DETERMINATION OF NORMATIVE DATA ON NON INVASIVE ELECTROCOCHLEOGRAPHY TEST IN MALAYSIAN ADULTS

By

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Dissertation Submitted In

Partial Fulfillment Of The Requirements

For The Degree of

Master Of Medicine

(Otorhinolaryngology- Head and Neck Surgery)

UNIVERSITI SAINS MALAYSIA

2015

ACKNOWLEDGEMENT

In the name of Allah , the most merciful and most greatful, with his blessing has allowed me to successfully complete this study. First and foremost, I would like to express my deep thanks and utmost gratitude to my supervisor Professor Dr Din Suhaimi Sidek for his assistance and contribution throughout the preparation and completion of this dissertation. My warmest appreciation and thankfulness is extended as well to Dr Nik Adilah Nik Othman , my co-supervisor for her support. Besides I am truly indebted and thankful to Dr Mohd Normani Zakaria who also acted as my co-supervisor who has given full commitment, persistent help and guidance towards the completion of this dissertation. It is also a great pleasure to thanks all the staffs in Department of Otorhinolaryngology and Department of Audiology, Pusat Pengajian Sains Perubatan Hospital University Sains Malaysia, Kubang Kerian for all their help.

Not forgetting, grateful thanks to all subjects who are willingly participated in this study. Finally to all my family members, I will forever cherish their continuous support and pray until this dissertation was successfully completed.

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LIST OF SYMBOL, ABBREVIATION AND NOMENCLATURE

ECochG	Electrocochleography
AER	Auditory evoked response
AP	Action potential
CM	Cochlear microphonic
SP	Summating potential
ABR	Auditory brain response
AEP	Auditory evoked potentials
EAC	External auditory canals
TM	Tympanic membrane
BM	Basilar membrane
ATP	Adenosine Triphosphate
AC	Alternating current
DC	Direct current
MD	Menierre's Disease
ELH	Endolymphatic hydrops
IT	Intratympanic
TT	Transtympanic
ET	Extratympanic
BBC	Broadband click
AN	Auditory neuropathy
OAE	Otoacoustic emission
IHC	Inner hair cell

OHC	Outer hair cell
EABR	Evoked auditory brainstem response
DP	Dendritic potential
CAP	Compound action potential
ABEP	Auditory brainstem evoked potential
HUSM	Hospital Universiti Sains Malaysia
PTA	Pure tone audiometry

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ABSTRAK

TAJUK KAJIAN : PENENTUAN DATA NORMATIF BAGI UJIAN ELEKTROKOKLEOGRAFI TIDAK INVASIF DI KALANGAN DEWASA DI MALAYSIA

Elektrokokleografi merupakan satu ujian respon elektrik otak (AER) yang digunakan untuk mengukur fungsi koklea dan saraf auditori melalui rangsangan bunyi yang diberikan.

Objektif

Tujuan kajian ini dijalankan adalah untuk mendapatkan data Elektrokokleografi di kalangan dewasa normal di Malaysia. Ia juga bertujuan membandingkan bacaan elektrokokleografi yang terdiri daripada potensi aksi (AP) , potensi penghasiltambahan (SP) dan nisbah potensi penghasiltambahan kepada potensi aksi (SP/AP) di antara elektrod yang diletakkan di bahagian atas dan bahagian bawah gegendang telinga. Kajian ini juga bertujuan membandingkan bacaan elektrokokleografi yang normal di antara subjek lelaki dan perempuan.

Kaedah kajian

Kajian ini merupakan kajian keratan rentas yang dijalankan di Klinik Audiologi, Pusat Pengajian Sains Perubatan HUSM bermula dari November 2011 sehingga Jun 2012. Seramai 30 orang dewasa yang terdiri daripada kakitangan Hospital Universiti SainsMalaysia , Kubang Kerian , Kelantan yang berumur 18 hingga 50 tahun telah dipilih melalui teknik persampelan rawak mudah.

Subjek dipastikan tidak mempunyai sebarang masalah telinga melalui pemeriksaan telinga menggunakan otoskop. Seterusnya subjek yang telah dipilih perlu menjalani ujian pendengaran audiometri nada tulen (PTA) untuk memastikan mereka mempunyai tahap pendengaran yang normal. Subjek yang memenuhi kedua-dua syarat ini akan menandatangani borang keizinan dan persetujuan untuk mengikuti kajian ini. Elektrod elektrokokleografi jenis timpanik dari Biologics digunakan dalam kajian ini. Gel akan diletakkan pada hujung elektrod sebelum dimasukkan ke dalam telinga. Dengan bantuan lampu kepala elektrod diletakkan di bahagian atas gegendang telinga dan diikuti dengan bahagian bawah gegendang pada waktu yang berbeza. Pada setiap kedudukan elektrod, rangsangan bunyi berupa bunyi klik jalur lebar pada kadar 95 dBHL pada kelajuan 7.1/s.

Keputusan

Data keputusan elektrokokleografi antara lelaki dan perempuan telah digabungkan kerana tidak ada perbezaan yang signifikan di antara kedua-dua kumpulan ini ($p > 0.05$). Oleh itu purata nisbah SP/AP ialah 0.31 untuk elektrod timpanik yang diletakkan di bahagian atas gegendang dan 0.30 untuk elektrod yang diletakkan di bahagian bawah gegendang. Purata bacaan AP pula ialah 0.72uV dan 0.66uV untuk elektrod yang diletakkan di bahagian atas dan bawah gegendang masing-masing. Nilai purata SP pula ialah 0.23uV untuk bahagian atas gegendang dan 0.20uV untuk bahagian bawah gegendang.

Kesimpulan

Bacaan data normal elektrokokleografi telah didapati daripada kajian ini. Nilai purata AP, SP dan nisbah SP/AP ialah masing- masing 0.69uV,0.21uV dan 0.31. Tidak ada perbezaan bacaan elektrokokleografi pada telinga kanan dan kiri di antara dua elektrod timpanik sama ada yang diletakkan di bahagian atas gegendang telinga atau di bahagian bawahnya dengan nilai p 0.49 ($p > 0.05$). Tidak ada perbezaan juga pada bacaan elektrokokleografi antara perempuan dan lelaki dengan nilai p 0.96 ($p > 0.05$).

