obtained at frequencies from 500 Hz through 4000 Hz using the above mentioned probe tone frequency. The ABR was used to screen out neural pathology.

ECochG was administered by seating the participants comfortably in a well illuminated acoustically treated test room with the ambient noise levels within ANSI specifications (ANSI S3.1-1999). The skin overlying the electrode sites were cleaned using Nuprep skin preparing gel prior to the electrode placement. For the preparation of ear canal skin, the same skin preparing gel was used with a swab stick. The electrodes were mounted using Ten20 conduction gel and surgical plaster. The electrode montage consisted of TIPtrode as the non-inverting electrode which was placed in the ear canal; inverting electrode was placed on the test ear mastoid; and ground was placed on the forehead. The inverting and ground electrodes were the regular disc type silver chloride electrodes. An adult-size TIPtrode was attached to insertion cushion on the TIPtrode tubing. Tiptrode plug was then compressed tightly and placed in the ear canal while pulling the pinna upward, backward, and slightly outward, in a circular movement. It was ensured that the impedance for each electrode was less than 5kΩ and the inter-electrode impedance difference was less than 2 kΩ. The protocol for ECochG has been shown in table 1.

ABR was administered with the electrode montage that included the placement of inverting electrode on the test ear mastoid, non-inverting electrode on the forehead and ground on the non-test ear mastoid. All the electrodes were the regular disc type silver chloride electrodes. The participant preparation and the impedance values required for the electrodes for ABR were similar to that of ECochG. The protocol for ABR has been shown in Table 1.

Response Measure

The latency of the action potential and wave I of ABR for rarefaction and condensation, and SP/AP ratio were measured for all the group of participants. From that the shift in the latencies between the condensation and rarefaction polarities were measured by subtracting one from the other.

Statistical Analysis

A descriptive statistics was done to obtain the mean and standard deviation for the measures.Since the data obtained was non-normally distributed, the non-parametric statistical analysis was done. This involved a Kruskal Wallis test for overall comparison and a Mann-Whitney U test for pairwise comparison. A Kappa analysis was also done for checking the agreement between the SP/AP ratio and AP latency difference between the condensation and rarefaction polarities of click.

Results

The present study was conducted with the aim of checking the utility of latency difference between the condensation and rarefaction polarity of action potential in the diagnosis of Meniere's disease. In addition, it was aimed at evaluating the utility of a similar difference for ABR wave I in the diagnosis of Meniere's disease. Furthermore, the study also aimed at checking the efficacy of SP/AP ratio in the diagnosis of Meniere's disease and comparing this method to the AP latency difference to find out which is a better tool for the diagnosis of Meniere's disease. To fulfil these aims, the participants were divided in to 3 groups. The results are discussed under the headings of AP latency difference, SP/AP ratio, and ABR latency difference to compare between groups. Also a correlation between SP/AP ratio, ABR latency difference, and AP latency difference was evaluated. For several comparisons, the unaffected ears of individuals with Meniere's disease were considered as a separate group.

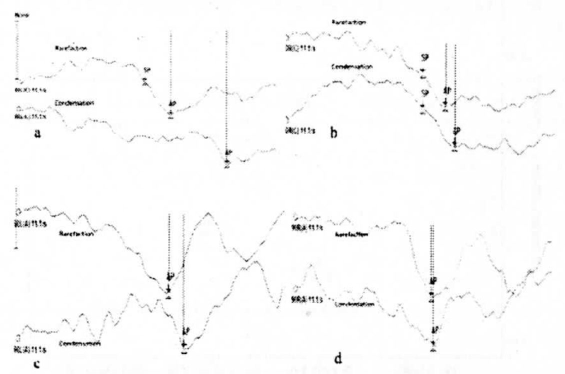

Figure 1: Representative AP waveforms (in alphabetic order) from affected ears with Meniere's disease, ears of healthy individuals, unaffected ears of individuals with Meniere's disease, and ears with sensorineural hearing loss.

AP Latency Difference between Condensation and Rarefaction Polarities of ECochG

All the participants within each of the three groups underwent ECochG and AP were identified in the condensation as well as the rarefaction polarities' waveforms. Sample ECochG waveforms from one participant from each of the groups are shown in Figure 1.

