Auditory Brainstem Responses Using Chained Stimuli of Multiple Frequency Tone Bursts

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May, 2016

CERTIFICATE

This is to certify that this dissertation titled **'Auditory Brainstem Responses Using Chained Stimuli of Multiple Frequency Tone Bursts'** is the bonafide work submitted as part fulfillment for the Degree if Master of Science in Audiology of the student with Registration No. 14AUD012. This has been carried out under the guidance of a faculty of this 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 dissertation titled **'Auditory Brainstem Responses Using Chained Stimuli of Multiple Frequency Tone Bursts'** has been prepared under my supervision and guidance. It is also certified that this has not been submitted earlier to any other University for the award of any other diploma or degree.

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DECLARATION

This dissertation titled **'Auditory Brainstem Responses Using Chained Stimuli of Multiple Frequency Tone Bursts'** is the result of my own study under the guidance of Dr. Sandeep M., Reader in Audiology, Department of Audiology, All India Institute of Speech and Hearing, and has not been submitted earlier to any other University for the award of any other diploma or degree.

May, 2016
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Dedicated to

AMMA

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Abstract

Auditory brainstem responses (ABRs) are clinically used to evaluate the peripheral auditory system. As one of its primary clinical application, ABRs serve to estimate hearing thresholds in in difficult to test population wherein reliable behavioral thresholds cannot be obtained. The present study proposed a novel technique called Multifrequency ABR (MFABR) using which frequency specific ABRs of multiple frequencies can be obtained simultaneously. The aim of this study was to validate MFABR as a time efficient and reliable clinical tool for estimating frequency specific hearing thresholds. Thirty normal hearing adults and 11 individuals with Sensorineural hearing loss in the age range of 20 to 50years participated in the study. The latency and amplitude of wave I, III and V were compared between conventional single frequency tone burst ABR and the MFABR techniques at 500Hz, 1000Hz, 2000Hz and 4000Hz. The MFABR thresholds were also correlated with behavioral audiometric thresholds at the four aforementioned frequencies to analyze the agreement between the two types of thresholds. Results showed that MFABRs did not differsignificantly from that of single frequency tone burst ABR to affect the clinical interpretations. MFABR thresholds were in close agreement with the pure tone thresholds thus validating it to be a reliable clinical tool to estimate frequency specific hearing. The total time taken for estimating thresholds across the four audiometric frequencies (500Hz, 1000Hz, 2000Hz & 4000Hz) is one-fourth of the time taken by single frequency tone bursts. Therefore it is a promising time efficient tool in diagnostic audiology, particularly in difficult to test population.

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Chapter 1

INTRODUCTION

Auditory brainstem responses (ABRs) are clinically used to evaluate the peripheral auditory system and the lower brainstem. As its primary clinical application, ABRs are used to estimate hearing thresholds in patients who are not able to provide reliable behavioral thresholds such as infants and malingering adults. (Coles, 1977; Hall, 1992; Stapells & Vancouver, 2000). The information thus derived is useful for inferring the degree of hearing loss, configuration of hearing loss, type of hearing loss and to an extent, the cause of hearing loss. This information in turn helps in fitting of hearing aids, facilitating early identification and rehabilitation (Hoke, Pantev, Ansa, Lutkenhoner & Herrmann, 1991). However, there are still limitations to ABR testing, not the least of which is the time duration of a test session particularly while estimating frequency specific ABR thresholds (Mitchell & Clemis, 1977; Jerger et al., 1985; Burkard et al., 1990; Hamill et al., 1991; Mitchell et al., 1994).

The testing duration of ABR is governed by three major factors; the number of averages required for an acceptable signal to noise ratio, the repetition rate of the stimulus and the number of frequencies for which the threshold is to be estimated. These three factors are particularly important in frequency-specific ABR testing, where the time required to obtain thresholds to a comprehensive number of stimulus frequencies usually exceeds the time which is available by patient sedation or cooperation (Mitchell & Clemis, 1977; Davis et al., 1985). Reducing the test time by increasing the repetition rate is limited by neural adaptation, which degrades the ABR's morphology (Smith & Brachman, 1982). Particularly, presentation rates above 20/s (Fowler & Noffsinger, 1983;

Campbell & Abbas, 1987), typically results in diminished ABR amplitudes (Leung, Slaven, Terkildsen & Osterhammel, 1975) and longer ABR latencies (Stapells & Picton, 1981; Leunget al., 1998). Because some reduction in Wave V amplitudes is tolerated, adapted rates of 25–40/s are acceptable in threshold testing (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; Hall, 2004) and paediatric population.

To avoid the adaptation effects caused by increasing the stimulus presentation rate in frequency specific ABR testing, some researchers have trailed alternative stimuli called ‘chained stimuli’. The tone bursts of different frequencies are chained one after the other with appropriate inter-stimulus interval to generate a chained stimulus. Instead of eliciting ABRs for tone bursts individually with high repetition rate, a chained stimulus involving all tone bursts in one stimulus can be used with lower repetition rate without causing adaptation. This approach interleaves several discrete stimuli and maximizes acquisition efficiency, while minimizing response adaptation. It is assumed that if the frequency of each discrete stimulus is different enough, then different populations of neurons will be stimulated in sequence, and adaptation will be minimized or avoided even if the inter-stimulus interval is reduced to as low as 10 milliseconds (Mitchell, Fausti & Frey, 1994; Mitchell, Henry, Kempton, Fausti & Trune, 1994). The conventional method used to obtain frequency specific ABR is to stimulate the auditory system with brief tone bursts with short rise times (Suzuki & Horiuchi, 1977; Klein & Teas, 1978; Kodera, Yamada, Yamane & Suzuki, 1978). This approach is limited, however, by its excessively long test time, approximately 2 hours (Stueve & O'Rourke, 2003; Karzon & Lieu, 2006).

1.1 Justification for the Study

To estimate hearing thresholds in difficult to test population, where in behavioral thresholds are not reliable, objective techniques such as click ABRs can be used. Click evoked ABRs predominantly estimates hearing between 1000Hz to 4000Hz (Emanuel, 2002) but these estimates are not frequency specific. However, it is one of the most preferred techniques due to its time efficiency.

Frequency specific auditory thresholds are vital for fitting hearing aids. Auditory evoked potentials such as tone burst ABR, Auditory steady state responses (ASSR) and Late latency responses (LLR) are known to be reliable techniques for estimating frequency specific hearing thresholds. However, these test procedures are not practiced in all clinical set ups due to time constraints. Approximately 2 hours are required for tone burst ABR (Stueve & O'Rourke, 2003; Karzon & Lieu, 2006), around 28 minutes for MASTER ASSR (Schmulian, Swanpoel & Hugo, 2005) and approximately 4 hours for LLR (Bell, Smith, Allen & Lutman, 2004) has been estimated. The estimated time duration for proposed technique (ABR using chained stimuli), is 30 minutes based on pilot study. Although ASSRs are quicker in acquisition of frequency specific auditory thresholds, they are highly contaminated by stimulus related artifacts resulting in high false positives (Gorga et al., 2004; Picton & John, 2004; Small & Stapelles, 2004). Even though it is possible to obtain frequency specific thresholds with the LLR, its susceptibility to the state of arousal, drugs and longer test duration curtails their usefulness. In such conditions ABR can be obtained for tone bursts using chained stimuli of multiple frequencies.