ABSTRACT

TITTLE : DETERMINATION OF NORMATIVE DATA ON NON INVASIVE ELECTROCOCHLEOGRAPHY TEST AMONG MALAYSIAN ADULTS

Electrocochleography (EcochG) is the measurement of an auditory evoked response (AER) to assess functional integrity of cochlea and auditory nerve. An AER is a response from auditory system elicited by an acoustic stimulus.

Objective

The study was conducted with the aim to obtain normative data of Electrocochleography (EcochG) among Malaysian adults. It is also done to compare EcochG outcomes amplitude of summating potential (SP), action potential (AP) and SP/AP ratio between two different placements of EcochG electrode at the upper part of tympanic membrane and lower part of tympanic membrane and the difference between male and female.

Methodology

This is a cross sectional study conducted at audiology clinic HUSM starting from November 2011 until June 2012. 30 adults who consist of HUSM staffs aged 18 to 50 years old were chosen using simple random sampling method. Subjects were confirmed to have no pathological ear by otoscopy and have normal hearing level on pure tone audiometry (PTA).Tympanic electrode by Biologics was used. The gel is applied at its tip prior to insertion.

With the help of head light,the electrode is introduced firstly at upper part of tympanic membrane until subject feels that it touches the membrane with the placement of insert earphone below the electrode. Broadband alternating clicks 95 dBHL at 7.1/s is given to the patient and result recorded. After recording of upper placement finished, the electrode is then placed at lower part of tympanic membrane with the insert earphone above it. Same stimulus given and result recorded.

Results

EcochG data between males and females are combined because there was no significant difference between them ($p > 0.05$). The mean SP/AP ratio is 0.31 for upper TM placement and 0.30 for lower TM placement. The mean for AP are 0.72uVand 0.66uV for upper TM and lower TM respectively where as mean SP is 0.23uV for upper TM and 0.20uV for lower TM.

Conclusion

The normative data for EcochG parameters were obtained. The mean for AP, SP and SP/AP ratios are 0.69u ,0.21uV and 0.31 respectively. There was no difference in EcochG reading of right and left ear between two different placements of tymptrode with p value of 0.49 ($p > 0.05$). There was also no difference in EcochG parameters between male and female with p value of 0.96 ($p > 0.05$).

CHAPTER 1

INTRODUCTION AND LITERATURE REVIEW

1.1 Background of Study

Electrocochleography (ECochG) is the measurement of an auditory evoked response (AER) to assess functional integrity of cochlea and auditory nerve. An AER is a response from auditory system elicited by an acoustic stimulus. To elicit an AER , sounds such as clicks and tones of varying intensities are played through an acoustic transducer. Auditory system activity in response to acoustic stimulus can be measured at several specific sites on head with electrodes. The cochlear potential of interest in clinical EcochG are auditory nerve compound action potential (AP), cochlear microphonic (CM) and summating potentials (SP).

ECochG began to be a useful clinical tool nearly 40 years following the discovery of CM in animals by Wever and Bray in cats (Lempert *et al*.,1950). Wever and Bray mistakenly concluded that this recording was generated by auditory nerve and named their discovery " Wever –Bray effect''. However the wave was concluded to be cochlear in origin and not from the auditory nerve by Hallowell Davis from Harvard (Moore ,1983). Fromm *et al.*(1935) were the first investigators to employ the ECochG technique in humans by inserting a wire electrode through tympanic membrane and recording the CM from niche of round window. Later Fisch and Ruben (1960) provided evidence of round window recordings of compound action potentials (AP) from both round window and eight cranial nerve in cats and mice. Ruben was the first person to use CM and AP clinically. Since ECochG was used by Ruben *et al*. in 1961 to monitor cochlear and acoustic nerve action potentials intraoperatively during otosclerosis surgery , many studies have been made of cochlear evoked potentials and their relationship in inner ear fuction (Ruben *et al*., 1960).

Summating potentials (SP), a stimulus related hair cell potential was first described by Tasaki and colleagues in 1954(Tasaki *et al*., 1954). It took more than 25 years before this component began to receive any meaningful clinical attention where Moffat *et al*. (1978) demonstrated in 1978 the significance of summating potential in the pathodynamics of endolymphatic hydrops and thus opened new possibilities for objective studies of inner ear disorders using ECochG. Dr Ernest J.Moore (Moore , 1971) was the first investigator to record the CM from surface electrode. In 1971 , Dr Moore conducted 5 experiments where he recorded CM and AP from 38 human subjects using surface electrodes.

Renewed and increased attention to all auditory evoked potentials (AEPs) in early 1970s was due to the discovery and clinical application of auditory brain response (ABR). The development and refinement of noninvasive recording techniques also facilitated clinical application of AEPs including ECochG. The technical capability to record cochlear and auditory nerve potentials in humans has brought to a variety of clinical applications for ECochG. The usage of ECochG in diagnosis, assessment and monitoring of Menierre's disease is of primary importance in addition to its usage in the diagnosis of auditory neuropathy and for the enhancement of wave I ABR.

Knowing the importance of ECochG especially in diagnosing Menierre's disease, we are conducting this study in order to get the normal values for the parameters involved in ECochG among normal Malaysian adult since no similar study was done before in this country. These normal values will be able to be the reference reading in comparing with the abnormal ones. Thus it will enable us to diagnose certain disease like Menierre's and auditory neuropathy.

1.2 Anatomy and Physiology of ear

To conduct the ECochG test, it is very important to understand the anatomy and physiology of the ear. The ear is divided into 3 parts namely external ear, middle ear and inner ear. ECochg electrode placements may involve external ear, or inner ear depending on type of electrode which will be explained in detail .

The external ear consist of auricle , external auditory canal (EAC) and tympanic membrane (TM). The EAC measures 25 mm from TM annulus to anterior lip of concha with diameter of 7 mm. The lateral one third of EAC comprises of cartilage , runs posterior superiorly . It is lined with hair and cerumen glands.The medial two third is bony meatus of temporal bone. EAC has two constrictions that are at the junction of lateral one third and medial two third. The second one is located 5mm lateral to TM.

