BILATERAL SIMULTANEOUS AUDITORY BRAIN STEM RESPONSE IN INDIVIDUALS WITH HEARING LOSS

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This Dissertation is submitted as part fulfilment

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CERTIFICATE

This is to certify that this dissertation entitled **'Bilateral Simultaneous Auditory Brainstem Response in individuals with hearing loss'** is the bonafide work submitted in part fulfilment for the degree of Master of Science (Audiology) of the student Registration Number: 18AUD006. This has been carried out under the guidance of the faculty of the institute and has not been submitted earlier to any other University for the award of any other Diploma or Degree.

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CERTIFICATE

This is to certify that this master's dissertation entitled **'Bilateral Simultaneous Auditory Brainstem Response in individuals with hearing loss'** has been prepared under my supervision and guidance. It is also being certified that this dissertation has not been submitted earlier to any other University for the award of any other Diploma or Degree.

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DECLARATION

This is to certify that this dissertation entitled **'Bilateral Simultaneous Auditory Brainstem Response in individuals with hearing loss'** is the result of my own study under the guidance of Dr. Sandeep M, Associate Professor in Audiology, Department of Audiology, All India Institute of Speech and Hearing, Mysore, and has not been submitted earlier to any other University for the award of any other Diploma or Degree.

Mysuru
May 2019

Register No. 18AUD006

Dedicated To,

My dear Parents

&

Beloved guide, Sandeep Sir.

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I would like to thank my parents for everything what I am today, I know your hopes and prayers are always there with me. You have taught me how to be independent and self-sufficient. Not all people get chance to live their life the way they want to be, but in that case, I am so lucky that you always trusted my choices. Today I feel so happy to tell you, I am proud to have you as my parents.

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Chapter 1

INTRODUCTION

Auditory brainstem responses (ABRs) evaluate the peripheral auditory system and the lower brainstem. Clinically, ABR is the most preferred objective tool to estimate hearing thresholds, if the behavioral thresholds are not reliable as is the case with infants and malingering adults. We can derive the degree of hearing loss, configuration of hearing loss, type of hearing loss, and, to some extent, even the cause of hearing loss, from the findings of ABR. All this information, in turn is useful in early identification and rehabilitation of hearing loss.

Tone-burst evoked ABR, despite being a gold-standard method to estimate frequency-specific hearing thresholds, is time consuming - the test completion time ranges from 1 to 3 hours (Stueve & O'Rourke, 2003; Karzon & Lieu, 2006). Click evoked ABR testing also can be time consuming. This means that the test may take more than 1 session to complete, particularly in infants and children, in whom it is carried out under sedation. Therefore, scientists have attempted to modify the stimulus and acquisition paradigms in order to improve time efficiency of ABR. Polonenko and Maddox (2019) invented parallel ABR (pABR), which uses randomly timed tone-burst stimuli to simultaneously acquire ABRs to 5 frequencies, from both the ears. ABRs recorded were found to be similar to the standard ABRs recorded serially. Latency and amplitude of the ABRs recorded by their paradigm suggest better frequency specificity. This technique, although promising for quick estimation of frequency specific hearing, requires complex algorithms for stimulus presentation as well as for response acquisition, which are not available in the clinical AEP equipments. This warrants a simple method that can be executed immediately in the clinical AEP equipments, for quick estimation of hearing.

It is also feasible to increase stimulus repetition rate in order to reduce the testing duration, but increasing the repetition rate is limited by neural adaptation, resulting in degraded ABR morphology (Smith & Brachman, 1982). Particularly, presentation rates above 20/s (Fowler & Noffsinger, 1983; Campbell & Abbas, 1987), typically results in diminished ABR amplitudes (Terkildsen & Osterhammel, 1975) and longer ABR latencies (Stapells & Picton, 1981; Leung et al., 1998). Some reduction in Wave V amplitude is tolerated; hence, adapted rates of 25–40/s are acceptable for threshold estimation (American Speech Language-Hearing Association, 1987). However, rates below 25/s are advisable to ensure clear ABR morphology, more so in neurodiagnostic evaluations (American Speech-Language Hearing Association, 1987) and pediatric population.

Recently, Maruthy, Gnanateja, Sebastian and Sruthi (2018) proposed a new technique termed 'Bilateral simultaneous ABR (BiSi-ABR)' in which ABRs for clicks were recorded simultaneously from the two ears. The technique is expected to cut down the testing time by half of the conventional method. They showed that the latency, amplitude and the threshold of ABR were similar to that of the conventional ABR in normal hearing adults.

1.1 Justification for the Study

Audiological testing typically requires several hours - more so in infants and children. In difficult to test population, physiological tests such as ABR and OAEs are mandatory in order to cross-check the results of behavioral tests. ABR requires a minimum of half an hour to establish the thresholds of the two ears. It is important to note that this testing time can get prolonged owing to the sleep time of infants and children. Therefore, it is necessary to invent and validate new techniques that lead to time-efficient audiological evaluation.

The technique (BiSi ABR) invented by Maruthy, et al. (2018) is shown to be time efficient in eliciting hearing thresholds using click ABRs in normal hearing adults. The findings can be generalized to individuals with hearing loss but would benefit if proven with scientific evidence. BiSi ABR involves presenting clicks alternately between the two ears with total stimulus rate being twice that used in standard ABR. The physiological processes such as recruitment and neural adaptations are known to be deviant in individuals with hearing loss compared to normal hearing adults. Due to these deviances, it is not impossible to expect ABRs of different characteristics than the standard ABR, in the BiSi ABR technique. Therefore, the present study aimed to compare ABRs obtained using BiSi ABR technique with that of standard ABRs in a group of individuals with cochlear hearing loss.

1.2 Objectives of the Study

1 Compare peak latency of Jewett waves obtained using BiSi ABR technique with that of standard ABRs, in individuals with sensorineural hearing loss.

2 Compare peak amplitude of Jewett waves obtained using BiSi ABR technique with that of standard ABRs, in individuals with sensorineural hearing loss.

3 Compare the threshold of ABR obtained using BiSi ABR technique with that obtained using standard ABRs, in individuals with sensorineural hearing loss.