Statistical analysis was done using Statistical Prediction for the Social Sciences (SPSS) software version 17. The waveforms were analyzed for latencies of action potential for rarefaction and condensation polarities and the difference between the two was obtained. The values so obtained were then subjected to *descriptive analysis* to obtain mean and standard deviations. The *mean* and *standard deviation* values for ears of healthy individuals, ears of individuals with sensorineural hearing loss, unaffected ears of individuals with Meniere's disease and affected ears of individuals with Meniere's disease were found to be *0.13 ms (S.D = 0.02), 0.13 ms (S.D = 0.02), 0.21ms (S.D = 0.02), and 0.47ms (S.D = 0.11)* respectively. The mean of AP latency difference in the affected ears of individuals with Meniere's disease was higher than the other two groups and also compared to their own unaffected ears. Likewise, the unaffected ears of individuals with Meniere's disease also produced larger mean latency difference value than the ears of healthy individuals and also those of the individuals with sensorineural hearing loss. The same has been depicted in Figure 2.

A *Kruskal Wallis test* was administered to compare between the ears of healthy individuals, ears with SNHL, unaffected ears of individuals with Meniere's disease and affected ears of individuals with Meniere's disease in terms of the difference between the Action potential latencies between rarefaction and condensation clicks. The results revealed *significant difference* between the latencies of the two polarities [$\chi^2(3) = 71.889$, $p = 0.000$]. A *post hoc analysis* was done using *Mann-*

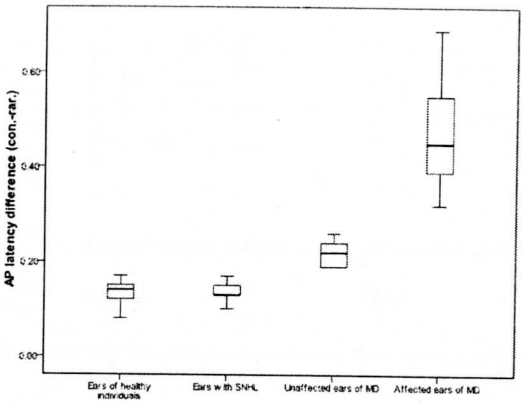

Figure 2: The box plot of AP latency difference between condensation and rarefaction polarities.

Whitney U test for pair wise comparison between all possible pairs. The pair wise comparison revealed a *significant difference* between all the pairs except between ears of healthy individuals and ears with SNHL. The latency difference between the polarities in the affected ears of individuals with Meniere's disease was also significantly different from the other groups. The latency difference was largest for the affected ears of individuals with Meniere's disease followed by their unaffected ears. The ears of healthy individuals and those of individuals with sensorineural hearing loss revealed lesser latency difference between the polarities than either of the above two and the two were comparable. The exact '*p*' and '*Z*' values are given in table 2.

ABR Wave I Latency Difference between Condensation and Rarefaction

All the participants within each of the groups underwent ABR and peaks (waves) were identified. Sample ABR waveforms from one participant from each of the groups are shown in Figure 3.

The waveforms were analyzed for latencies of wave I of ABR for rarefaction and condensation polarities and the difference between the two was obtained. The values thus obtained were then subjected to descriptive analysis. The ears of healthy individuals produced a *mean* ABR wave I latency difference of *0.08 ms (S.D. = 0.03)* between the two polarities used in the study. The difference for ears with sensorineural hearing loss, unaffected ears of Meniere's disease, and affected ears of Meniere's disease was *0.08 ms (S.D = 0.03), 0.13ms (S.D = 0.02),* and *0.32 ms (S.D = 0.07)* respectively. A graphical illustration of the same has been put forward in Figure 4.

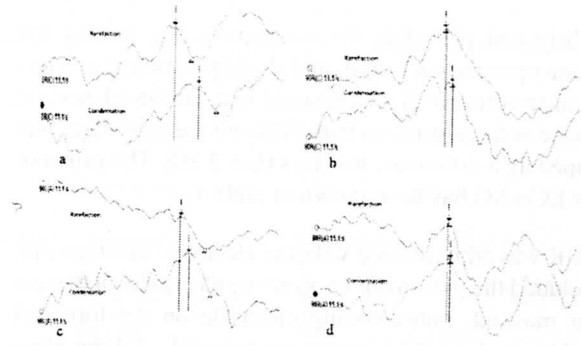

Figure 3: Panel 'a', 'b', 'c' and 'd' represent the ABR waveforms obtained from ears of individuals with Meniere's disease, ears of healthy individuals, unaffected ears of individuals with Meniere's disease, and ears with sensorineural hearing loss respectively.