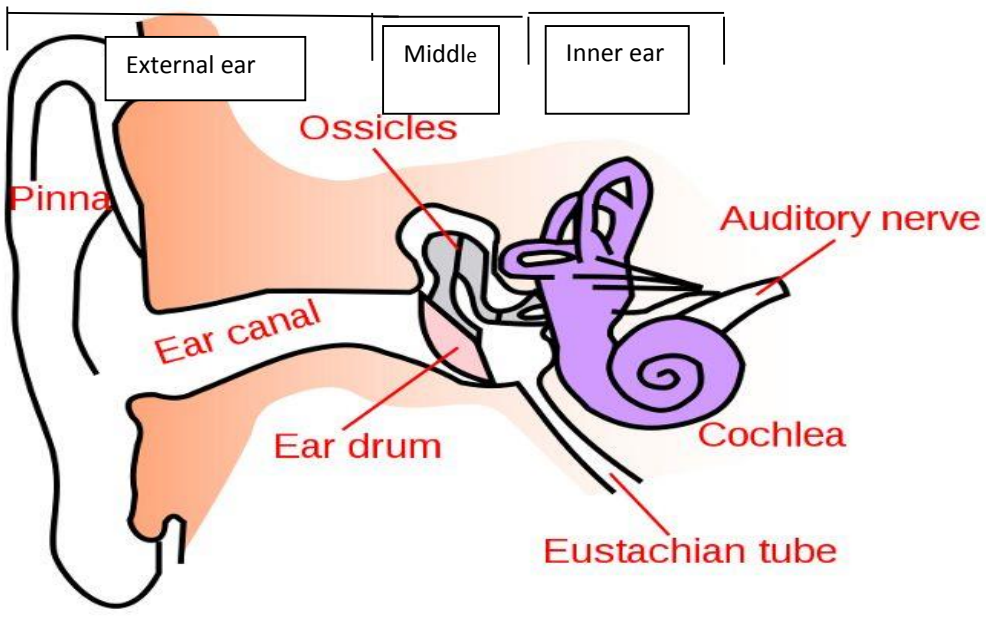

Figure 1.1: Parts of the ear.

A study done by Resmus *et al.* (2002) showed a highly significant difference in size between males and females external auditory canal (p = 0.0003) .

Tympanic membrane is a thin fibrous structure covered externally with layer of stratified squamous epithelium and internally low columnar epithelium. Fibrous tissue (lamina propria) which provide structure for TM is in between these layers. Most of its circumference is thickened to form fibrous cartilaginous ring called tympanic annulus.TM is the most medial of EAC. It measures about 10mm in diameter and approximately 85 mm^2 in surface area. It slant, making 55° angle to the floor. The TM is divided into pars tensa dan pars flacida. TM can be divided into 4 quadrants by a line drawn across the diameter of ear drum in the axis of handle of malleus and another intersecting the first at right angles at the umbo. The 4 quadrants are anterosuperior, anteroinferior , posterosuperior and posteroinferior quadrant.

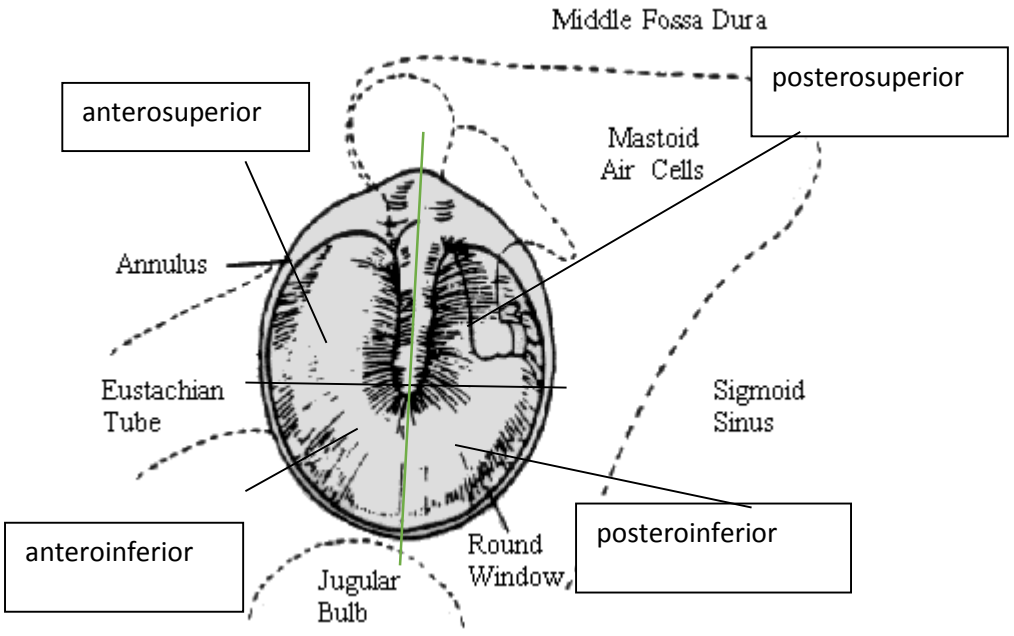

Figure 1.2 : The four quadrant of Tympanic membrane

The sound stimulus from extratympanic and tympanic ECochG electrode must pass through the middle ear structures in order to reach the cochlea. Middle ear can be likened to a six sided box with a roof, floor, medial, lateral, anterior and posterior wall. The vertical (distance from floor to roof) and anteroposterior diameter of cavity are each about 15 mm. The transverse diameter measures about 6 mm above and 4 mm below, opposite the centre of TM (between umbo and middle ear mucosa at level of promontory) is only 2 mm as illustrated by figure below.