There are only fewer studies assessing acquisition of ABR with multiple frequency and multiple intensity tone bursts (Mitchell, Fausti & Frey, 1994; Mitchell, Kempton, Creedon & Trune, 1996; Curtin, Mitchell, Kempton, Creedon & Trune, 1999). One set of studies (Mitchell et al., 1996; Mitchell et al., 1999) are done on mice at frequencies above 8000Hz and the results obtained cannot be directly generalized to human population. In the study by Mitchell, Fausti & Frey (1994) on humans, they did not use stimulus frequencies below 8kHz, which limits the applicablity of the results to study hearing thresholds in human beings.

Since there is a need for acquisition of ABR responses across frequencies within relatively less time duration, ABR using chained stimuli with multiple frequency tone bursts seems to be a promising tool. However, the technique needs to be clinically validated.

1.2 Aim of the Study

To validate ABRs elicited by multi frequency chain of tone burst (MFTB) as a clinical tool for recording frequency specific ABRs.

1.3 Objectives of the Study

The two objectives of the present study were,

- To compare latency and amplitude of ABR elicited by single frequency tone bursts (SFTB) with that of ABRs elicited by (MFTB) at 110dB SPL
- To estimate ABR thresholds using MFTB and compare with that of puretone hearing thresholds at 500Hz, 1000Hz, 2000Hz and 4000Hz

1.4 Hypothesis

The null hypothesis of the present study is that there is no significant difference in the latency and amplitude between ABR elicited by multifrequency tone burst MFTB and ABR elicited by single frequency tone burst (SFTB).

Chapter 2

REVIEW OF LITERATURE

Hearing threshold estimation plays a significant role in appropriate diagnosis and rehabilitation. Conventionally, threshold is estimated using behavioral methods such as puretone audiometry, behavioral audiometry and visual reinforcement audiometry depending on the age of the patient. Frequency specific threshold estimation is crucial in young children and other difficult to test population (Coles, 1977; Hall, 1992; Stapells & Vancouver, 2000) to facilitate early identification, precise fitting of hearing aids and rehabilitation (Hoke, Pantev, Ansa, Lutkenhoner & Herrmann, 1991). Inconsistent behavioral thresholds necessitates the use of objective methods to estimate frequency specific auditory thresholds. The advent of auditory brainstem responses (ABRs) raised the hopes of audiologists substantially to estimate auditory thresholds in patients who are not able to provide reliable behavioral thresholds. Click evoked ABRs are generally used in threshold estimation due to its fast acquisition compared to other techniques. However, click being a broadband stimulus do not represent accurate measures of hearing thresholds for any specific frequency, and may completely miss or underestimate hearing loss in particular frequency regions (Eggermont & Don, 1980; Stapells et al., 1994). Hence, frequency specific auditory thresholds are essential for accurate diagnosis and hearing aid fitting.

2.1 Methods to obtain Frequency Specific Auditory Brainstem Responses

There are three general methods to obtain frequency specific information from ABR (Stapells., 1994). They are masking method, derived band technique and the tonal method. The conventional tonal method which is used to obtain frequency specific ABR, stimulates the auditory system with brief tone bursts of short rise times (Suzuki & Horiuchi, 1977; Klein & Teas, 1978; Kodera, Yamada, Yamane & Suzuki, 1978). This approach is limited, however by its excessively long testing time of approximately 2 hours (Karzon & Lieu, 2006; Stueve & O'Rourke, 2003). Furthermore, at high intensities, tone bursts leads to significant spectral splatter degrading the frequency specificity. Consequently, masking techniques have been suggested to obtain frequency specific responses. The masker is meant to eliminate unwanted non-frequency-specific contributions to the ABR by selectively masking cochlear regions which are outside the region to be stimulated either by using notched-noise masking or high-pass masking noise (Terkildsen, 1975; Picton, 1979; Stapells & Picton, 1981; Pratt & Bleich, 1982; Jacobson, 1983; Stapells, 1990; Beattie & Kennedy, 1992; Beattie, 1992; Conijn, 1992; Abdala & Folsom, 1995; Oates & Stapells, 1997). Alternatively, the neural activity in specified cochlear regions can also be selectively suppressed by computing the off-line difference-waveform between the masked and unmasked responses by using derived response technique (Eggermont, 1976; Don & Eggermont, 1978; Eggermont & Don, 1980; Kramer, 1992; Nousak & Stapells, 1992; Donaldson & Ruth, 1993; Don, 1994, 1997; Oates & Stapells, 1997) or by using pure-tone masking methods (Folsom, 1984, 1985; Pantev, 1985; Klein, 1983; Klein & Mills, 1981; Mackersie, 1993; Wu & Stapells, 1994).

2.1.1 Auditory Brainstem Responses for Tone Bursts

Gorga, Kaminski and Jesteadt (1988) recorded ABR from 20 normal hearing individuals using tone-burst stimuli which was gated with cosine-squared functions. Responses were obtained for a wide range of frequencies and intensities. In the results, they found that the ABR thresholds were higher than behavioral puretone thresholds for all the frequencies and more so for lower frequencies such as 250Hz and 500Hz. Inter-subject variability was also greater for lower frequencies. Wave-V latencies decreased with increase in frequency and intensity. Better responses at higher frequencies were attributed to shorter rise times of the tone burst. The rapid rise times at higher frequencies result in greater discharge synchrony, which in turn results in greater amplitude of the response relative to the background noise. Additionally, the basal end of the cochlea has greater nerve fiber density per unit area when compared to apical turns which also is likely to have contributed, according to Spoendlin (1972). This increased density results in a greater number of neural fibers discharging synchronously for high frequency stimuli.

Dündar et al. (2014) compared thresholds of tone-burst ABR and puretone audiometry. Eighty patients with sensorineural hearing loss were part of their study. Tone-burst ABR thresholds were estimated at 500Hz, 2000Hz and 4000Hz, and the differences between tone-burst ABR thresholds and pure-tone thresholds were calculated. The mean differences was found to be 4.75dB, 6.25dB, and 4.87dB at 500Hz, 2000Hz and 4000Hz respectively.

Suzuki, Kodera and Kaga (1982) compared ABR and behavioral thresholds at 500Hz and 1000Hz, and reported that ABR thresholds were higher than behavioral thresholds. Hayes, Jerger and Jerger (1982) reported that there is an inherent difference in our ability to elicit an ABR for lower frequencies. The greater variability in the differences between ABR and behavioral thresholds for lower frequencies may be the limiting factor in using tone-burst ABRs to predict behavioral thresholds. However, utility of tone burst ABR to obtain frequency specific responses for all frequencies is limited by its excessively long test time of approximately 2 hours (Stueve & O'Rourke, 2003; Karzon & Lieu, 2006).