Chapter 2

REVIEW OF LITERATURE

According to the Cross- check principle (Jerger & Hayes, 1976), auditory test results should not be accepted and used in the diagnosis of hearing loss until it is confirmed or cross-checked by one more independent measure, preferably an objective test. In light of cross-check principle, auditory evoked potentials are being used to cross-verify the results of behavioural hearing tests in difficult to test population. This becomes particularly necessary in infants wherein the behavioural thresholds are not reliable for obvious reasons. Yet, owing to their sleep time, there is limited time available for recording auditory evoked potentials. In many instances, the situation warrants testing in multiple sessions. Therefore, there is a dire need for techniques that cut-down recording time of auditory evoked potentials in infants.

Auditory brainstem responses (ABR) is used worldwide to assess multiple clinical aspects of the human hearing system. These include, hearing threshold estimation, diagnosing cause of hearing loos pathology and even locating it in the auditory pathway. In threshold estimation, the mid frequency and the high frequency components of the ABR wave is very important for determining the latencies and estimating the hearing threshold. Click ABR correlates with the average threshold in the region of 1kHz to 4 kHz range (Eggermont,1982; stapells, 1989). ABR is also one of the best tools available for newborn screening with its sensitivity ranging from 42% (Desai et al., 1997) to 100% (Swigonski et al., 1987; Watkin et al., 1991;Shimizu et al., 1990; Smyth et al., 1990). Specificity ranges from 70% (Swigonski et al., 1987) to 100% (Durieux-Smith et al., 1991).

The presence of wave V and its latency often play an important role in lesion testing sites. In most studies, the overall sensitivity of absolute latency measurements in the detection of eighth nerve lesions was over 90% (Bauch, Rose, & Harner, 1982; Bauch, Olsen, & Harner, 1983; Jerger & Mauldin, 1978; Jerger & Johnson, 1988; Selters & Brackmann, 1977). In the identification of eighth-nerve lesions, Prosser and Arslan (1987) reported exactly 100 % sensitivity through the measurements of wave V latency. False-positive rates were indeed variable around 9 and 33 % (Bauch et al., 1982; Clemis & McGee, 1979; Selters & Brackmann, 1979).

Drift, Brocaar and VanZanten (1987) conducted a study where the click ABR was used to estimate the hearing threshold for adults (209 ears) with cochlear hearing loss. They found that maximum correlation coefficient was obtained in mean of 2 kHz and 4 kHz pure-tone thresholds and it was found to be 0.93. The other studies have reported correlation coefficient of 0.48 (Jerger & Mauldin, 1978), 0.65 (Coats & Martin 1984), 0.85 (Bellman et al.,1984). The minimum standard error of the estimate (defined as the mean difference between ABR & the corresponding PTA) is found to be 19.0dB (Bellman et al., 1984), 15.8 dB and (Jerger & Mouldin, 1978).

Werner, Folsom and Rickard (1993) conducted a study in infants and adults with normal hearing to find age-related improvements observed in auditory sensitivity by comparing ABR and behavioural thresholds. There were a total of 355 participants including 3 months (190), 6 months (125) and 18-30 years (40) old individuals. Tone pips of 1, 4 and 8 kHz were used to elicit ABRs. Results showed a positive correlation between ABR and behavioural threshold, and the difference between the two ranged from 10 to 20 dB. Gorga et al. (1988) showed similar findings in adults with normal hearing using similar frequency-specific stimuli.

Oezdamar et al. (1994) recorded ABR using an automated algorithm in a large population of infants, young children, adolescents, and a range of adults from young adulthood to old age, having hearing loss. The participants had either sensorineural, conductive or mixed hearing loss of varying degree. The behavioural thresholds (PTA1 & PTA 2) was compared with ABR thresholds. They found ABR thresholds to have best correlation with PTA 2. The authors also reported that, excluding time lost to artifact-rejected sweeps, on an average, 12.6 minutes were needed to test one ear with within ±5 dB accuracy.

Jerger (1978) assess the correlation between ABR and behavioural threshold in 275 individuals with various degrees of hearing loss. Their findings indicated that ABR threshold is a lot dependant on the hearing sensitivity in 1kHz to 4 kHz region.

ABR can be recorded with different type of stimuli, which can be either a broadband click or frequency-specific tone burst. Click evoked ABR estimate hearing sensitivity between 1 to 4 kHz region (Emanuel, 2002). Althout frequency-specific responses are obtained using tone bursts, it requires more than 2 hours to estimate hearing sensitivity in the audiometric frequencies of the two ears (Stueve & O’Rourke, 2003; Karzon & Lieu, 2006).

2.1 Methods to improve the time efficiency of ABR

Hecox and Galambos were the first to talk about the use of ABR for hearing threshold estimation. Later, various researchers have modified the stimulus or the acquisition parameters to improve the morphology of the ABR waveform and to reduce the time of testing.

2.1.1 Increasing the rate of stimulus presentation

Increasing the testing rate can decrease the testing time, but it is limited by neural adaptation, resulting in degraded ABR morphology (Smith & Brachman, 1982). Particularly, presentation rates above 20/s, typically results in diminished ABR amplitudes (Fowler & Noffsinger, 1983; Campbell & Abbas, 1987) and longer ABR latencies (Stapells & Picton, 1981; Leung et al., 1998).

Campbell and Abbas (1987) recorded ABR in 28 (20 with hearing loss of cochlear origin and 8 with retro cochlear pathology) adults with asymmetric sensorineural hearing loss and assessed the effect of repetition rate on ABR in tumour and nontumor patients. Clicks were presented at rates of 9.7, 39.7, 49.7, and 59.7 per second and responses were obtained. They found that the presence of hearing loss didn’t bring much change in the latency of the Vth peak. On an average the variations in the rate didn’t have much significant effect.