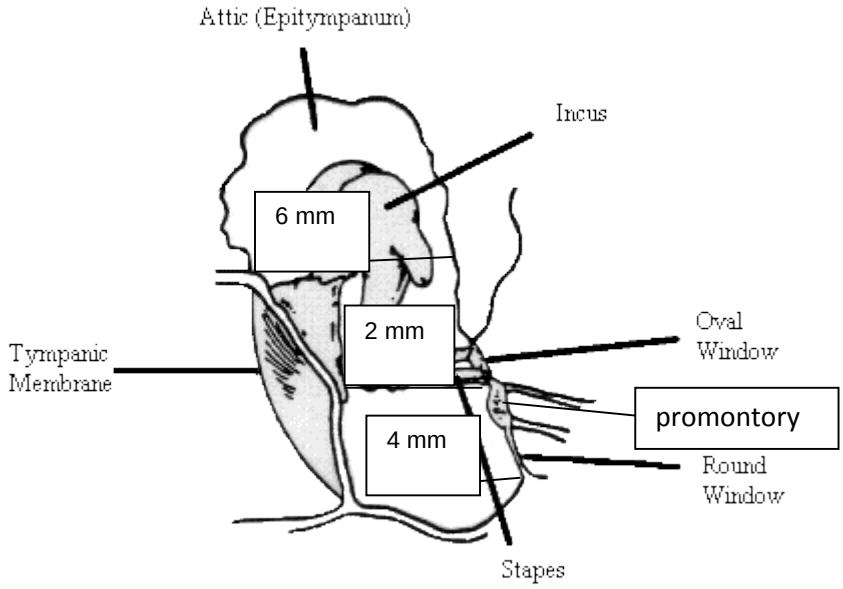

Figure 1.3 : The middle ear cavity

The ECochG electrode can also be fixed in the inner ear either at round window or promontory (Fig 1.3). Another structure of interest is the cochlea. The bony cochlea is a coiled tube making 2.5 to 2.75 turns round a central pyramid of bone called the modiolus.The promontory is the bony bulge due to basal coil of cochlear forming one of the structure in the medial wall of

tympanic cavity. The bony cochlea contains 3 compartments that are scala vestibule, scala tympani and scala media or membranous cochlea. Membranous cochlea is a blind coiled tube formed by the basilar membrane which support organ of corti, the Reissner's membrane which separate it from scala vestibule and stria vascularis. The organ of Corti is a band like structure situated on the basilar membrane and contains auditory sensory cells which are called inner hair cell and outer hair cells (Figure 1. 4).

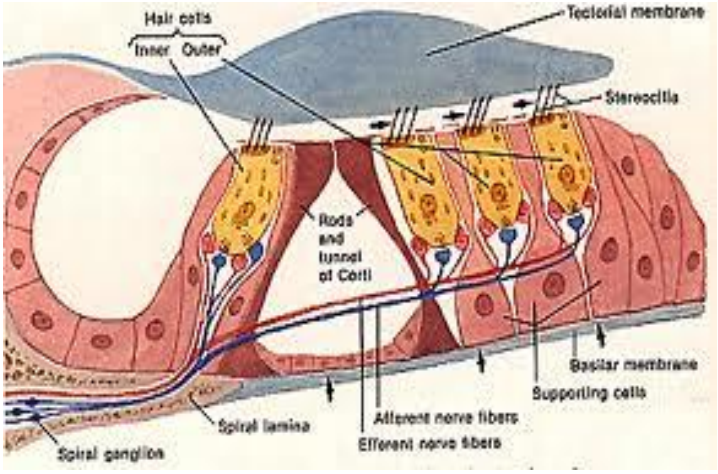

Figure 1.4 : Organ of corti

In cochlear physiology, basilar membrane (BM) and hair cells function as a sharply tuned frequency analyzing mechanism (Kohlloffalcue ,1972). Once acoustic energy reaches tympanic membrane , it is converted into mechanical energy and carried on to inner ear through middle ear bones. As the stapes pushes the oval window , pressure wave in perilymph inside cochlea causes the BM to vibrate. Place of maximum vibration amplitude depends on sound frequency. The area of maximum displacement in the BM will cause the hair cells and supporting structure to move. During the upward displacement of BM and hair cells, the stereocillia and kinocillia of hair cells move against the tectorial membrane. Bending of stereocillia towards the modiolus will cause the mechanically gated ion channels to open

allowing potassium and calcium ion to enter. An alternating current (AC) flows through the hair bearing surface and this increase in the flow or decrease in the resistance has the same frequency as BM movement and hence the acoustic stimulus frequency. This AC voltage is called cochlear microphonics (CM), which mimics the stimulus. The hair cells function as a tranducer, converting the mechanical movement of BM into electrical voltage. Adenosine tri-phosphate (ATP) from the stria vascularis provides the energy for conversion. This potential derived from the CM initiate chemical processes in hair cells that lead to the release of neurotransmitter in the synaptic cleft between the hair cells and spiral ganglion neurons. The neurotransmitters rapidly diffuse and combine with the receptor cells in their specific locations. This results in a built up of postsynaptic potential or generator potential in the unmyelinated nerve endings. When a certain threshold value is reached, generator potential depolarizes the first neuron. The axon stimulation by depolarization results in AP. SP as the stimulus – related potential of cochlear is the direct current (DC) response of the hair cells as they move in conjunction with BM.

1.3 Electrocochleogram components

As stated earlier , the cochlear microphonic (CM), compound action potential (AP) and summating potential (SP) are the 3 components of interest in cochlear potential to be studied in ECochG.

1.3.1 Cochlea microphonic

CM which is an alternating current (AC) electrical potential present throughout whole duration of acoustic stimulus which is predominantly generated by outer hair cells of cochlear (Patuzzi,Yates ,Jonston ,1989). This voltage reflects the instantaneous displacement of basilar membrane along some distance within the cochlea (Ferraro and Durrant, 2002).This distance is defined by effective site and method of recording and conditions of stimulus. As reflected by CM, organ of Corti acts as a microphone, but the transducers are numerous as each hair cell produce a receptor potential that is substantially AC. The historical popularity of CM in laboratory derives from its link to cochlear transduction, from well demonstrated sensitivity to the health of cochlear partition and certainly because it can be recorded from within or near the cochlea. This latter factor is facilitated by the CM's considerable magnitude compared to other electrical phenomena associated with the auditory periphery. However the utility of CM in differential diagnosis of inner ear versus auditory nerve disorder has yet to be establish. Even though reductions in CM magnitude have been reported for various disorders such as Menierre's disease or endolymphatic hydrops (Gibson and Beagley, 1976), these features tend to reflect general rather than specific cochlear pathology.