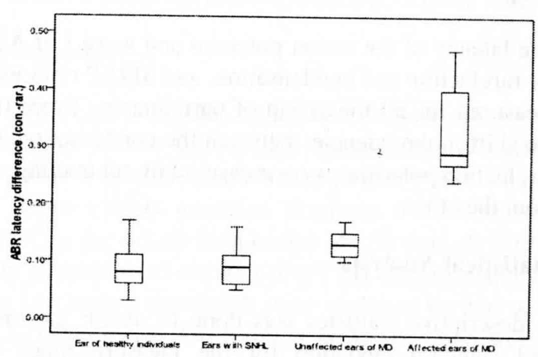

Figure 4: The box plot of the of ABR latency difference between condensation and rarefaction polarities.

A *Kruskal Wallis test* was administered to compare the groups in terms of the latency difference between rarefaction and condensation polarities for wave I of ABR. The results revealed *a significant difference* between the groups [$\chi^2(3) = 60.358$, $p = 0.000$]. A pair wise comparison was done using the *Mann-Whitney U test statistic* which revealed the latency difference of ABR be-

Table 2: 'Z' and 'p' values of Mann-Whitney U test for AP latency difference between condensation and rarefaction polarities

	Ears of healthy individuals	Ears of SNHL	Unaffected ears of MD	Affected ears of MD
Ears of SNHL	Z = -0.653 p = 0.514	- -	Z = -5.805 p = 0.000	Z = -4.968 p = 0.000
Unaffected ears of MD	Z = -5.530 p = 0.000	- -	- -	Z = -4.843 p = 0.000
Affected ears of MD	Z = -6.601 p = 0.000	- -	- -	- -

Table 3: 'Z' and 'p' values of Mann- Whitney U test for ABR latency difference between condensation and rarefaction polarities

	Ears of healthy individuals	Ears of SNHL	Unaffected ears of MD	Affected ears of MD
Ears of SNHL	Z = -0.579	-	Z = -3.415	Z = -5.798
	p = 0.563	-	p = 0.001	p = 0.000
Unaffected ears of MD	Z = -3.749	-	-	Z = -4.844
	p = 0.000	-	-	p = 0.000
Affected ears of MD	Z = -6.588	-	-	-
	p = 0.000	-	-	-

tween the polarities in the affected ears of individuals with Meniere's disease to be *significantly different* from all of the groups (ears of healthy individuals, ears with SNHL, & unaffected ears of individuals with Meniere's disease). The comparison between ears of healthy individuals and those of sensorineural hearing loss showed *no significant difference*. The latency difference between the polarities in the unaffected ears of individuals with Meniere's disease was *significantly different* from all others. The latency difference was greatest for the affected ears of Meniere's followed by their unaffected ears. The other two groups produced nearly equivalent latency differences. The 'Z' and 'p' values for the pairwise comparisons also have been shown in table 3.

SP/AP Ratio

The ECochG waveforms obtained from each individual were analyzed. The SP/AP amplitudes were obtained and their ratio was computed and subjected to *descriptive analysis*. The SP/AP amplitude ratio was highest for the affected ears of individuals with Meniere's disease [*Mean = 0.43, S.D = 0.19*]. The ears with sensorineural hearing loss [*Mean = 0.26, S.D = 0.07*] produced comparable SP/AP ratio values to the ears of healthy individuals [*Mean = 0.26, S.D = 0.07*] and also the unaffected ears of Meniere's disease [*Mean = 0.26, S.D = 0.07*]. A graphical representation of the same has been provided in Figure 5.

A *Kruskal Wallis test* was administered to compare the four groups in terms of SP/AP ratio. The results revealed a *significant difference* in SP/AP amplitude ratio between the groups [$\chi^2(3) = 11.31$, $p = 0.01$]. A *post hoc analysis* was done using *Mann-Whitney U test* for pair wise comparison between all possible pairs. The affected ears of Meniere's disease were found to be *significantly different* from all others on the pair wise comparison. This apart, there was *no significant difference* between other pairs. The *'p'* and *'Z'* values of pairwise comparison have been given in table 4.