Orsini (2004) reported that ABRs obtained by tone bursts which have brief stimulus onset may cause excessive spectral splatter due to the response elicited by adjacent regions of the cochlea which in turn reduces the frequency specificity of the ABR. It was suggested that introducing notched noise along with the tone burst, limits the evoked response to those frequencies within the notch, thereby reducing the likelihood of spectral splatter and improving frequency specificity.

2.1.2 Masking Methods in ABRs to Elicit Frequency Specific Responses

Ipsilateral masking is used for eliciting frequency specific ABRs. Noise with specific frequency characteristics is presented to the test ear, along with the ABR eliciting stimulus to reduce or eliminate certain portions of the cochlea from contributing to the ABR. The frequency specific ABRs were acquired by using masking methods such as notched noise method, pure-tone masking profiles and high pass masking noise method.

Orsini (2004) recorded standard tone burst ABR and a notched noise tone burst ABR in 25 participants with normal hearing and 16 participants with bilateral sensorineural hearing loss. Notched noise masking used in conjunction with the tone burst ABR was meant to limit the ABR to those frequencies within the notch and reduce spectral splatter and in turn increases frequency specificity.

Beattie and Spence (1991) used notched noise method to estimate frequency specific responses. They reported that high noise levels are essential to mask clicks (95dB SPL of BBN is required to mask a 65 dB nHL click) which in turn would lead to tolerance issues. Also, high ABR thresholds were obtained in notched noise method. Based on their results they suggested tone bursts to be more promising stimuli for assessing the frequency specific ABRs than notch noise method.

Folsom (1984) presented simultaneous pure-tone maskers at half octave intervals of the stimulus center frequency. Masking profiles were obtained at two intensities (60 & 40dB SL). The measured wave V latency and amplitude shifts as a result of the discrete-frequency maskers showed masking profiles at 40dB SL to be narrow and centered around stimulus frequency. Whereas, masking profiles at 60dB SL showed high frequency spread of the cochlear excitation area.

The studies have also exemplified the possibilities to obtain frequency specific responses using filtered clicks along with puretone masking. Nevertheless, it is depended upon the intensity at which it is delivered and low intensity level condition revealed narrow masking profiles which are centered around the dominant stimulus frequency. Using low-frequency tonal stimuli has to be approached with a caution while attempting to assess hearing sensitivity in the apical region of cochlea and stimuli should be combined with high-pass masking noise to assure the frequency specificity at moderate intensity levels and above.

High pass masking noise method is also used to increase frequency specificity in ABRs (Don & Eggermont, 1978; Kileny, 1981; Laukli, 1983; Stapells et al., 1985). High pass noise masking method is reported to provide larger amplitudes than notched noise, thus leading to greater response identifiability. High pass noise also is advantageous because it requires less complex instrumentation than notch noise. However, tone bursts in high pass noise are not as frequency specific as tone bursts in notch noise because the stimulus includes all frequencies below the cutoff frequency. However, for frequencies below 1000Hz it can still serve to be a good tool to elicit frequency specific information.

Don and Eggermont (1978, 1980) gave a novel technique called derived band technique to obtain frequency specific ABRs. In this, ABR is recorded for clicks and then with high pass noise of different cut off frequencies. Subsequently an offline subtraction of 2 ABRs elicited with high pass noise of 2 adjacent cut off frequencies (for example, 500Hz and 1000Hz) will give derived band ABRs. The assumption of the technique is that these responses differ only in the contribution of the frequency region between the cut-off frequencies of the maskers. Therefore the subtracted response originates from a limited frequency region only. Although this assumption seems true, and the technique has been experimentally validated, it is again time consuming, needs computer storage, and because of the subtraction of two responses, signal to noise ratio of the responses decrease. Furthermore, contribution from the region below 500Hz for ABR elicited by clicks is probably minimal (Don & Eggermont, 1978; Don et al., 1979; Thiimmler et al., 1981; Laukli et al., 1988; Gorga et al., 1988) and therefore may not elicit identifiable responses in the 500Hz band.

2.2.3 Other Objective Techniques to Obtain Frequency Specific Auditory Thresholds

Auditory evoked potentials such as Auditory steady state response (ASSR) and Late latency response (LLR) also provide frequency specific information. However, these test procedures are not practiced in all clinical set up due to time constraints. Around 28 minutes are required to acquire threshold using MASTER ASSR (Schmulian, Swanpoel & Hugo, 2005) and approximately 4 hours for LLR (Bell, Smith, Allen & Lutman, 2004) has been estimated. The use of the N1-P2 cortical auditory evoked response in the estimation of hearing sensitivity is well established, with most studies suggesting that threshold estimation in adults is accurate within 10-20 dB.

Lightfoot and Kennedy (2006) showed that the mean agreement between audiometric and electrophysiological threshold was 6.5dB and 94% of threshold estimates were within 15 dB. Apeksha and Devi (2010) showed that aided LLRs can also be used to elicit frequency specific responses using speech stimulus such as /ba/ (spectral energy concentration in low frequency), /ga/ (syllable dominated by mid frequency spectral energy) and /da/ (syllable dominated by the high frequency spectral content) to estimate hearing threshold. Results showed that aided ALLR can help in the selection of hearing aids as it mimics the hearing aid processing. However, LLRs are susceptible to the state of arousal and drugs, as well as its longer test duration curtails its practical utility in case of infants and children.

Werff, Brown, Gienapp and Clay (2002) compared ASSR and ABR thresholds in children. They found strong correlation between click ABR thresholds and the ASSR thresholds. The study showed that ASSR can provide a reasonable alternative to the ABR for estimating frequency specific audiometric thresholds in very young children.

Cone-wesson, Dowel, Tomlin and Rance (2002) compared ASSR with those of click and tone burst evoked ABRs. They studied whether the ASSR threshold estimated in infants and children could be used to predict the puretone threshold. Results showed that the tone burst ABR thresholds and ASSR thresholds were similar when both were detected with an automatic detection algorithm and that threshold estimates varied with frequency, stimulus rate, and detection method. These findings supported the use of ASSRs to estimate puretone threshold in infants, children and adults with hearing loss and also with normal hearing sensitivity. However ASSRs in spite of being quick in estimating frequency specific hearing, are highly contaminated by stimulus related artifacts resulting in high false positives (Stapells, 2004) and therefore is not a preferred clinical tool. Hence, there is a need for an alternate, quick and efficient electrophysiological technique for frequency specific threshold estimation at multiple frequencies.

2.2 ABR for Multi Frequency Chain of Tone Bursts

Multi frequency ABR (MFABR) is a new technique, promising to be a valuable addition to the audiological test battery. There have been several interesting studies of tone bursts on estimating frequency specific hearing thresholds using multi frequency chain of tone bursts.