Furthermore examination of CM with confidence that recording represents the true potential remains challenging in clinical setting. Since CM mimics the waveform of the evoking signal, it is difficult to separate from stimulus artifact, therefore its measurement has been considered less suitable for clinical ECochG.

1.3.2 Summating potential

Summating potential (SP) is another observable part of ECochG waveform which is least understood cochlear potential. The SP is a complex response comprising several components. Like the CM, the SP is also stimulus related but generated by inner hair cells of cochlea (Ferraro, 2002, Hall, 2007). It is a reflection of the displacement time pattern of cochlear partition. As CM mirrors the stimulus waveform, the SP displays a rectified, direct current (DC) version of this pattern more representative of stimulus envelope (Ferraro ,2002, Hall, 2007). The SP appears as a unidirectional shift in the CM baseline, the polarity of which is dictated by an interactive effect between stimulus parameters (ie frequency and intensity) and the location of recording electrode. When recorded from tympanic membrane (TM) or ear canal electrode, the SP is often seen as a downward (negative) deflection persisting for the duration of acoustic stimulus.

Because of its complexity, the role of SP in hearing function remains unclear. As DC responses to AC stimuli, however at least some of its components are thought to represent nonlinearities associated with the transduction processes in cochlea (Tasaki *et al*., 1954, Whitfield and Ross, 1965, Gallic *et al*., 1985, Ruth, 1994). By definition, rectification (ie AC to DC conversion)

is a nonlinear process but whether or not the SP actually reflected intracellular receptor potentials was uncertain for a period of time following its discovery. However , SP like potentials have since been observed inside hair cells and it is now clear and that the SP is not an epiphenomenon (Dallos , 1973). It is also has long been known that the SP is also sensitive to mechanical and electrical biasing (Durrant and Gans ,1977). The nonlinear nature of SP has made it useful for monitoring certain clinical conditions such as Menierre's disease (MD)or endolymphatic hydrops (ELH) which may augment nonlinearitis in the transduction process where SPs displayed are enlarged in comparison to SPs of normally hearing subjects or patients with cochlear disorder other than MD/ELH. Conventional rationale for this finding is that an increase in endolymph volume creates mechanical biasing of vibration of organ of Corti to which again SP is sensitive. Whether this increased distortion is mechanical and /or electrical has not been resolved (Durrant and Gans, 1977). Other factors such as biochemical or vascular changes may also be responsible for enlarged SP in MD/ELH. Regardless of the specific pathophysiology, measurement of the SP to help diagnose, assess and monitor MD/ELH has emerged as a primary application for modern day ECochG

1.3.3 Action potential

Action potential is another component recorded via EcochG which represent the summed response of numerous, at times thousands of auditory nerve fibres firing synchronously. It is produced by fibres within the distal portion of auditory nerve (Hall, 2007). AP is usually larger than SP with latency of approximately 1.5 ms (Hall, 2007) When evoked by click stimuli the

term “ whole nerve AP ‘’ is applied since theoretically the click has a nearly flat spectrum over the frequency range of interest and thus vibrate essentially the entire basilar membrane. As recorded clinically however and regardless of stimulus , the AP is clearly a compound action potential where the response of a population of neurons rather than a single unit. A stimulus with a narrower bandwith such as toneburst excites a more limited segment of the membrane and consequently a more restricted population of nerve fibres. More important is the fact that these very different stimuli clicks and toneburst fail to achieve their respective objectives. That is the spectrum of clicks that actually reaches the cochlea generally is far from flat due to combined earphone, ear canal and middle ear response characteristics. Likewise the cochlear response to toneburst is far from discrete due to their spectra and limited cochlear resolution. Thus clicks do not excite ‘whole ‘ nerve and even tonebursts excite several points of vibration along basilar membrane.

A high degree of synchrony of neural firing is essential to producing a well-defined AP, which accounts for the popularity of click and brief –onset toneburst as evoking stimuli. In either case the response to moderately intense stimulation (ie 70dB nHL or more) tends to be dominated by neural contributions from basal or high-frequency end of the cochlea, at least in normal ears and pathological ears with no worse than moderate hearing lost

(Kiang ,1965). Since the velocity of the travelling wave is the highest in this region, phase shifts caused by cochlear mechanics are minimal. The AP , like CM is an AC voltage. Unlike either of cochlear potentials whose waveforms reflect the displacement-time pattern of cochlear partition (ie CM and SP), the AP waveform is characterized by a series of brief, predominantly negative peaks of representative of the distribution of underlying neural firings. At suprathreshold stimulus levels, the first and largest of these peaks is referred to as N1, which

is the same component as wave 1 of the ABR and as such arises from distal portion of the auditory nerve (Moller and Janette, 1983).. AP peaks beyond N1 (such as N2 and N3) are analogous to corresponding ABR component (ie waves II and III) but have received little if any clinical attention in ECochG.

For clinical purposes, AP magnitude and latency appear to be the most useful features. The former is a reflection of the number of nerve fibres firing. Since the afferent fibres of auditory nerve primarily innervate the inner hair cells, AP magnitude also can be viewed as a reflection of inner hair cell output. AP latency which is analogous to the 'absolute latency' for ABR components, represent the time between stimulus onset and peak of N1. This value incorporates stimulus travel time from the output of the transducer to the inner ear, travelling wave propagation time along the basilar membrane and time consumed activating synaptic transmission between hair cells and first order neurons. As with all waves of the ABR, reductions in signal intensity at suprathreshold levels for the AP are accompanied by absolute latency prolongations and reductions in N1 magnitude leading to eventual disappearance into the electrical noise floor. Since its initial recording in humans in 1960, the AP has been the most widely studied product of EcochG.