Relationship between AP Latency Difference and SP/AP Ratio in the Affected Ears of the Individuals with Meniere's Disease

The present study aimed at evaluating a relationship between AP latency difference and SP/AP ratio in individuals with Meniere's disease. The *Spearman's correlation analysis* was used to obtain the relationship between the difference in AP latencies in rarefaction and condensation polarities and SP/AP ratio in the affected ear of MD. The results showed the existence of *slight negative correlation* (Viera & Garrett, 2005) between the two which was statistically *not significant* [$r_s = -0.070$, $p = 0.797$]. Figure 6 shows the scatter plot illustrating this relationship.

Another statistical tool used was the *Kappa coefficient analysis*. For this, the AP latency difference values were converted into categorical data of Meniere's and non-Meniere's disease ears by using the mean reference values from the available research regarding the two variables. The mean value of AP latency difference of ≥ 0.40ms (Orchik, Ge & Shea, 1998) and SP/AP ratio of ≥ 0.35 (Ohashi, Nishino, Arai, Hyodo & Takatsu, 2009) was used to categorize the data into Meniere's and Non-Meniere's ears. The SP was present in only 16 ears (out of 21 ears) of the individuals with Meniere's disease and hence *Kappa correlation analysis* was done using only these many ears. The results revealed *slight correlation* (Viera & Garrett, 2005) which was statistically

Table 4: 'Z' and 'p' values of Mann- Whitney U test of SP/AP ratio

	Ears of healthy individuals	Ears of SNHL	Unaffected ears of MD	Affected ears of MD
Ears of SNHL	Z = -6.14	-	Z = -0.45	Z = - 2.314
	p = 0.53	-	p = 0.653	p = 0.021
Unaffected ears of MD	Z = -0.77	-	-	Z = -2.147
	p = 0.93	-	-	p = 0.032
Affected ears of MD	Z = - 2.991	-	-	-
	p = 0.003	-	-	-

not significant [$K = 0.127, p = 0.61$]. There was agreement for positive results of Meniere's disease for 7 ears (out of 16) and negative results for 2 ears. The overall agreement between tests for Meniere's disease diagnosis was only 56.25%. This implies that a correct diagnosis of Meniere's disease versus non-Meniere's disease was made in only 56.25% of individuals when using a positive criterion on both the methods. When the diagnosis of MD was based on the positive results on either of the two methods, the identification of MD increased to 85%.

Relationship between ABR Wave I Latency and SP/AP Ratio in the Affected Ears of Individuals with Meniere's Disease.

One of the objectives of the study was to check if the ABR wave I latency difference between condensation and rarefaction polarities could yield results that could help in the diagnosis of Meniere's disease. A *Spearman's correlation analysis* was used to correlate the difference in ABR wave I latencies and SP/AP ratio in the affected ear of individual with MD. The results showed *slight negative correlation* (Viera & Garrett, 2005) between the two which was statistically *not significant* [$r_s=-0.131, p = 0.630$]. The same has been illustrated in Figure 7.

Relationship between AP Latency Difference and ABR Wave I Latency Difference in the Affected Ears of Individuals with Meniere's Disease

A *Spearman's correlation analysis* was used to establish the relationship between the difference in AP latencies and ABR wave I latencies in the affected ears of individuals with Meniere's disease. The results revealed an *almost perfect positive correlation* (Viera & Garrett, 2005) between the two set of variables, and this was statistically *significant* [$r_s= 0.938, p = 0.000$]. The same has been illustrated in Figure 8.

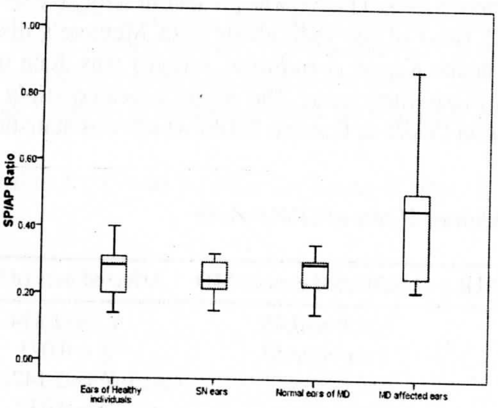

Figure 5: The box plot of the SP/AP amplitude ratio.