Mitchell, Kempton, Creedon and Trune (1996) obtained ABR in mice, for single tone burst and multiple stimulus sequence of tone bursts. The latency and amplitude functions were noted in both the conditions. The tone bursts of 4kHz to 32kHz were used as stimuli. The multiple stimulus sequence consisted of 20 tone-burst sequences of four different frequencies, at five different intensities, each separated by 12ms. Comparison of ABRs for single frequency tone bursts with that of 20 stimulus train showed that there are no significant differences in thresholds. Also, the response latencies or amplitudes showed no significant differences, indicating that the responses from multiple stimuli sequences were not adapted or affected in terms of latency and amplitude of responses. The findings suggested that the use of 20-stimulus train can result in a significant time reduction for acquisition of data compared to single tone burst stimuli. These findings demonstrated the practicality of the acquisition of ABR at different frequencies using a multiple sequence of tone-bursts at different frequencies and intensities. However, the study was carried out on mice and not on human population and also the stimulus frequencies in the current study are above 4kHz till 32kHz. Hence the results of the study cannot be generalized due to structural and functional differences between the two species. Further, the test frequencies are higher and the results are not applicable to lower audiometric frequencies.

Mitchell, Fausti and Frey (1994) had also used a similar stimulus for eliciting frequency specific ABRs. Stimuli were tone bursts at 21 frequencies, from 1000Hz to 32,000Hz approximately in 1/4-octave steps. These tone bursts had a duration of 2ms, with rise/fall time of 1ms and no plateau, and were produced by gating a continuous sine wave from a synthesizer with an electronic switch. Five experiments in guinea pigs using single and paired tone-burst stimuli were conducted. The intra-pair time and frequency were varied to determine when adaptation measured by a latency delay occurred. Results showed that the adaptation effects are minimal when the time separation is 10ms or greater in paired-stimulus. Adaptation was reported to be generally less if the frequency of the second stimulus was either above or below that of the first stimulus in paired stimulus. However, this study has been conducted on guinea pigs for a frequency range of 1kHz to 32kHz which again cannot be generalized for human population.

Fausti, Mitchell, Frey, Henry and O’Connor, (1994) recorded ABRs for high-frequency tone bursts in two different methods in a single session. Ten normal hearing subjects participated in the study. Step 1 involved presentation of four high-frequency tone burst stimuli (14kHz, 12kHz, 10kHz and 8kHz) individually to elicit ABRs. Step 2 involved presentation of multiple stimulus sequence with stimulus onsets separated by

10ms. Wave V latencies from the multiple stimulus sequences were compared to those presented individually. Results showed that there was a small but statistically significant longer latencies observed for all stimuli following the initial stimulus (14kHz) in the multiple sequence. Test-retest reliability was good between multiple and single conditions. These findings of the above study support the development of this technique for clinical auditory monitoring for threshold estimation with relatively lesser time duration. However, the above study has not been done for frequencies below 8kHz, which limits the applicablity of the results to estimate hearing thresholds in the audiometric frequencies.

Petoe, Bradley and Wilson (2009) analyzed the variance in latency of Wave V for ABRs evoked by conventional tone bursts and chained stimuli of tone-pulse series stimulation with simultaneous Gliding high pass noise Masker-‘GHINOMA’). Results showed that frequency-specific ABR can be obtained in less time compared to conventional tone burst stimuli, without compromising on the quality of response.

Overall, the literature suggests that the test-retest reliability of chained stimuli is good and the responses are similar to that with single frequency tone burst. Considering that ABR for chained stimulus is time efficient, its clinical utility if validated in audiometric frequencies seems promising.

Chapter 3

METHOD

The present study aimed to validate multi frequency auditory brainstem responses (MFABR) as a clinical tool for recording frequency specific auditory brainstem responses (ABRs). The null hypothesis stated was that there is no significant difference in the latency and amplitude of MFABR compared to single frequency tone burst ABR (SFABR). To test the hypothesis, the following method was adopted.

3.1 Participants

Two groups of participants were used in the study. Group 1 included 30 normal hearing adults while group 2 included 10 adults (11 ears) with cochlear hearing loss. Individuals of both the groups were in the age group of 20 to 50 years. They were native speakers of Kannada and geographically located in and around Mysore. All the participants had normal middle ear functioning with no other relevant neurological or otological dysfunction. They willingly participated in the study and gave written consent for the same.

Participants in the group 1 (NH group) had normal hearing sensitivity as assessed on puretone audiometry. The puretone hearing thresholds were within 15dB HL at octave frequencies between 250Hz and 8000Hz. On the other hand, participants in the group 2 had sensorineural hearing loss (SNHL) of primarily cochlear in origin. The degree of hearing loss was either of mild (PTA of 26-40 dB HL) or moderate (PTA of 41-55 dB HL) in the participants of the group and the configuration of the audiogram was either flat or gradually sloping. In group 2, there were 2 participants with mild hearing loss and 9 participants with moderate hearing loss.

3.2 Test Stimulus

Tone bursts (TBs) of 500Hz, 1000Hz, 2000Hz and 4000Hz were used to elicit frequency specific auditory brainstem responses. They were generated using Praat software (version 5.3.36) with 2-0-2 envelope and Hanning window. Accordingly the duration of the stimuli for 4000Hz, 2000Hz, 1000Hz and 500Hz TBs were 1ms, 2ms, 4ms and 8ms respectively.

The output SPL of each of the four TBs was recorded using an SLM (Bruel and Kjaer with Pressure-field 1" microphone type 4144) using standard settings. Tone bursts were routed through ER3A insert receivers connected to the Biologic Navigator Pro EP system and were played at 110dB SPL. The amplitudes of the generated TBs were then manipulated such that the peak SPL was 110dB SPL at each of the frequencies.

The individual TBs were then played to 20 normal hearing individuals to obtain the minimum dB SPL required to perceive them. The stimulus was routed through insert receivers and was presented at the rate of 9.1/s. The average of the threshold of 20 individuals for tone burst of each frequency was calculated. This value was used to derive ABR threshold in terms of nHL.

To generate a multi frequency chain of tone bursts (MFTB), the same four tone bursts were sequentially linked in the order of 4000Hz, 2000Hz, 1000Hz, and 500Hz with onset to onset interval being 20ms. Depending on the stimulus duration, the inter-stimulus interval was (offset of a tone burst to onset of subsequent tone burst) was 19ms (between 4000Hz & 2000Hz), 18ms (between 2000Hz & 1000Hz), 16ms (between 1000Hz & 500Hz) and 12ms (between 500Hz & 4000Hz). The total duration of the

MFTB was 68ms. Figure 3.1 shows waveform of the MFTB and Figure 3.2 shows the spectrum of the same.