1.4 Electrocochleography recording approaches

There are four approaches to ECochG recording depending on the position of ECochG electrode (Bonucci and Hyppolito ,2009) . First approach is intratympanic (IT) when the electrode is placed in round window (usually during surgery).Second approach is transtympanic (TT) where the active electrode is placed in promontory closed to round window. Third type is by tympanic membrane (TM) when the electrode is placed close to tympanic membrane in posteroinferior quadrant and the last approach is extratympanic (ET) when the electrode is placed in the external auditory meatus. The IT and TT ECochG method are invasive procedure. TT approaches to ECochG were introduced in late 1960s and are still used widely in countries other than United States (Yoshie *et al*., 1967).The main advantage of this recording technique is the close proximity of recording needle electrode to the cochlea which enables large ECochG response waveform to be obtained with a minimal signal averaging required(Ferraro and Durrant, 2002). However there are several limitations to this method. As an invasive technique it requires a physician to place the recording needle electrode. This can restrict the test to medical settings and consequently make it an expensive test to perform. In addition , even with the local anaesthesia, the penetration of a needle through tympanic membrane can be a painful experience for patient (,Bullen and Arerberg, 1990, Ferraro and Durrant, 2002).

ET and TM ECochG method are less invasive, performed with an electrode resting against the skin of ear canal or surface of tympanic membrane (Bullen and Arerberg, 1990, Ferraro and Durrant, 2002). Pioneering work in ET recordings was performed by Sohmer and Feinmesser (1967), Coats and Dickey (1970) and Cullen *et al*. (1972), among others.

By comparison, ECochG responses recorded from ET and TM sites require more signal averaging and tend to yield smaller component magnitudes than TT or IT recordings. However the biggest advantage of ET and TM approaches is that they can be performed in nonmedical setting with minimal discomfort which is more tolerable to patient, obviating the need for sedation and local anesthesia as well as not necessarily be performed by a physician. Another factor that facilitated the use of ET or TM ECochG relates to the advances in electrode design and the practice of using the TM as a recording site. The TM offers a good and practical compromise between ear canal and TT or IT placement with respect to component magnitudes and consequently signal averaging time (Ruth and Lempert, 1989). Perhaps most importantly for clinical purpose is the waveform patterns that lead to interpretation of the TT and IT electrocochleogram tend to be preserved in TM recordings (Ferraro, Thediger *et al*,. 1994) even though IT and TT ECochG produces response amplitudes that are 5 to 10 times greater than those obtained with tympanic electrode while response obtained with extratympanic ECochG diminish rapidly with increasing electrode distance from tympanic membrane (Coats ,1986). Ferraro and Ferguson (1989) also showed that ECochg components recorded from TM displayed magnitudes that were at least twice as large as corresponding measurement made from ear canal (Ferraro and Furgeson ,1989). When performed correctly , TM ECochG should cause minimal- to-no discomfort to the patient.

There were many studies on improving the recording approach and comparing between these technique of recordings. Federico and Serena (2009) had presented an alternative technique by introducing a conducting liquid inserted into the ear canal to act as a distributed electrical interface between TM and external electrode. The concept proposed relies on a recording

electrode able to work without any direct contact with sensitive TM. As a conducting liquid, a water based saline solution can be used. Its high conductivity allows a continuous and stable electrical connection with TM and not necessarily to insert the electrode deeply into the ear canal.

Bonucci and Hyppolito (2009) on the other hand compared the use of TM electrode and ET electrode. Their study group consisted of 23 individuals with normal hearing with none of them had history of auditory or vestibular disease or metabolic changes. Threshold tonal audiometry and impedanciometry were performed to confirm the normality of audiometry thresholds. Recording started with TM electrode first placed close to the posteroinferior quadrant of TM. Immediately after the end of evaluation with TM electrode and its removal, ET electrode was placed in the external auditory meatus. The results showed no significant difference between ET and TM electrode with a mean SP/AP ratio of 0.30 and 0.32 were obtained respectively. They concluded that both electrodes were effective for EcochG evaluation but extratympanic one was easier to insert and did not cause discomfort. The TM electrode produce tracings of greater amplitude and of better reproducibility.

Another study done by Noguchi *et al*. in 1999 comparing tympanic versus transtympanic recording in electrocochleography. In their study 15 subject were evaluated from which 9 volunteers with normal hearing and 6 patients with sensorineural hearing loss. The TM electrode was placed at the posterior inferior quadrant of tympanic membrane while the TT EcochG was fixed on the promontory near round window niche.In this study, TM and TT EcochG yielded nearly identical detection threshold, input-output curves and waveforms for both CM and AP measurements.