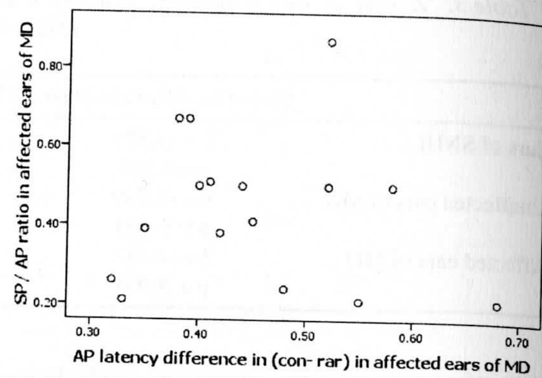

Figure 6: The scatter plot showing the relationship between SP/AP ratio and AP latency difference in the affected ears of individuals with Meniere's disease.

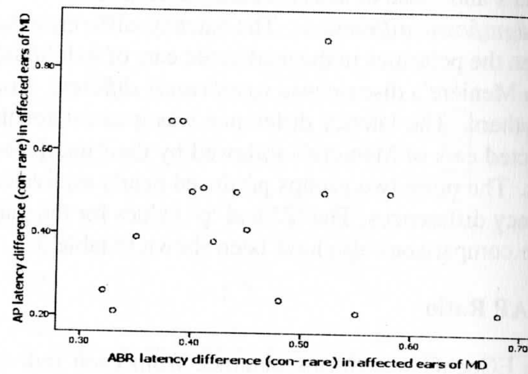

Figure 7: The scatter plot showing the correlation between SP/AP ratio and ABR wave I latency difference in the affected ears of individuals with Meniere's disease.

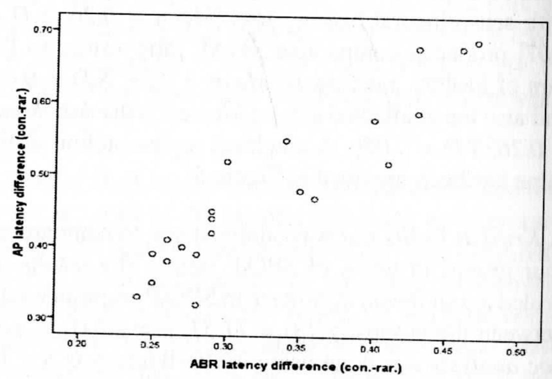

Figure 8: The scatter plot showing the relationship between AP latency difference and ABR wave I latency difference in the affected ears of individuals with Meniere's disease.

Discussion

AP Latency Difference between Condensation and Rarefaction Polarities of ECochG.