2.1.2 ABR using Chained Stimuli

Petoe, Bradley and Wilson (2009) recorded ABRs for chained stimuli in order to obtain frequency-specific ABR waveforms in less time than conventional stimuli, without sacrificing the 'quality' of waveforms obtained. They compared the conventional tone burst

ABR and ABR using the chained stimuli. The technique used was Gliding high-pass Noise Masker (GHINOMA; Hoke et al., 1991), The GHINOMA-evoked ABRs were acquired from 33 volunteers, aged between 18 to 55 years. The responses of the chained stimuli were found to be similar to that of conventional stimuli when acquiring ABRs for a range of 8 test frequencies and the time savings of ~24%. The waves had clearer morphologies, and larger wave V amplitudes for the chained stimuli.

Mamatha (2016) conducted a study using a novel stimuli consisting of a chain of tone bursts of different frequencies. This method was called as Multi Frequency auditory brainstem response (MFABR). They compared single frequency and multi frequency ABRs in 30 adults with normal hearing and 11 individuals with hearing loss. The latency and amplitude of wave I, III and V were compared between the two methods. The ABRs were found to be similar in their characteristics. But the hearing sensitivity at four audiometric frequencies (0.5, 1, 2 & 4kHz) could be estimated in 1/4th of the time required otherwise.

2.1.3. Maximum Length Sequence Analysis

Weber and Roush (1995) introduced maximum length sequence analysis (MLSA) with rapid click rates to examine its potential benefits in newborn hearing screening using ABRs. ABRs were acquired with conventional signal averaging at four stimulus intensity levels (50 dB, 40 dB, 30 dB, and 20 dB nHL) using a click rate of 33.3/sec. These responses were directly compared with the ABRs acquired with MLSA using a rate of 227.3/sec. Results showed that ABRs recorded with MLSA and conventional signal averaging were very similar. Due to increased repetition rate, the testing time was significantly lesser compared to conventional recording paradigm.

2.2 Auditory Steady State Responses (ASSR)

Stueve and O'Rourke (2003) evaluated click ABR, tone burst ABR, ASSR and ear-specific behavioural thresholds in 76 children (46 boys and 30 girls) ranging in age from 1-125 months. They found that ASSR time of testing ranged from 20 - 60 min depending on the hearing thresholds. There is, however, doubt about the validity of ASSR thresholds at high stimulation rates and the total time to complete the ASSR assessment in the clinics may not be any better than ABR (Schmulian, Swanepoel, & Hugo, 2005). In addition, actual hearing levels and ASSR thresholds are in better agreement for children with severe to profound hearing loss. The actual hearing levels and ASSR thresholds agreement is not so high for those with a hearing loss of mild to moderate degree (Rance, Rickards, Cohen, De Vidi, & Clark, 1995; Sininger, 2003).

Rance et al. (2005) reported that ASSR testing cannot reliably differentiate between normal ears and those with mildly elevated hearing levels. Rather, click ABR can be considered as more useful method for differentially diagnosing an ear with normal hearing sensitivity and an elevated hearing levels (Bachmann & Hall, 1998; Schmulian et al., 2005). Thus, the ABR remains as the gold standard tool for determining hearing threshold evaluations in young infants.

2.3 The Dichotic Multiple Stimulus ASSR

Schmulian, Swanepoel, and Hugo (2005) examined the precision of the multiple frequency ASSR in predicting the pure-tone thresholds at frequencies like 0.5, 1, 2, and 4.0 kHz in comparison with an ABR used (click and tone burst at 0.5 kHz) in a total of 25 participants with hearing impairments. The threshold was estimated in both the paradigms and the testing time was compared. Recording time for the steady state protocol was about 28 minutes when compared to 24 minutes (with standard deviations of 11 and 9 minutes respectively) of the ABR protocol. Multi-frequency ASSR could predict the thresholds with reasonable accuracy, while some configurations of hearing loss showed inaccuracies for low-frequency estimates.Multiple-ASSR and tone-ABR (Air-Conduction Stimulus) results were obtained in infants and young children with hearing loss or hearing loss. For each group (normal or hearing loss), and for both groups combined, the correlations between ASSR and ABR thresholds, linear regressions, and ASSR-minus-ABR threshold differential scores were calculated. Multiple ASSR thresholds (in dB HL) thresholds were highly correlated (r=5,97) with tone-ABR (in dB nHL) thresholds for 500, 1000, 2000 and 4000 Hz.

Researchers found that dichotic multiple ASSR stimulation was very quick, requiring a total of approximately 4 to 6 minutes to complete testings in infants with normal-hearing (Janssen & Stapells 2009; van Maanen & Stapells 2009). It's about 50 to 70% of the time necessary for the conventional tone-ABR in normal infants; in infants with elevated thresholds, in the very first step, the multiple ASSR indicated "elevated" only slightly quicker, requiring approximately 80 to 90% of the conventional tone-ABR time (Janssen & Stapells, 2009).

2.4 Bilateral Simultaneous Auditory Brainstem Response

A novel paradigm called ‘Bilateral Simultaneous (BiSi) ABR’ was proposed recently by Maruthy, Gnanateja, Sebastian and Sruthi (2018). Twenty-five individuals (with hearing sensitivity within the normal limits) were chosen for the study. The ABRs were recorded in both conventional ABR paradigm and BiSi ABR paradigm and were compared. In the two BiSi-ABR conditions, both the ears were stimulated using clicks with an inter-aural interval of 16 ms between the clicks presented to the two ears. They found that thresholds and amplitude of ABR obtained from the BiSi ABR method and conventional ABR was not different. Only half the testing time was required estimate the thresholds using BiSi ABR compared to standard method.

Chapter 3

METHODS

A within-subject single group design was used in the study. Auditory brainstem responses (ABR) were recorded using two paradigms (conventional ABR & Bilateral Simultaneous ABR) and their characteristics were compared with each other. The details of the method used are given in the subsequent sections.

3.1 Participants

Thirteen adults in the age range of 20 to 50 years (mean age: 42.5 years) participated in the study. They had bilateral sensorineural hearing loss predominantly of cochlear origin. The degree of hearing loss ranged from mild (pure tone average between 26 & 40 dB HL) to moderately severe (PTA between 56 & 70 dB HL). The configuration of the audiogram was either flat or gradually sloping. There was no evidence of retro-cochlear lesion in the click evoked ABRs recorded in them. The thirteen participants were tested for ABR in both the ears, resulting in data of 26 ears.