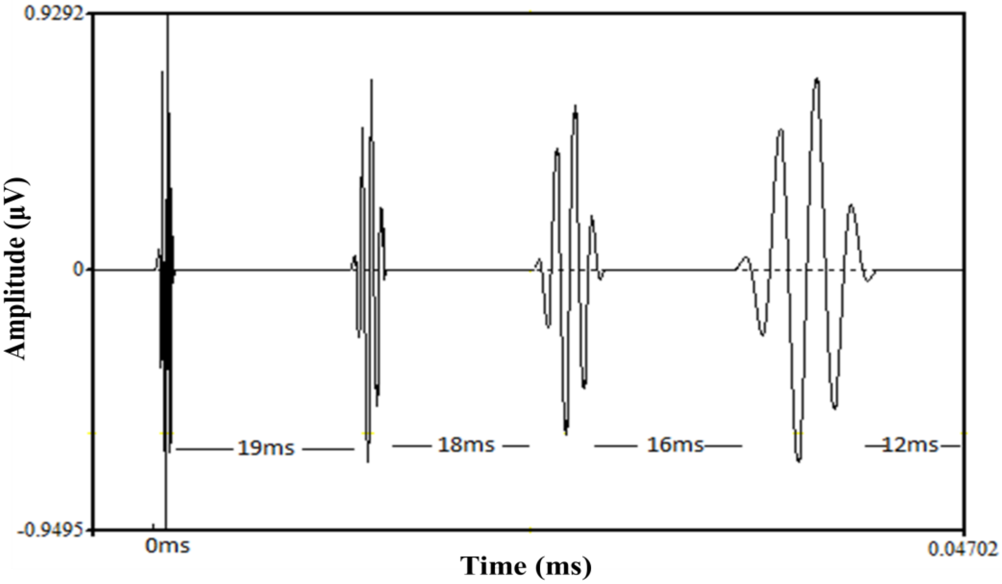

Figure 3.1: *Waveform of the Multi frequency chain of tone bursts*.

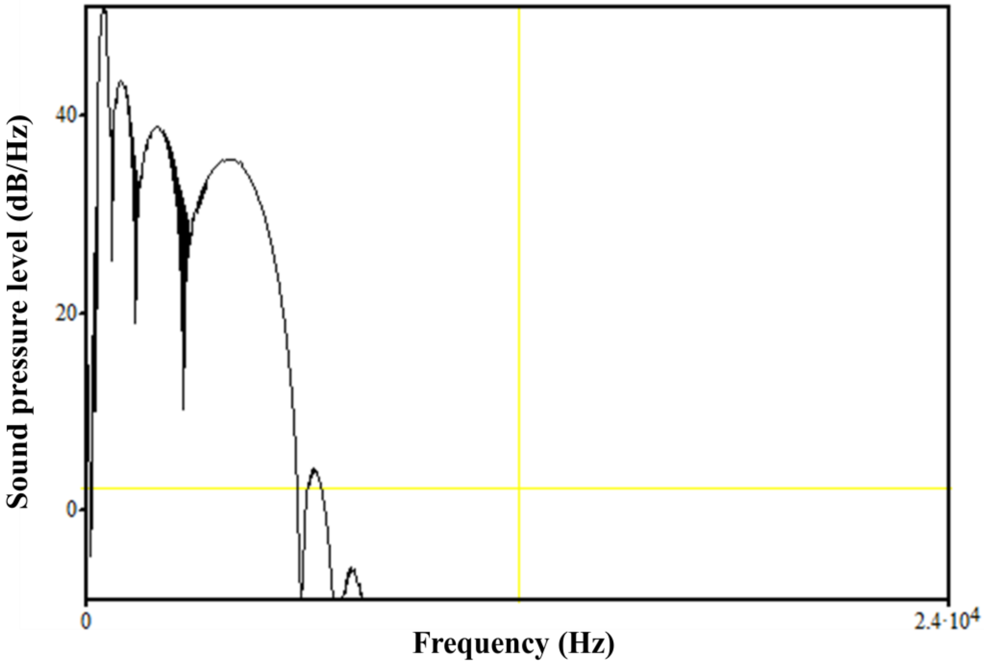

Figure 3.2: *Spectrum of the Multi frequency chain of tone burst.*

3.3 Instrumentation

Several technical equipments were used in the present study for various purposes such as generation of test stimulus, preliminary audiological evaluations and experimental evaluations.

A calibrated diagnostic audiometer was used for puretone audiometry with (GSI-61) with TDH-39 supra aural headphones and Radio ear-B71 bone vibrator. A GSI-Tympstar middle ear analyser was used to record tympanogram and acoustic reflex thresholds. A Biologic Navigator Pro AEP Acquisition system with impedance matched insert receiver was used for acquiring ABRs.

3.4 Test Environment

All the audiological tests were carried out in an air conditioned sound treated room where the noise levels were within permissible limits (ANSI S-3, 1991). The ABR recordings were carried out in a air conditioned and electrically shielded room (Electrophysiology Lab of dept of Audiology, AIISH) where the noise levels were below 40dB SPL at the testing area.

3.5 Test Procedure

The test procedure involved preliminary audiological evaluations to qualify the individuals as participants and the actual experimental procedures.

3.5.1 Preliminary Audiological Evaluations

Pure tone thresholds were estimated in both the ears using modified Hughson and Westlake procedure (Carhart & Jerger, 1959). Hearing thresholds were estimated at octave frequencies between 250Hz and 8000Hz for air conduction and from 250Hz to

4000Hz for bone conduction stimulation. Thresholds were tracked using bracketing method.

Immittance evaluation involved recording tympanograms and acoustic reflexes. A 226 Hz probe tone at approximately 85dBSPL was used to obtain the tympanograms by varying the air pressure in the ear canal from +200 to -400 daPa. Ipsilateral and contralateral acoustic reflex thresholds were measured for 500 Hz, 1000 Hz, 2000 Hz, and 4000 Hz using the same probe tone frequency. The static admittance and peak pressure were recorded to rule out middle ear pathologies in both the groups. Participants with type 'A' or 'As' tympanogram with reflexes present were selected for the study.

Click evoked ABR was recorded to check the integrity of neural pathway at the level of brainstem prior to MFABR. Specifically, it was meant to rule out retro cochlear pathologies. Only if the results of click ABR were normal, the individual was considered to record MFABR. The conventional settings and parameters were used for recording click ABRs.

3.5.2 Recording Frequency Specific ABR using Tone bursts

The participants were seated on reclining chair and were instructed to relax and minimize extraneous movements. The surface electrode sites were cleaned before placing electrodes and inter electrode impedance was maintained below 2kOhms. Three silver chloride disc electrodes were placed in vertical montage with Cz being positive, M2 being negative and M1 being the ground electrode sites, and the EEG was recorded. Two types of stimuli were used to elicit frequency specific ABR; the conventional single frequency tone burst and the MFTB. Table 3.1 gives the stimulus and acquisition parameters used to record the frequency specific ABR for TBs.

Table 3.1: *Stimulus and Acquisition parameters used to record the MFABR*

Stimulus Parameters	
Stimulus	➢ Single frequency tone burst ➢ Multi frequency chain of tone bursts
Polarity	Rarefaction
Transducer	Insert ear phone
Repetition rate	9.1/sec
Intensity	➢ 110dB SPL in SFABR & MFABR ➢ Lower intensities up to ABR threshold in MFABR
Type of stimulation	Monaural
Acquisition Parameters	
Montage	Vertical
Electrode sites	➢ Cz (+ve) ➢ M2 (-ve) ➢ M1 (Gnd)
Filters setting	100Hz - 1500Hz
Amplification	1,00,000 times
Artifact rejection	20μV
Analysis time	85ms
Total no. averages	2000
Data points	1024
Test ear	Right

Two sets of ABRs were obtained for each participant. First set consisted of ABRs for single frequency TBs recorded at only 110dB SPL. The frequency of TBs were 500Hz, 1000Hz, 2000Hz and 4000Hz. The second set consisted of ABRs for MFTB at 110dB SPL and the lower intensities till threshold. The stimulus intensity in MFTB was reduced in 20dB steps till 50dB SPL and threshold was tracked in 10 dB steps below 50dB SPL. The threshold in MFABR was defined as the lowest intensity at which ABR was present at any one frequency. All the recordings were replicated and only replicable responses were considered for further analysis.