From the results of the present study it was evident that the mean AP latency difference between condensation and rarefaction polarities of AP was higher for the affected ears of the individuals with Meniere's disease compared to ears of healthy individuals, ears with sensorineural hearing loss and also their own unaffected ears. The present study did not compare the rarefaction and condensation polarities separately across the groups. However, the findings in literature have shown the difference to be prominent for condensation polarity (Saas, Densert, Magnussen, Whitaker, 1998). The authors reported no difference for rarefaction polarity between the healthy individuals, individuals with sensorineural hearing loss and those with Meniere's disease; however the individuals with Meniere's disease revealed longer latency of AP for condensation polarity than the other two groups of their study. This probably may be the reason for the larger difference between the latencies of the two polarities in individuals with Meniere's disease even in the present study. The prolongation of latency for condensation clicks alone may be explained on the basis of postulations of Tonndorf (1976) and the impact of hydrops on the travelling wave velocity (Eggermont & Odenthal, 1974). Tonndorf (1976), through his cochlear model, postulated that the basilar membrane, when loaded with endolymphatic hydrops, undergoes a downward displacement. Eggermont et al. (1974) studied the mode of the excitation in human cochlea and demonstrated that the latency of the AP was dependent on the velocity of the travelling wave, especially in cases with endolymphatic hydrops. The travelling wave was more affected in response to a condensation clicks than to rarefaction clicks due to the load of endolymphatic hydrops, and this resulted in a latency prolongation for condensation polarity. Therefore, the increased stiffness and change in position of the basilar membrane is likely to influence the pattern of the travelling wave motion, thereby aiding the explanation of the increased latency difference between the polarities in the individuals with Meniere's disease. The results of the present study are in agreement with the findings in the literature about the AP latency difference in Meniere's disease. Saas et al. (1998) conducted a study using transtympanic electrode placement on 30 individuals with Meniere's disease whose pure tone average thresholds ranged between 20 and 65dB. In addition, their study also used 11 patients with cochlear hearing loss of other aetiologies with pure tone average ranging between 30 and 60 dB and also 10 healthy subjects. They reported a mean difference in AP latencies between condensation and rarefaction of 0.02 ms, 0.01ms, and 0.32ms respectively in ears of healthy individuals, ears with sensorineural hearing loss, and ears of individuals with Meniere's disease. The findings of the present study revealed a similar pattern across the groups. However, the values obtained were higher (0.13 ms, 0.13 ms, and 0.47 ms in the same order as above). The values observed in the present study were appreciably higher for all the three groups of Saas et al. (1998). The differences in the values between the present study and Saas et al. (1998) could be related to the differences in the site of electrode placement. They used a transtympanic (near field) placement of the non-inverting electrode as against the extratympanic (far field) placement in the present study. Another study by Chen, Kang, Yeh and Wang (2004) used extratympanic electrode placement on ears of 10 healthy individuals and 33 individuals with Meniere's disease. They obtained a mean AP latency shift of 0.55 ms in the ears of individuals Meniere's disease and 0.11 ms in the ears of healthy individuals. The values observed in the present study were similar to those reported by Chen et al. which probably may be related to the use of similar method, including the extratympanic electrode placement in both the studies. So it could be concluded that the latency difference of AP between the polarities is greater in individuals with Meniere's disease irrespective of the site of electrode placement generally used for ECochG recordings. However, the cut-off values for Meniere's disease diagnosis could vary depending on the site of placement of electrodes. This calls for obtaining separate clinical values for different electrode placements for the diagnosis of Meniere's disease using ECochG.

The study revealed another finding of interest. The unaffected ears of individuals with Meniere's disease showed significant deviation in terms of latency difference between the polarities from the ears with sensorineural hearing loss and those with healthy individuals. The latency difference was*significantly* larger for the unaffected ears of individuals with Meniere's disease than their healthy and sensorineural counterparts. The findings in the literature has shown that, though Meniere's disease generally begins as a unilateral condition, it has a tendency to progress to the other ear within 2-7 years of its onset in the first ear in more than 50% of the individuals (Morrison, 1981., Salvinelli et al., 1998; Jackson & Silverstein, 2002., Saeed & Penny, 2011). Similar views were echoed by Huffelen, Mateijsen and Wit (1998) who obtained smaller OAE amplitudes in unaffected ears of individuals with Meniere's disease than the ears of normal hearing adults. They attributed this to the early manifestation of bilateral Meniere's disease. The findings in the present study also showed a similar trend, though for AP. The findings of the present studyindicate that the latency difference of AP between the polarities could be useful in the early detection of onset of bilateral Meniere's in the individuals who are already suffering from the unilateral condition.

ABR Wave I Latency Difference between Condensation and Rarefaction.