All the participants had normal middle ear functioning, which was confirmed with the help of a middle ear immittance testing. There were no other relevant neurological or otological dysfunctions. A written informed consent was obtained from the participants for their participation. The study abided to the ethical guidelines stipulated for biobehavioral research in human subjects at the All India Institute of Speech and Hearing, Mysuru.

3.2 Stimulus and Presentation Paradigm

Broadband clicks with instantaneous rise/fall time were used to elicit ABRs. The stimulus and presentation paradigm used for BiSi ABR were the same as that of Maruthy, et al. (2018). The stimulus was generated using MATLAB (Mathworks Inc., Natick, Massachusetts, USA).

There were two stimuli generated, each with a duration of 17.5 ms. The first stimulus had a 100µs click in it at the onset, followed by a silence for the next 17.5 ms. This stimulus was fed to the right channel of the stimulus module (meant to be presented only to the right ear) in Advance research module of Intelligent Hearing systems (IHS) equipment. The second stimulus with the same duration had silence in the first 17.5 ms and ended with a 100µs click. This stimulus was fed to the left channel of the stimulus module. Before loading them into IHS equipment, the stimuli were converted into '.stim' format, compatible to be used in the equipment.

In the standard ABR paradigm, the stimuli were presented monaurally. In each participant, right ear was tested first followed by left ear. Whereas in the BiSi stimulus paradigm, the two stimuli were presented simultaneously to the two ears. Due to different location of the clicks in the two stimuli (in one at the onset and the in the other at the offset), clicks were delivered alternately to the two ears with an interaural time delay of 17.5ms. In each ear, clicks were presented at 30.1 Hz, which resulted in a total repetition rate of 60.2 Hz. The stimulus presentation in BiSi paradigm is schematically represented Figure 3.1.

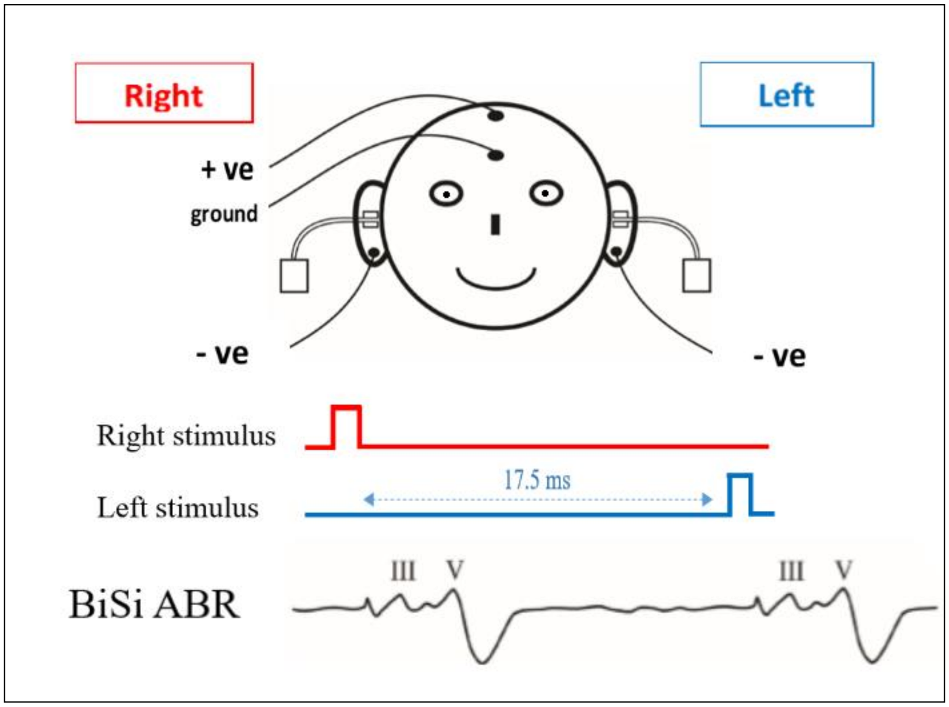

Figure 3.1: *Representation of stimulus delivery in BiSi-ABR paradigm.*

The stimuli were calibrated both objectively and subjectively. The objective calibration was done with the help of a sound level meter. In objective calibration, the output of the instrument was measured with the sound level meter in dBSPL and it was compared with the intensity levels given in the instrument. Subjective calibration was done by finding the mean detection thresholds (in dBSPL) for the clicks in 10 normal hearing participants. The mean threshold in dBSPL became 0 dBnHL This correction factor were fed to the advance research module of IHS and the ABR testing was carried out accordingly.

3.3 Test Environment

All the audiological testing was carried out in an acoustically treated room where the noise levels were within permissible limits (ANSI S3.1; 1991). The room used for recording ABR was also electrically shielded.

3.4 Test Procedure

3.4.1 Preliminary examination

The potential participants were subjected to puretone audiometry, speech audiometry, immittance evaluation, otoacoustic emissions and click ABRs to ensure that they possess all the necessary characteristics to serve as participants.

Puretone thresholds were estimated using a calibrated Inventis Piano diagnostic audiometer. Both air conduction and bone conduction thresholds were estimated using modified Hughson-Westlake procedure (Carhart & Jerger. 1959). The air conduction thresholds were obtained at octave frequencies between 0.25 and 8 kHz, while the bone conduction thresholds were estimated between 0.25 and 4 kHz.

Immittance evaluation was carried out using a calibrated diagnostic GSI tympstar immittance meter. Tympanogram and acoustic reflexes were recorded from both the ears using a probe tone of 226 Hz. Ipsilateral and contralateral acoustic reflex thresholds were estimated for pure tones of 0.5, 1, 2 and 4 kHz.

Transient evoked otoacoustic emissions for 80µs clicks were recorded using ILO-292 Echoport plus. The clicks were presented in nonlinear stimulus paradigm at 75dBpkSPL.

The SNR and amplitude of otoacoustic emissions were noted down at octave frequencies between 1 and 6 kHz.

Click evoked ABRs were recorded using standard protocol recommended by Hall (2007) for site of lesion testing. The responses were interpreted based on the absolute and relative latencies of Jewett waves, and V/I amplitude ratio.