3.6 Response Analysis

The averaged ABRs were visually analyzed to mark the presence of Jewett waves, I, III and V. The responses were analyzed by 4 audiologists experienced in the area of electrophysiology. They judged a response to be present or absent, based on replicability, negative slopes and latency characteristics. Peak latency and Peak-to-peak amplitude (i.e., the amplitude change between peak and trough) of the waves present were noted down from each individual wave. Threshold of ABR was judged based on the lowest intensity at which an ABR (wave V) was visually detected in the waveform. The ABR threshold (in dB SPL) was tracked at each frequency in the MFABR. The thresholds which are obtained in dB SPL was then converted into dB nHL by adding the respective correction factor (mentioned in 3.2).

3.7 Data Analysis

Data were entered on a spreadsheet and correct entry was confirmed prior to analysis. The data was imported into IBM SPSS statistics (version 21) for analysis. The group data was analyzed to derive mean and standard deviation of the response parameters. The data of the NH group and SNHL group were treated separately. Initially the data were tested for its distribution using Shapiro-Wilk test of normality. Accordingly, either paired t test or Wilcoxon singed rank test was used. Spearman’s rank test was used to test the relation between thresholds of MFABR and pure-tone thresholds at each frequency.

Chapter 4

RESULTS

The present study aimed to test whether multi-frequency ABR (MFABR) is a valid method to test the frequency specific hearing sensitivity. The frequency specific ABRs were elicited using two different types of stimuli; conventional single frequency tone bursts (SFTB) and the multi frequency chain of tone bursts (MFTB). Results obtained in the present study are reported under the following headings.

1. Results of the test of normality
2. Comparison of ABR for SFTB (SFABR) and MFTB (MFABR) at 110dB SPL
3. Agreement between MFABR threshold and puretone hearing threshold
4. Prevalence of wave I, III and V at different intensities at the four test frequencies in MFABR

4.1 Results of Test of Normality

The group data was initially tested for its distribution using Shapiro-wilk test of normality. This was done separately for the data of normal hearing group and the hearing loss group. There were a total of 48 parameters tested for normality in each group which included latency and amplitude of I, III and V elicited by the 2 stimulus types (SFTB & MFTB) at 4 different frequencies (500Hz, 1kHz, 2kHz, & 4kHz). Table 4.1 gives the results of Shapiro-Wilk test of normality for each response parameter and accordingly the statistical test chosen for within-group comparisons in normal hearing group. Similarly, Table 4.2 gives the results of Shapiro-Wilk test of normality for each response parameter and accordingly the statistical test chosen for within-group comparisons in sensorineural hearing loss group (SNHL). In general, if the data was normally distributed, a parametric test was used and if the data was not normally distributed, non-parametric test was used.

Table 4.1: *Results of Shapiro-Wilk test of normality for each response parameter and statistical test chosen for within-group comparisons in normal hearing group*

Frequency			Latency (ms) (N = 30)		Amplitude (μV) (N= 30)	
	Normal hearing		Statistic (df = 18)	Test chosen for within group comparisons	Statistic (df = 17)	Test chosen for within group comparisons
4000Hz	I	SF	0.938*	Paired t-test	0.937*	Paired t-test
		MF	0.934*	Paired t-test	0.903*	Paired t-test
	III	SF	0.931*	Paired t-test	0.956*	Paired t-test
		MF	0.924*	Paired t-test	0.929*	Paired t-test
	V	SF	0.937*	Paired t-test	0.926*	Paired t-test
		MF	0.937*	Paired t-test	0.947*	Paired t-test
2000Hz	I	SF	0.966*	Paired t-test	0.956*	Paired t-test
		MF	0.952*	Paired t-test	0.895*	Paired t-test
	III	SF	0.940*	Paired t-test	0.977*	Paired t-test
		MF	0.963*	Paired t-test	0.941*	Paired t-test
	V	SF	0.966*	Paired t-test	0.901*	Paired t-test
		MF	0.959*	Paired t-test	0.962*	Paired t-test
1000Hz	I	SF	0.889	Wilcoxon signed rank	0.978*	Paired t-test
		MF	0.937*	Paired t-test	0.884	Wilcoxon signed rank
	III	SF	0.939*	Paired t-test	0.967*	Paired t-test
		MF	0.911*	Paired t-test	0.953*	Paired t-test
	V	SF	0.883	Wilcoxon signed rank	0.923*	Paired t-test
		MF	0.883	Wilcoxon signed rank	0.956*	Paired t-test
500Hz	I	SF	0.921*	Paired t-test	0.881	Wilcoxon signed rank
		MF	0.910*	Paired t-test	0.759	Wilcoxon signed rank
	III	SF	0.914*	Paired t-test	0.932*	Paired t-test
		MF	0.914*	Paired t-test	0.853	Wilcoxon signed rank
	V	SF	0.889	Wilcoxon signed rank	0.966*	Paired t-test
		MF	0.901*	Paired t-test	0.932*	Paired t-test

Note: *p >0.05

Table 4.2: *Results of Shapiro-Wilk test of normality for each response parameter and the statistical test chosen for within group comparisons in sensorineural hearing loss group*

Frequency	SNHL		Latency (ms) (N = 11) Statistic (df = 7)	Latency (ms) (N = 11) Test chosen for within group comparisons	Amplitude (µV) (N= 11) Statistic (df = 7)	Amplitude (µV) (N= 11) Test chosen for within group comparisons
4000Hz	I	SF	0.852*	Paired t-test	0.636	Paired t-test
		MF	0.777	Wilcoxon signed rank	0.828*	Paired t-test
	III	SF	0.844*	Paired t-test	0.853*	Paired t-test
		MF	0.875*	Paired t-test	0.729	Wilcoxon signed rank
	V	SF	0.927*	Paired t-test	0.878*	Paired t-test
		MF	0.881*	Paired t-test	0.878*	Paired t-test
2000Hz	I	SF	0.843*	Paired t-test	0.649	Wilcoxon signed rank
		MF	0.979*	Paired t-test	0.840*	Paired t-test
	III	SF	0.803	Wilcoxon signed rank	0.902*	Paired t-test
		MF	0.743	Wilcoxon signed rank	0.596	Wilcoxon signed rank
	V	SF	0.916*	Paired t-test	0.900*	Paired t-test
		MF	0.919*	Paired t-test	0.962*	Paired t-test
1000Hz	I	SF	0.896*	Paired t-test	0.797	Wilcoxon signed rank
		MF	0.895*	Paired t-test	0.953*	Paired t-test
	III	SF	0.827*	Paired t-test	0.962*	Paired t-test
		MF	0.821*	Paired t-test	0.894*	Paired t-test
	V	SF	0.928*	Paired t-test	0.971*	Paired t-test
		MF	0.965*	Paired t-test	0.949*	Paired t-test
500Hz	I	SF	0.887*	Paired t-test	0.939*	Paired t-test
		MF	0.770	Wilcoxon signed rank	0.984*	Paired t-test
	III	SF	0.967*	Paired t-test	0.853*	Paired t-test
		MF	0.860*	Paired t-test	0.729	Wilcoxon signed rank
	V	SF	0.980*	Paired t-test	0.887*	Paired t-test
		MF	0.980*	Paired t-test	0.764	Wilcoxon signed rank