The results of the present study indicated towards a greater difference in Meniere's disease in terms of the latency difference between condensation and rarefaction click-evoked wave I of ABR. Tietze and Pantev (1986) reported a mean difference of 0.06 ms in ABR wave I latency between condensation and rarefaction polarities in normal hearing individuals. For high-level clicks, the wave I (Coats & Martin, 1977) or eighth nerve action potential (Peake & Kiang, 1962) has been reported to be approximately 0.2 ms earlier for rarefaction than for condensation stimuli. Contrary to this, Beattie (1988) found no significant differences between the latencies for human wave I elicited by rarefaction and condensation clicks. The findings of the present study are in agreement with those of Coats and Martin (1977) and in disagreement with Beattie (1988). However, these values were very small and the test-retest reliability of up to 0.3 ms has been reported (Hall, 2007) for different waves, including wave I of ABR. Thus such small deviations in normals could be ignored. The absence of or very small phase-related latency difference is expected for normal-hearing subjects because the normal click-evoked ABR is dominated by high-frequency neural responses (Don & Eggermont, 1978), which are not significantly affected by stimulus phase. However in the ears with Meniere's disease, the changes due to endolymphatic hydrops has been documented to result in prolongation of AP for condensation polarity, thereby by increasing the latency difference of AP between the two polarities (Saas et al., 1998; Chen et al., 2004). Since the wave I of ABR corresponds to the AP (Moller et al., 1983; Hall & Antonelli, 2001), a similar prolongation of latency for condensation polarity is justified. However, the present study is one of the first that has used ABR for the diagnosis of Meniere's disease and there are no other studies that reported about the usefulness of ABR in the diagnosis of Meniere's disease. The present study also revealed another intriguing finding. The unaffected ears of individuals with Meniere's disease revealed significantly larger difference between the latency of wave I of ABR between the polarities compared to the ears of healthy individuals and the ears with sensorineural hearing loss. This may be an early sign of progression of the disease to the unaffected ear in the individuals with unilateral Meniere's disease. There are a number of studies that have reported a tendency of Meniere's disease to progress to the other ear within 2-7 years of its onset in the first in more than 50% of the cases (Morrison, 1981; Salvinelli et al., 1998; Jackson & Silverstein, 2002; Saeed & Penny, 2004). But there are no studies that have used ABR wave I latency difference between the polarities and demonstrated such a finding. However, the reports using OAEs have shown that the unaffected ears of individuals with Meniere's disease had significantly lower amplitudes and the authors discussed this as an early sign of progression to bilateral condition (Huffelen et al., 1998). On similar lines the findings of present study may be considered an early sign for progression to bilateral Meniere's disease. So the present study shows that the technique of latency difference between condensation and rarefaction not only aids the diagnosis of Meniere's disease in the affected ears but also is capable of predicting its spread in the unaffected ear.

SP/ AP Ratio

The mean SP/AP amplitude ratios in the affected ears of individuals with Meniere's disease was higher when compared to ears of healthy individuals, ears of individuals with sensorineural hearing loss, and also the unaffected ears of individuals with Meniere's disease in the present study. The mean SP/AP ratios in these were 0.26, 0.24, 0.26, and 0.43 respectively. Similar patterns of findings have been reported in literature about SP/AP ratio (Mori et al., 1987; Chen et al., 2004). Mori et al. (1987) conducted a study in which they found the mean SP/AP ratio of 0.22, 0.20, and 0.63 respectively in ears of healthy individuals, ears of individuals with sensorineural hearing loss, and ears with Meniere's disease. Chen et al. (2004) obtained a mean SP/AP ratio of 0.46 in the individuals with Meniere's disease and 0.22 in the ears of healthy individuals. The differences between the ratio values observed in the present study and that by Mori et al. (1987) may be because of the differences in the method and also the presence of a higher variability within the group with Meniere's disease in terms of higher standard deviation for the Meniere's group in their study. The present study used Tiptrode placed at the entrance of the ear canal as the non-inverting electrode as against silver ball electrode placed near the tympanic membrane at a distance of 3 mm in the study by Mori et al. (1987). Also, the standard deviation obtained was 0.19 in the present study as opposed to 0.44 in Mori et al. (1987). Furthermore, the volatile nature of the Meniere's disease itself, which causes high variability in the test results usually, may have contributed to the differences between their study and the present study. However, Chen et al. (2004) used the same electrode placement (extratympanic) as the present study and obtained a mean SP/AP ratio of 0.46 in Meniere's disease and 0.22 in normal hearing individuals. These findings are similar to the ones observed in the present study and thus it probably extends further support to reasons of the differences observed between the present study and the study by Mori et al. (1987).

Relationship between AP Latency Difference and SP/AP Ratio in the Affected Ears of the Individuals with Meniere's Disease.

The present study revealed the existence of *no significant* correlation between AP latency difference and SP/AP ratio. Similar findings have also been reported by Ohashi et al. (2009). This disagreement between the techniques may be attributed to the differences in the physiology of the AP and SP generation. The AP waveform is characterized by a series of brief, predominantly negative peaks representing the distribution of underlying neural firings. The response to moderately intense stimulation tends to be dominated by neural contributions from the basal or high frequency end of the cochlea (Kiang, 1965), at least in normal ears and pathologic ears no worse than moderate hearing loss. The AP magnitude can also be viewed as a reflection of inner hair cell output. The SP is a complex response made up of several components. It reflects the displacement time pattern of cochlear partition. The SP is stimulus related and generated by the hair cells of the organ of Corti (Dallos, 1973). The SP manifests itself as a shift in the CM baseline, the direction of which is indicated and dictated by an interactive effect between stimulus parameters and the location of the recording electrode (Dallos, 1973). In general, the ECochG waveform recorded from patients with suspected endolymphatic hydrops is often characterized by an enhanced summating potential (Ferraro, Arenberg & Hassanein, 1985).The rationale usually given for this finding is that an increase in endolymph volume alters the hydromechanical characteristics of the inner ear because of the resultant increase in intra-labyrinthine pressure. When this occurs, the normal vibratory asymmetry of the basilar membrane is augmented. Since the SP supposedly reflects this vibratory asymmetry, it too will be enhanced during a hydropic state. However, AP has a distinctly different physiology and hence the presentation in hydropic pathology may accordingly be different.. This probably may explain the disagreement between the two techniques for the diagnosis of MD and calls for further studies to clarify the reasons.