3.4.2 Experimental test procedure

Puretone hearing thresholds estimated during the preliminary examination were used to derive the pure tone average. This served as the estimate of behavioral hearing thresholds.

For the ABR recordings, the participants were seated on a cushioned recliner chair. They were briefed about the procedure of recording ABR. They were instructed to relax their head and neck region, and to minimize the extraneous body movements. The Intelligent Hearing System's AEP equipment with Advanced research module was used to record ABRs. ABR were simultaneously recorded from two channels with vertical electrode montage. The electrode sites were Cz (non-inverting), A1 and A2 (inverting), and Fpz (ground) as per the 10-20 classification system. The electrode sites were cleaned with Nuprep skin preparation gel and the silver chloride disc electrodes were placed using conducting paste.

ABRs were recorded once for the standard stimulus paradigm and once for the BiSi paradigm. In the standard paradigm, ABRs were recorded for the two ears separately while in the BiSi paradigm, they were recorded simultaneously. The stimulus and acquisition parameters used to record ABRs are given in Table 3.1. The order of paradigms was counterbalanced across participants. In both the paradigms, ABRs were initially recorded at 90dBnHL. If the responses were present, stimulus intensity was reduced in steps of 10dB to track ABR threshold in the two ears. Near the ABR threshold, the intensity was varied in 5 dB steps. All the recordings were repeated at least once to ensure replicability. The exact time taken to estimate the ABR thresholds in minutes was noted down for the two procedures.

Table 3.1: Stimulus and acquisition parameters used to record ABRs in the standard and BiSi paradigms

Stimulus Parameters	
Stimulus	Broad band clicks 1) In standard monoaural 2) In BiSi paradigm
Polarity	Rarefaction
Transducer	Insert ear phone
Repetition rate	30.1/s in each ear
Intensity	90dB nHL and lower intensities till ABR threshold
Type of stimulation	Monoaural for standard ABR Binaural for BiSi ABR
Acquisition parameters	
Montage	Vertical
Electrode sites	Inverting: left (A1) & right (A2)
	Non inverting: vertex (Cz)
	Ground: Fpz
Filter setting	100-1500 Hz

Amplification	1,00,000 times
Artifact rejection	20 µV
Analysis window	30 ms
Total no; averages	2000
Data points	1024

3.5 Response Analysis

Figure 3.2 shows the representative waves recorded in the two paradigms. The replicated responses were visually inspected by two audiologists, experienced in the field of electrophysiology. They were blinded to the purpose of the study. They were instructed to mark the peaks of the Jewett waves, if present. The peaks were marked only on the ipsilateral recordings. The latency and amplitude of the marked waves were noted down. The peak latency and amplitude of wave I, III and V (in instance of presence of the wave) were noted down at 90 dB nHL. At lower intensities, peak latency and amplitude of only the wave V were noted down. ABR threshold was noted down as the lowest intensity at which wave V was recordable.

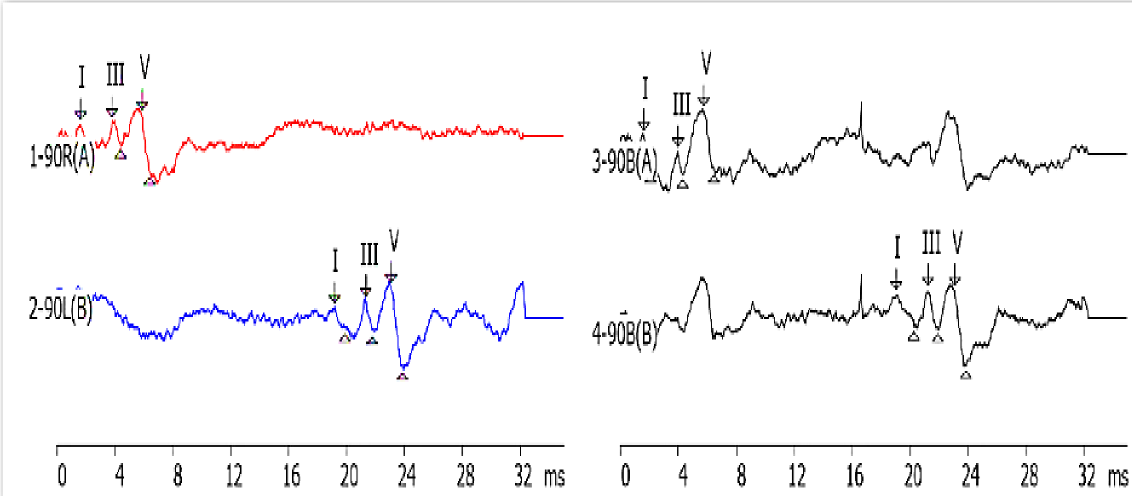

Figure 3.2: *The ABR waveforms of one representative participant using the BiSi-ABR technique and the standard method at 90dBnHL. The waveforms shown on the left side are standard ABRs (red; right, blue; left) recorded for right and left ear stimulation respectively. The waveforms shown on the right side are the BiSi ABRs recorded for right and left ear stimulation (in the order). The click onsets in the right ear start at 0 ms while onset of click is at 17.5 ms in the left ear.*

Chapter 4

RESULTS

The study aimed to test whether Bilateral simultaneous auditory brainstem response (BiSi ABR) technique can be a valid tool to estimate the hearing thresholds with less time than the standard ABR. The click evoked ABRs were elicited by BiSi ABR paradigm and the standard ABR paradigm. Figure 4.1 shows ABRs recorded in the two paradigms from the right ear of a representative participant. The figure shows ABRs recorded at multiple intensities with ABR threshold being 55dBnHL. The ABRs recorded at 90 dBnHL had wave I, III and V. With the decrease in intensity, earlier waves disappeared and wave V was the last one to disappear.