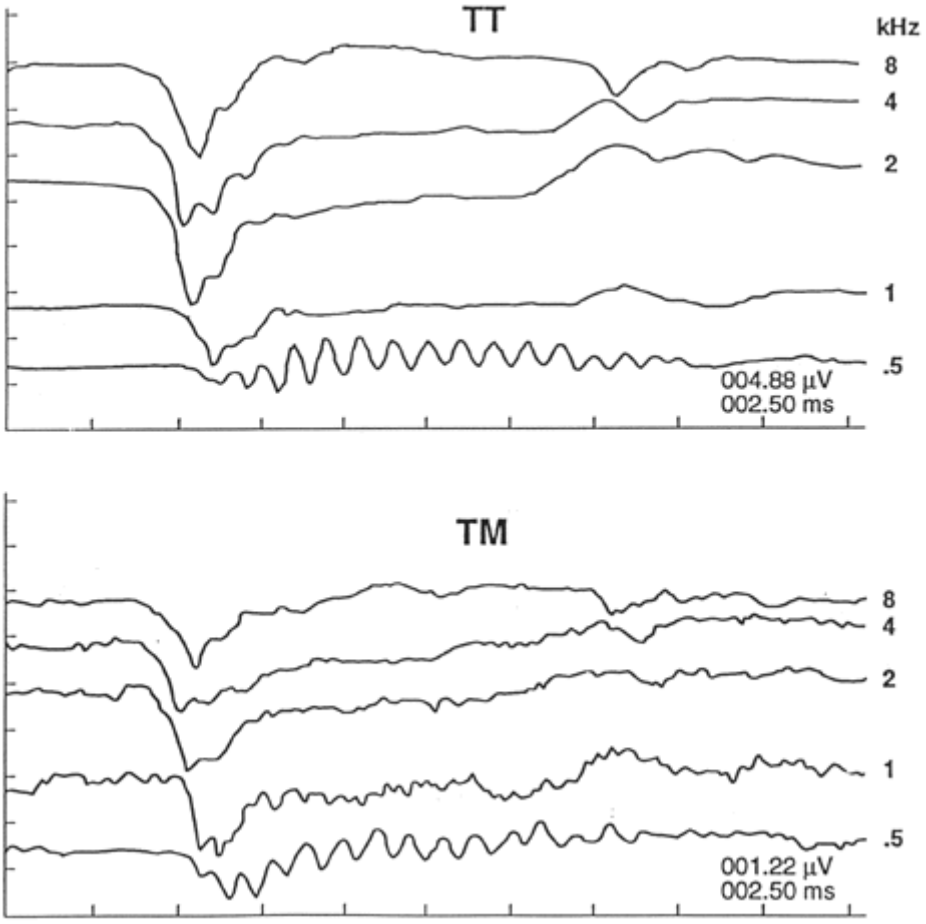

Figure 1.5 : Tonebursts SPs at several frequencies recorded from both TM and TT (promontory) of same patient. Although magnitudes of TM response are approximately ¼ that of promontory response (note the amplitude scale), the corresponding pattern of the TM and TT recordings at each frequency are virtually identical (Ferraro 2003).

1.5 Electrocochleogram recording parameters

Selection of recording parameters for ECochG varies according to the components of interest. Since these components generally occur within a latency epoch of 5 msec following stimulus onset, they can be considered to be in family of early-latency or short latency AEPs. As members of same family, ECochG components and ABR can be recorded using similar parameters. A notable exception occurs in the selection of the bandpass of the preamplifier for ECochG when SP is of interest that is the filter setting must be wide enough to accommodate both a quasi-steady- state DC component (the SP) and an AC component with a fundamental frequency of approximately 1 kHz (the AP). Other difference involve the electrode array and the number of samples to be averaged.

1.5.1. Electrode array

For an electrode array displays the AP as downward (negative) deflection, primary electrode (i.e. the electrode connected to the positive or noninverting input of the differential preamplifier) should rest on the TM. Sites for secondary (negative or inverting) electrode include the vertex of the scalp, high forehead, contralateral earlobe or mastoid process. The nasion, ipsilateral earlobe or ipsilateral mastoid may serve as sites for the electrode connected to ‘common’ or ‘ground’ input to the preamplifier. If AP is preferred to be displayed as an upward deflection, simply reversed the positive and negative inputs to the preamplifier.

1.5.2 Timebase

As indicated above, ECochG components generally occur within first few milliseconds after stimulus onset. For brief transient stimuli (such as clicks) we use a timebase (or signal averaging window) of 10 msec which also allows for visualization of ABR components that follow N1. For longer duration stimuli (such as tonebursts) , timebase should extend beyond duration of the stimulus envelope so that the entire response is observable within the averaging window.

1.5.3. Amplification factor

Amplification factor is selected to maximize the signal-to –noise ratio for a given recording condition. The amount needed for suitable recordings of the SP and/or AP for ET measurements generally ranges between 20000 and 100000 times , where as the factor for TT recordings can be much lower (by 5 to 10 times). The sensitivity setting of the computer's analog-to-digital converter also must be taken into account. The goal is to amplify enough to extract a good (and real) response without triggering the artifact rejection routine inordinately throughout the recording.

1.5.4. Analog Filter Setting

SP as fundamentally a DC potential could last as long as the stimulus of any duration. Ideally a DC recording amplifier is needed to record this component. However particularly for the amount of gain needed, such amplifiers are notoriously unstable for electrophysiological recordings. Fortunately the SP as evoked for practical or clinical purposes is only quasi – steady – state,permitting the use of AC coupled amplifier typically found in commercially manufactured AEP units. The low pass (or high frequencies cut off) setting of filter should be set to allow transmission of AC components of interest. Filter setting for CM recordings would depend on the frequencies of evoking stimuli.

1.5.5 Repetitions

Number of individual responses to extract a well defined electrocochleogram from background noise varies with recording conditions or approach and also the subject's degree of hearing loss. TT recordings require fewer repetitions than ET approaches while more repetitions may be necessary for subjects with hearing loss than normal subjects.

1.5.6. Stimuli

As mentioned earlier, the broadband click (BBC) is a popular stimulus for short latency auditory evoked potentials (AEPs) because it excites synchronous discharges from a large population of neurons to produce well-defined peaks in the response.100msec is a popular choice for the duration of the electrical pulse driving the transducer because the first spectral null for a click of this duration occurs at 10000 Hz (i.e 1/100 msec). Since the duration of both the CM and SP are stimulus dependent, the brevity of the click makes it a less than ideal stimulus for studying either of these potentials. Despite this limitation, the use of clicks has proven effective in evoking the SP-AP complex for ECochG applications related to MD/ELH.

Although the click continues to remain popular, toneburst stimuli also have been used in several ECochG studies involving MD/ELH populations (Levine *et al*.,1992). Tone burst provide a higher degree of response frequency-specificity than clicks which can be useful for monitoring cochlear status in progressive disorders where hearing may not be affected at all frequencies. In addition, the use of longer stimuli allows for better visualization of SP and CM (Durrant and Ferraro, 1991).

Stimulus polarity depends on the initial deflection of the transducer diaphragm and an important factor for ECochG. Presenting clicks or tonebursts in alternating polarity inhibits presence of stimulus artifact and CM as their phases are locked to the signal. Stimulus artifact can sometimes be large enough to obscure early ECochG components , and CM generally

overshadows both SP and AP features that are problematic when these latter two components potentials are component of interest. Alternating stimulus polarity can be applied to help overcome this problem. Stimulus artifact is indeed quite large for ECochG. The nature of ET and TM electrodes is that they tend to have high impedence and are vulnerable to radiation from transducer and other electrical sources in the environment.

1.6 Interpretation of Electrocochleogram

Component magnitude and temporal features form the bases for interpreting the electrocochleogram. Component magnitude (Fig 1. 6) can be measured as absolute values or peak to peak amplitudes of SP and AP (defined as single point – on the left panel) or using a baseline reference (on the right panel) (Margolis , Levine *et al*., 1952). The reason for this choice relates to the considerable lability of the baseline amplitude for ET recordings. Study done by Ferraro in 2003 normal SP amplitudes measure from TM to 95 dB HL clicks range from 0.1 – 0.8 microvolt with a mean of 0.4 microvolt while AP amplitudes range from 0.6 to 2.7 microvolts , with mean of 1.4 microvolts. AP- N1 latency is measured from stimulus onset to the peak of N1 and should be identical to the latency of ABR wave I. At 95 dBHL, their normal N1 latencies range from 1.3 -1.7 ms with a mean of approximately 1.5 ms. When using a tubal insert transducer, these values will be delayed by approximately 0.9ms.