Note: *p >0.05

4.2 Comparison of ABR for SFTB (SFABR) and ABR for MFTB (MFABR) at 110dB SPL

The ABR was elicited by two types of stimuli at 110dB SPL and the corresponding responses were compared in terms of its latency and amplitude. This was done for latency and amplitude of wave I, III and V at the four test frequencies (500Hz, 1000Hz, 2000Hz & 4000Hz), separately for the data of normal hearing group and SNHL group. The results obtained are reported separately for latency and amplitude.

Figure 4.1 shows a set of SFABRs (at 500Hz, 1000Hz, 2000Hz & 4000Hz) and the corresponding MFABRs recorded at 110dB SPL in a representative participant.

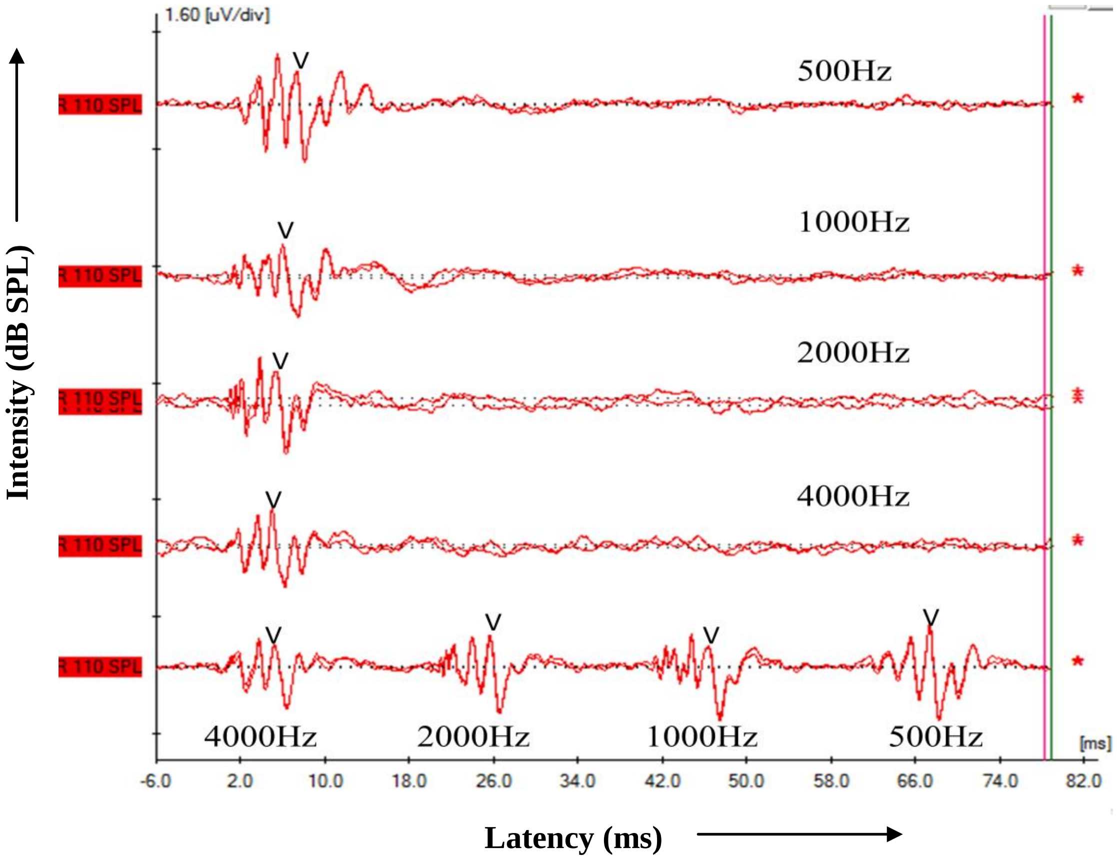

Figure 4.1 A set of SFABRs (at 500Hz, 1000Hz, 2000Hz & 4000Hz) and the corresponding MFABRs recorded at 110dB SPL in a representative participant.

4.2.1 Results of Peak Latency

Table 4.3 gives the mean and standard deviation of peak latency of wave I, III and V at four different frequencies (4000Hz, 2000Hz, 1000Hz & 500Hz) elicited using two different stimulus types (SFTB & MFTB).

On comparing across frequencies in *normal hearing group*, it was observed that the mean latencies get prolonged as the frequency of the tone burst decreases. This was true for both SFTB and MFTB. When SFTB were used, the mean shift in latency was 0.37ms, 0.63ms, and 0.70ms when test frequency shifted from 4000Hz to 2000Hz, 2000Hz to 1000Hz, and 1000Hz to 500Hz respectively. On the other hand when MFTB was used, the mean shift in latency was 0.43ms, 0.64ms, and 0.66ms when test frequency shifted from 4000Hz to 2000Hz, 2000Hz to 1000Hz, and 1000Hz to 500Hz respectively.

On comparing the two types of stimuli in normal hearing group, the mean latencies were prolonged when elicited by MFTB compared to that elicited by SFTB at all frequencies except at 500Hz (wave I & III). At 500Hz, mean latency of wave I and III were prolonged when elicited with SFTB compared to that of MFTB.

On comparing across frequencies in *SNHL group*, it was observed that in SFTB, the average shift in latency was 0.23ms, 0.54ms, and 0.89ms when test frequency shifted from 4000Hz to 2000Hz, 2000Hz to 1000Hz, and 1000Hz to 500Hz respectively. On the other hand when MFTB was used, the mean shift in latency was 0.33ms, 0.51ms, and 0.85ms when test frequency shifted from 4000Hz to 2000Hz, 2000Hz to 1000Hz, and 1000Hz to 500Hz respectively.