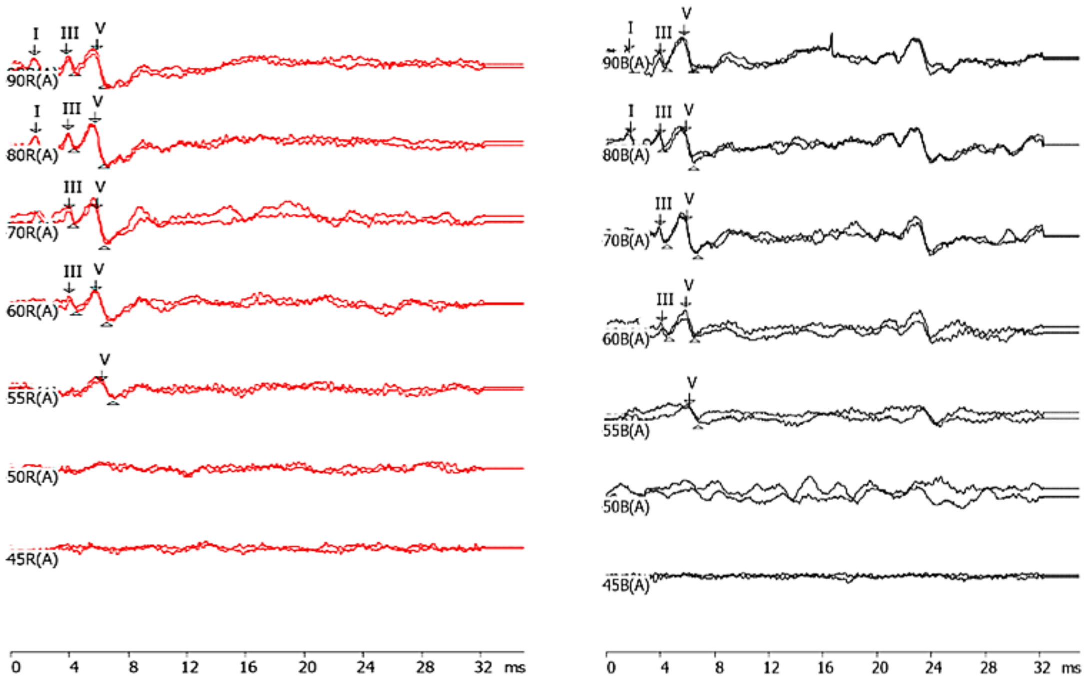

Figure 4.1: ABRs recorded in the two paradigms from the right ear of a representative participant. The left panel shows the recordings of *standard ABR (red) and the right panel* shows the recordings of *BiSi ABR (black).*

In order to meaningfully compare the two paradigms, it was important to derive the percentage of occurrence (operationally termed as prevalence) of wave I, III and V in the study group. The percentages would give an idea about the sample size available for comparison in each of these waves. This was particularly needed considering that the participants had up to moderately severe degree of sensorineural hearing loss, due to which, ABRs were not expected to have all the three of wave I, III and V, even at 90dBnHL in all the participants.

The prevalence of wave I, III and V at 90 dBnHL in the ABRs recorded in the two paradigms are given in Table 4.1. The prevalence is calculated in percentage. It reflects the number of ears in which a particular wave was present out of 26 possible occurrences (total number of ears in which ABRs were recorded). The prevalence of all the three waves was same in the two paradigms. All the 26 ears had wave V, while wave I and III were present in only subgroup of the participants even at 90 dBnHL.

Table 4.1: P*revalence of* wave I, III and V at 90 dBnHL in the ABRs recorded in the two paradigms

Wave	Standard ABR	BiSi ABR
I	34.6%	34.6%
III	57.7%	57.7%
V	100%	100%

The group data of latency, amplitude and thresholds of wave I, III and V were tested for their distribution using Shapiro-wilks test of normality. The results showed that most variables had non-normal distribution ($p > 0.05$) warranting the use of non-parametric test for statistical comparisons. The results obtained are reported under the following headings:

1. Comparison of latency of ABR between the two paradigms
2. Comparison of amplitude of ABR between the two paradigms
3. Comparison of ABR thresholds estimated in the two paradigms
4. Agreement between PTA and ABR thresholds
5. Comparison of Testing Time between Standard and BiSi Paradigms

5.1 Comparison of Latency of ABR between the Two Paradigms

Table 4.2 gives the median and interquartile range of latency of wave I, III and V obtained in the two paradigms. The median latency of all three waves were slightly different between the two paradigms. However, the differences were not signfincantly different as tested on Wilcoxon signed rank test (results shown in Table 4.2).

Table 4.2: Median and interquartile range of latency of wave I, III and V obtained at 90 dBnHL in the two paradigms. It also shows the results of Wilcoxon's sign rank test

Wave	Descriptive	Standard ABR	BiSi ABR	/Z/	*p*
I	Median (ms)	1.70	1.70	1.548	0.122
	Interquartile range	0.38	0.40		
III	Median (ms)	3.90	4.0	0.409	0.683
	Interquartile range	0.23	0.35		
V	Median (ms)	5.95	5.95	0.244	0.807
	Interquartile range	0.50	0.57		

5.2 Comparison of Amplitude of ABR between the Two Paradigms

Table 4.3 gives the median and interquartile range of amplitude of wave I, III and V obtained in the two paradigms. The median amplitude of all three waves although were slightly different between the two paradigms, results of Wilcoxon signed rank test revealed that the differences were not statistically significant (results shown in Table 4.3).

Table 4.3: Median and interquartile range of amplitude of wave I, III and V obtained at 90 dBnHL in the two paradigms. It also shows the results of Wilcoxon's sign rank test

Wave	Descriptive	Standard ABR	BiSi ABR	/Z/	*p*
I	Median (ms)	0.18	0.19	1.752	0.080
	Interquartile range	0.09	0.08		
III	Median (ms)	0.19	0.16	0.851	0.395
	Interquartile range	0.08	0.07		
V	Median (ms)	0.37	0.45	0.329	0.742
	Interquartile range	0.30	0.20		

5.3 Comparison of ABR thresholds estimated in the two paradigms

Table 4..4 gives the median ABR thresholds estimated in the two paradigms. The median ABR threshold was same (65dBnHL) in both the paradigms. Wilcoxon signed rank test showed no significant difference between the two median thresholds.