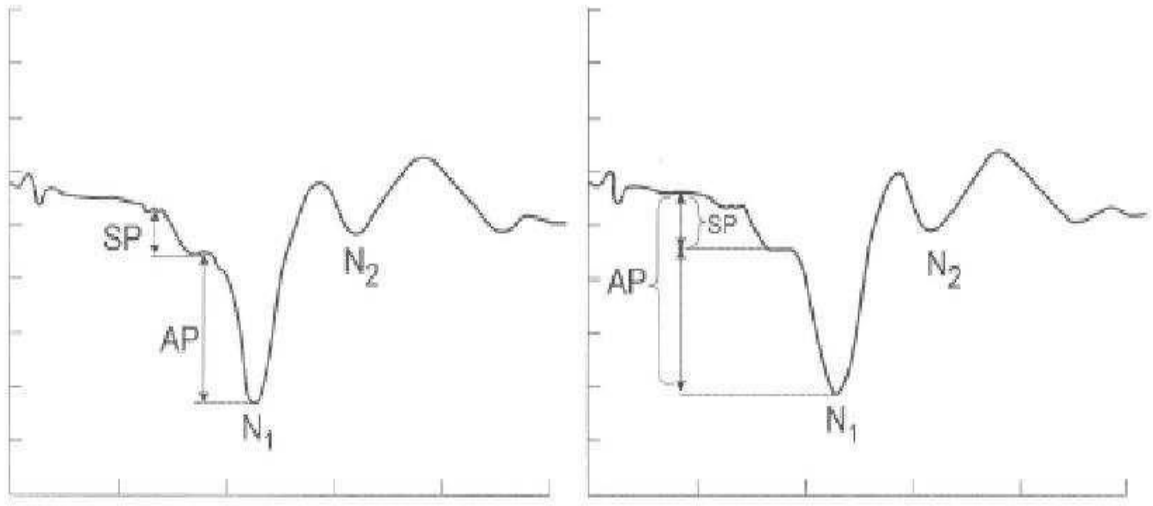

Figure 1.6 : Normal electrocochleogram from tympanic membrane to clicks presented in alternating polarity at 80 dBHL. The amplitude of summating potential (SP) and action potential (AP) can be measured from peak to trough (left panel) or with reference to a baseline value (right panel). Amplitude /time scale is 1.25 microvolts / 1 milisecond per gradiation. Insert phone delay is 0.90 ms (Ferraro, 2003).

Also as shown in Figure 1.6, SP and AP amplitudes are made from leading edge of both components. The resultant values are used to derive the SP/AP amplitude ratio. Their mean SP/AP amplitude ratio to click stimuli for normal subjects approximately 0.25 +/- 0.10 SD.

1.7 Electrocochleogram applications

1.7.1 .Evaluation of menierre's disease / endolymphatic hydrops

ECochG has emerged as one of the more powerful tools in diagnosis, assessment and monitoring of MD/ELH, primarily through the measurement of SP and AP. In particular it is now well documented that the electrocochleograms of patient with MD/ELH often display abnormally enlarged SP magnitude(Ferraro *et al*., 1983,Ferraro and Krishnan, 2002). The conventional rationale for this finding is that an increase in endolymph volume creates mechanical biasing of vibration of organ of Corti to which SP is sensitive. Whether the nature of this increased distortion is mechanical or /and electrical has not been resolved. Other factors such as biochemical or vascular changes may also be responsible (Staller, 1986). An enlarged SP/AP magnitude ratio to click stimuli should be considered a positive finding for ELH.

Although the specificity of ECochG in the diagnosis of MD/ELH has been reported to be higher than 90% (Ferraro *et al*., 1983, Murphy *et al*., 1997), the incidence of an enlarged SP and SP/AP magnitude ratio in the general Menierre's population is only approximately 55% - 65% (Margolis ,1995, Ferraro and Tibrik, 1999). The episodic nature of MD/ELH certainly play a role in the sensitivity of any diagnostic tool used for this disorder. Sensitivity is expected to vary according to when the test was administered in the course of disease. EcochG is more sensitive to test the patient when they are experiencing symptoms. Other approaches to increasing the sensitivity of ECochG include measuring the AP-N1 latency difference between responses to condensation versus rarefaction clicks. According to Margolis , Rieks *et al*. (1995) , a difference greater than 0.38 ms is a positive finding for endolymphatic hydrops.

1.7 .2. Auditory neuropathy

Auditory neuropathy (AN) is classified by normal cochlear mechanical function, shown by present otoacoustic emissions (OAE) and/or cochlea microphonic waveforms, but absent or severely disrupted synchronous neural activity, observed as an absent or grossly abnormal auditory brainstem response (ABR) waveform (Starr ,1996). A consequence of this broad classification is that AN may encompass multiple sites of lesion, including disruption to inner hair cells, the primary afferent synapse,or the auditory brainstem (Starr ,1996, Rance , 2005). Therefore, more accurate classification of AN into specific sites of lesion is needed. Scalp recording techniques, typically used for ABR measurements, have shown variable amounts of cochlear activity.

However, round-window electrocochleography provides a higher-quality recording of basally located hair cell and dendritic currents, which are in closer proximity to the recording electrode, this is important in the differential diagnosis of cochlear disruptions, such as AN, where the generation of action potentials relies on a cascade of events that is, vibration of the basilar membrane,which is enhanced by outer hair cell (OHC) activity, causes depolarisation of inner hair cells (IHCs), which leads to transmitter release and the generation of excitatory postsynaptic currents, ultimately initiating action potentials. The extracellular potentials that are generated by these events, and can be measured from the round window, include the cochlear microphonic (CM), the summating potential (SP), the dendritic potential (DP), and