In the present study the agreement between the two measures was found only for 9 ears. This implied that a Meniere's disease versus non-Meniere's disease diagnosis was appropriately made in only 56.25 % of the individuals when using a criterion of positive results on both techniques. However, when the criterion was changed to positive result on either of the two, 85 % of the cases were diagnosed as Meniere's disease. So both these techniques should be used in the protocol for the diagnosis of Meniere's disease as the two are likely to give complementary information, thereby supplementing in the diagnosis. It might be interesting to note if there would be a correlation between the agreement of the two tests and the stage of the Meniere's disease diagnosed as per AAO-HNS (1995). However, due to smaller sample size, a correlation of this kind could not be taken up. This may be considered in future studies using the two techniques and if found to correlate, it could well become an objective way of staging Meniere's disease.

Relationship between ABR Wave I Latency Difference and SP/AP Ratio in the Affected Ears of the Individuals with Meniere's Disease

The results of the present study revealed a lack of relationship between ABR wave I latency difference and SP/AP ratio in the affected ears of the individuals with Meniere's disease. Lack of agreement may be due to the differences in the physiology of generation of wave I of ABR and SP. Wave I of ABR is generated at the distal part of the auditory nerve (Wada & Starr, 1983) whereas SP is generated from the hair cells in the cochlea (Dallos, 1973). The two are likely to represent different aspects of physiology owing to these different structures (hair cells versus nerve fibers) involvement. Further, there are no such studies in the literature that compare latency difference between the two polarities for wave I of ABR and SP/AP in individuals with Meniere's disease. Present study is one of the first of this kind and the findings indicate towards a lack of correlation between this technique and the more established SP/AP amplitude ratio in the diagnosis of Meniere's disease. However, wave I of ABR has been reported to correspond to AP of ECochG (Moller & Janetta, 1983; Hall& Antonelli, 2001) and a similar lack of correlation of AP with SP/AP ratio (Ohashi et al., 2009) could explain the results of the lack of correlation so found.

Relationship between AP Latency Difference and ABR Wave I Latency Difference in the Affected Ears of Individuals with Meniere's Disease

The present study indicated a *strong correlation* between AP latency difference and ABR wave I latency difference in the affected ears of individuals with Meniere's disease. Tonndorf (1976), through his cochlear model, postulated that the basilar membrane undergoes a downward displacement when loaded with an excessive amount of endolymph. Distortion at the level of the basilar membrane will generally be reflected at the auditory nerve fibers in terms of the neural responses. Since wave I of ABR reflects the activity in the distal portion of the auditory nerve (Wada & Starr, 1983) and also corresponds to AP (Moller & Janetta, 1983, Hall & Antonelli, 2001), the finding of a strong correlation is expected and justified.There are no such studies in the literature that compare the latency difference of wave I of ABR and AP latency difference between the two polarities. So, the findings of the present study support the utility of latency difference between the polarities in the diagnosis of Meniere's disease, atleast to the same degree as that of AP latency difference between the polarities.

Conclusions

The latency difference of AP between condensation and rarefaction polarities can be an useful tool for the diagnosis of Meniere's disease. A similar difference for ABR wave I can also be used effectively for its diagnosis. The techniques of AP latency difference and ABR latency difference are better suited to the diagnosis of Meniere's disease than SP/AP amplitude ratio. However a larger data point needs to be used for the further validation of the results. Additionally, a combination of SP/AP ratio and AP latency shift would increase the chance of a positive diagnosis of Meniere's disease.

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