Table 4.4: The median and the inter quartile deviation of ABR threshold estimated using standard and BiSi paradigm. The results of Wilcoxon signed rank test is also given

Descriptive	Standard ABR	BiSi ABR	/Z/	*p*
Median (dBnHL)	65	65	0.816	0.414
Interquartile range	10	7.5		

4.4 Agreement between PTA and ABR thresholds

Agreement between PTA and ABR threshold were determined using measures of correlation and agreement (Bland-Altman Plots). The strength and direction of association between ABR thresholds and PTA was derived based on Spearman's correlation coefficient (R^2). Figure 4.2 and 4.3 show the scatter plots depicting the relationship between PTA and ABR thresholds, separately for the two paradigms. There was a significant high positive correlation between PTA and ABR thresholds. This was true for both the ABR paradigms. The correlation was higher (R^2 = 0.90, $p < 0.05$) for BiSi paradigm compared to standard paradigm (R^2 = 0.086, $p < 0.05$)

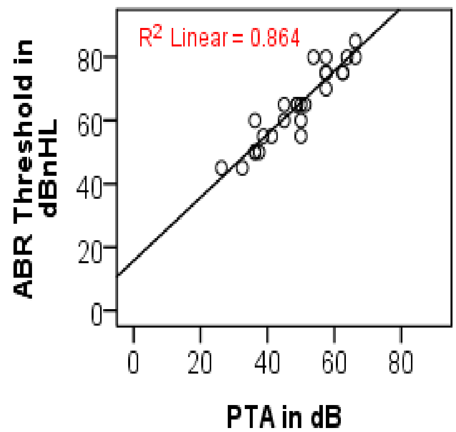

Figure 4.2: *Scatter plot depicting the relationship between PTA, and ABR thresholds derived using standard paradigm.*

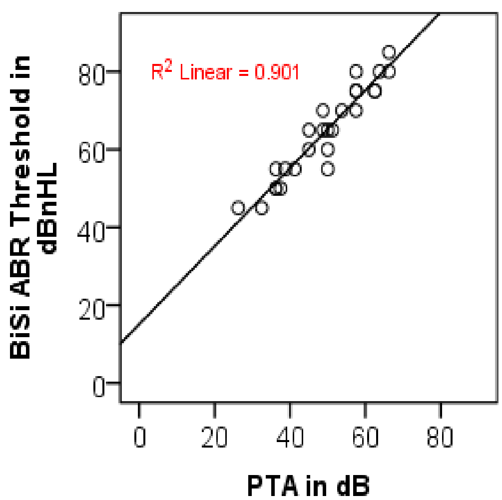

Figure 4.3: *Scatter plot depicting the relationship between PTA, and ABR thresholds derived using BiSi paradigm.*

To derive the agreement between PTA and ABR thresholds, the difference plots were constructed using the mean of ABR threshold and PTA thresholds on *x*-axis and the difference between the two thresholds on *y*-axis. One sample *t*-test was performed to obtain the bias (i.e., mean) value, which indicated absolute difference between the ABR threshold and PTA (Figure 4.4 & 4.5). The upper and lower 95% cut-off of agreements were calculated using the formula *"1.96*SD± bias,"* as given by Bland and Altman (1986). The bias value obtained for the standard ABR and BiSi ABR were 15.63 dB and 15.24 dB respectively. The 95% cut-off of agreement for standard ABR was 6.99 and 24.25 (lower & upper). For BiSi ABR, it was 7.97 dB nHL and 22.51 dB nHL respectively.

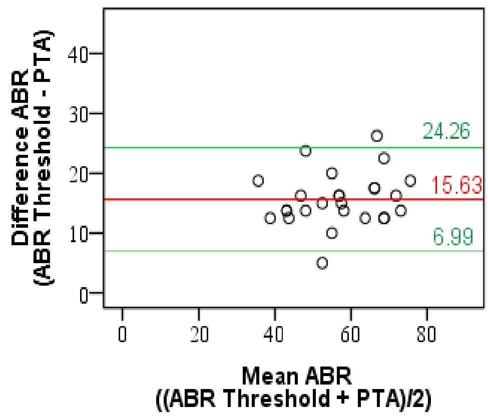

Figure 4.4. The difference plot of standard ABR threshold (dB nHL) and PTA (dBHL). The red line indicates the bias value and the green lines indicate the upper and lower 95% cut-off of agreement.

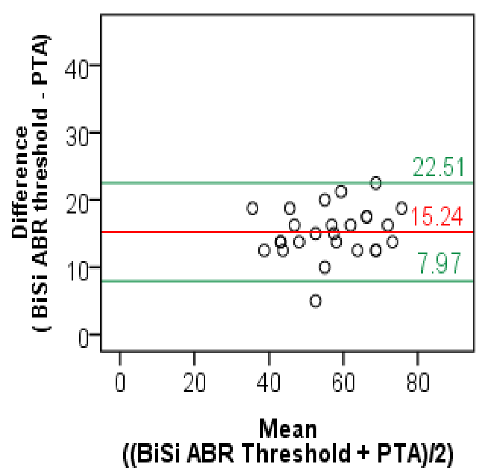

Figure 4.5. The difference plot of BiSi ABR threshold (dB nHL) and PTA (dBHL). The red line indicates the bias value and the green lines indicate the upper and lower 95% cut-off of agreement.

4.5 Comparison of Testing Time between Standard and BiSi Paradigms

The time taken for ABR threshold estimation of two ears of one participant was noted down for the two paradigms. Table 4.5 gives the median time in minutes, separately for the three degrees of hearing loss. The time taken in BiSi paradigm was only half the time needed to estimate thresholds using standard paradigm. The testing time decreased with increase in the degree of hearing loss.

Table 4.5 *The median testing time for estimating ABR thresholds using the two paradigms, shown separately for the three degrees of hearing loss*

Degree of hearing loss	Standard ABR (in min)	BiSiABR (in min)
Mild	40	20
	30	15
	18	9

Chapter 5

DISCUSSION

The present was taken up to validate the Simultaneous Auditory Brainstem Response as a clinical tool of recording the neural responses from the brainstem in less time compared to the conventional ABR. The study also tried to correlate the threshold obtained using BiSi ABR technique to the Pure Tone Average. The findings obtained are discussed under following headings:

1. Characteristics of BiSi ABR in comparison to standard ABR
2. Accuracy of hearing threshold estimation using BiSi ABR
3. Time efficiency of BiSi ABR
4. Potential for BiSi ABR to be a valid routine clinical tool

5.1 Characteristics of BiSi ABR in Comparison to Standard ABR

The present study compared the latency, amplitude and threshold obtained in BiSi ABR to that of standard ABR. The threshold and amplitude comparisons were made only for wave I, III, and V at 90 dBnHL. In the present study there was no significant difference between the paradigms in their latency of wave I, III as well as V. There was also no difference in the prevalence of these waves between the two paradigms. Maruthy, Gnanateja, Sebastian and Sruthi (2018) also found a similar result in individuals with normal hearing sensitivity.

This study also revealed that there was no significant difference in the amplitude of Jewet waves between both the two paradigms. This finding is in congruence with the previous study done by Maruthy et al. (2018). There was a reduction in amplitude with the decrease of the intensity. Both the method showed no difference because the amount the energy of stimulus reached the ear from both the paradigm was the same and probable it created a similar amount of neural synchrony and thereby similar amplitudes.

Regardless of the degree of hearing loss, in majority of the ears (23/26) the derived thresholds were within 5dB between the two paradigms. Taken together, the results of latency, amplitude and threshold support that the findings in BiSi ABR is same as that of standard ABRs. Therefore, it does not compromise the characteristics of ABR in any way. The two paradigms are different in terms of number of stimuli presented per second.

5.2. Accuracy of hearing threshold estimation using BiSi ABR

The correlation of PTA and ABR threshold was tested separately for the thresholds in the two paradigms. BiSi ABR thresholds had high positive correlation with PTA as well the thresholds of standard ABR paradigm. The findings suggest that hearing sensitivity estimated using BiSi ABR will have same precision as that standard ABR. Therefore, apart from having similar latency, amplitude and prevalence to that of standard ABR, BiSi ABR estimated comparable thresholds. Across different degrees of hearing loss, the thresholds of BiSi ABR is going to be elevated with hearing sensitivity.

The PTA and ABR threshold agreement was found to be 15.63 dB for the conventional ABR and 15.24 for the BiSi ABR which are comparable.

5.3 Time Efficiency of BiSi ABR

This was one of the major objectives of the study and this proved BiSi ABR to be one of the most time efficient tool in hearing threshold estimation. There was a significant reduction in the time of testing - the testing time was reduced by half in BiSi ABR compared to the conventional ABR. This finding is very much similar to that of the recent study done by Maruthy, et al. (2018). The effective repetition rate is double that of the conventional ABR which helps to reduce the time of testing. Using the intra ear time of the stimulus presentation for testing the other ear helped this tool to significantly bring down the time of testing. Even though the effective repetition rate of the stimuli doubled from 30.1/s to 60.2/s, if we consider only one ear, the rate remained at 30.1/s which made this paradigm no different from the standard ABR in terms of accuracy. This proves that the BiSi ABR testing of 2 individuals can be completed with the same time taken to complete one patient using the standard ABR.

5.4 Potential for BiSi ABR to be a Valid Routine Clinical Tool

The study strongly supports that BiSi ABR is a time efficient objective tool for the hearing threshold estimation. The time taken for the BiSi ABR is half that of the conventional ABR. With such significant reduction in testing time, the clinicians will be able to test twice the number of patients in a clinic. Furthermore, it will be a very helpful tool to conduct test in difficult to test population, in screening infants and even while obtaining stacked ABR.

Despite of all the advantages, one disadvantage may be the possibility of cross hearing. The masked ABR cannot be done with the procedure but by using insert ear phones most of the chances of cross hearing and thereby false responses can be reduced.

Chapter 6

SUMMARY AND CONCLUSIONS

Auditory Brainstem Response (ABR) being one of the mostly preferred physiological test for hearing threshold estimation as well as neuro-diagnostics in the field of audiology, lots of researchers have come up with modifications and inventions of methods to improve the time efficiency of ABR recording. The current study aimed to validate Binaural simultaneous (BiSi) paradigm invented by Maruthy, Gnanateja, Sebastian, Sruthi (2018) in a group of adults with sensorineural hearing loss.

Thirteen adults (26 ears) in the age range of 20 to 50 years, having mild- moderately severe sensorineual hearing loss participated in the study. The study incorporated a within-subject single-group research design. The stimulus was a pair of broadband clicks concatenated with interstimulus interval of 17.5 ms. All odd stimu;I were presented to the right ear while the even stimuli went to the left ear. The clicks were presented at 60.2 per second repetition rate, wherein the effective rate presented to the individual ear was 30.1 per second. The paradigm was meant to record ABR simultaneously from two ears, thereby reducing the recording time to half the time required for standard ABRs. ABRs recorded in the BiSi paradigm were compared with standard ABRs in terms of their prevalence of Jewett waves, latency, amplitude, and the estimated threshold.

Wilcoxon's signed rank test was used to compare the ABRs recorded in the two paradigms. Results showed no significant difference in latency, amplitude as well as ABR threshold. The prevalence of Jewett waves at 90dB nHL also remained same between the two paradigms. The results of Spearman correlation and the test of agreement (Bland-

Altman plots) revealed a strong agreement between behavioral and the ABR threshold estimated using BiSi paradigm. Although the difference was marginal, the agreement was better with BiSi ABR than standard ABR. The recording time of ABR was only half of that of standard ABR.

The findings reveal that ABRs recorded using BiSi paradigm has characteristics same as that of standard ABR. Therefore, is no negative influence of the paradigm even at threshold level. Considering that it provides the same information as standard ABR in only half of its time, it is strongly recommended to use BiSi paradigm in the audiology clinics. Although it is validated for hearing threshold estimation, the findings support the use of BiSi paradigm even for neuro-diagnostic purposes. The only demerit of this technique is that it requires a stimulus presentation module wherein two different stimuli can be presented to the two ears, as in Advanced research module of IHS equipment.

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