Table 4.3: *Mean and standard deviation (SD) of peak latency of wave I, III and V recorded by single frequency tone burst (SFTB) and multi frequency chain of tone bursts (MFTB) in normal hearing and SNHL groups*

Group	Stimulus frequency	Stimulus Type	I		III		V	
			Mean (ms)	SD	Mean (ms)	SD	Mean (ms)	SD
Normal Hearing	4kHz	SF	1.82	0.11	3.79	0.13	5.54	0.25
		MF	1.82	0.11	3.82	0.14	5.56	0.24
	2kHz	SF	2.22	0.19	4.23	0.21	5.91	0.32
		MF	2.22	0.19	4.25	0.20	5.99	0.35
	1kHz	SF	2.84	0.38	4.68	0.16	6.54	0.28
		MF	2.86	0.38	4.78	0.24	6.63	0.30
	500Hz	SF	3.24	0.35	5.22	0.33	7.24	0.27
		MF	3.12	0.31	5.16	0.37	7.29	0.28
SNHL	4kHz	SF	2.05	0.26	4.12	0.24	5.93	0.13
		MF	2.07	0.24	4.06	0.18	5.96	0.15
	2kHz	SF	2.51	0.30	4.40	0.18	6.16	0.17
		MF	2.43	0.19	4.47	0.16	6.29	0.17
	1kHz	SF	3.38	0.43	5.21	0.53	6.70	0.31
		MF	3.40	0.40	5.23	0.56	6.80	0.30
	500Hz	SF	4.03	0.29	5.77	0.52	7.59	0.38
		MF	3.97	0.27	5.93	0.36	7.65	0.40

On comparing the two types of stimuli in SNHL group, the mean latencies were prolonged when elicited by MFTB compared to that elicited by SFTB at all frequencies except at wave III of 4000Hz, wave I of 2000Hz and 500Hz. In these exceptions, the mean latencies were prolonged when elicited with SFTB compared to that of MFTB.

Paired t-test was carried out to test whether the observed mean differences in latency between SFTB and MFTB were statistically significant. This was tested at each test frequency. Results of paired t-test in the *normal hearing group* (Table 4.4) showed that there is no significant difference (p>0.05) between the ABRs elicited by the two types of stimuli in wave I of 4000Hz, wave I and III of 2000Hz and wave III of 500Hz. However wave III and V of 4000Hz, wave V of 2000Hz, wave III of 1000Hz and wave I of 500Hz elicited by MFTB were significantly different from SFTB. On close inspection of the mean differences in instances where there was a statistically significant difference, it was found that the mean difference ranged from 0.02ms (Wave V at 4kHz) to 0.12ms (wave I at 500Hz).

Table 4.4: *Results of Paired t-test comparing latencies of wave I, III and V between SFABR and MFABR at four different stimulus frequencies in normal hearing group*

Frequency	Wave	't'	p	df
4000Hz	I	-0.694	0.493	30
	III	-3.519	0.001*	30
	V	-2.905	0.007*	30
2000Hz	I	-0.133	0.896	27
	III	-1.299	0.205	28
	V	-3.257	0.003*	30
1000Hz	III	-4.730	0.000*	27
500Hz	I	2.107	0.048*	20
	III	0.784	0.442	21

Wilcoxon Signed Rank test showed that there was no significant difference (p>0.05) seen between SFTB and MFTB in wave I of 1000Hz (Table 4.5). Whereas there was a significant difference between the two stimulus types for wave V of 1000Hz and 500Hz. Again the inspection of the mean differences in these two instances were 0.09ms and 0.05ms at 1000Hz and 500Hz respectively.

Table 4.5: *Results of Wilcoxon signed rank test comparing latencies of wave I and V between SFABR and MFABR in normal hearing group*

Frequency	Wave	/Z/	p
1000Hz	I	0.115	0.908
	V	3.173	0.002*
500Hz	V	3.623	0.000*

In *SNHL group*, paired t-test was carried out to test whether the observed mean differences in latency between SFABR and MFABR were statistically significant. Results of paired t-test (Table 4.6) showed that there is no significant difference (p>0.05) between the ABRs elicited by the two types of stimuli in wave I, III and V of 4000Hz and 1000Hz, wave I and V of 2000Hz, wave I and III of 500Hz . However, wave V of 500Hz elicited by MFTB was significantly different from SFTB and the mean difference in this condition was 0.06ms.

Wilcoxon Signed Rank test (Table 4.7) showed that there was no significant difference (p>0.05) between SFABR and MFABR in the peak latency of any of the waves at the four test frequencies except for wave III of 2000Hz. In wave III of 2000Hz, the mean difference in latency was 0.07ms.

Table 4.6: *Results of Paired t-test comparing latencies of wave III and V between SFABR and MFABR at four different stimulus frequencies in SNHL group*

Frequency	Wave	't'	p	df
4000Hz	III	1.000	0.351	7
	V	-1.764	0.108	10
2000Hz	V	-2.013	0.072	10
1000Hz	III	-2.000	0.081	8
	V	-1.990	0.075	10
500Hz	V	-3.646	0.004*	10

Table 4.7: *Results of Wilcoxon signed rank test comparing latencies of wave I and III between SFABR and MFABR at four different stimulus frequencies in SNHL group*

Frequency	Wave	/Z/	p
4000Hz	I	1.000	0.317
2000Hz	I	0.368	0.713
	III	2.456	0.014*
1000Hz	I	1.633	0.102
500Hz	I	0.378	0.705
	III	1.512	0.131

4.2.2 Results of Response Amplitude

The peak to peak amplitude of wave I, III and V elicited by the two types of stimuli (SFTB & MFTB) were analysed for mean and standard deviation at each of the frequencies, in the two groups of participants (Normal group & SNHL). The results are given in Table 4.8.

On comparing SFTB and MFTB, there were mean differences in the amplitudes observed. The differences in amplitude ranged between 0.01µV(wave V of 1000Hz) and highest value of 0.18µV(wave V of 500Hz) in normal hearing individuals. The mean amplitudes were higher in SFABR compared to MFABR in normal hearing individuals.

The mean amplitude increased as the frequency increased at wave I of MFABR. However, the similar trend was not seen in other peaks of either SFABR or MFABR .

Table 4.8: *Mean and standard deviation (SD) of amplitude of wave I, III and V recorded by single frequency tone burst (SFTB) and multi frequency of tone burst chain (MFTB) in normal hearing and SNHL groups*

Group	Stimulus frequency	Stimulus	I		III		V	
			Mean (µV)	SD	Mean (µV)	SD	Mean (µV)	SD
Normal Hearing	4kHz	SF	0.39	0.14	0.41	0.16	0.47	0.22
		MF	0.32	0.09	0.35	0.12	0.44	0.11
	2kHz	SF	0.34	0.11	0.39	0.16	0.61	0.24
		MF	0.31	0.10	0.37	0.14	0.58	0.18
	1kHz	SF	0.32	0.09	0.39	0.13	0.69	0.26
		MF	0.29	0.15	0.32	0.15	0.68	0.21
	500Hz	SF	0.36	0.22	0.51	0.27	0.77	0.59
		MF	0.28	0.19	0.41	0.26	0.59	0.27
SNHL	4kHz	SF	0.28	0.31	0.23	0.11	0.35	0.18
		MF	0.19	0.05	0.33	0.30	0.32	0.11
	2kHz	SF	0.18	0.17	0.25	0.14	0.42	0.14
		MF	0.32	0.27	0.27	0.22	0.42	0.10
	1kHz	SF	0.44	0.37	0.26	0.23	0.50	0.16
		MF	0.19	0.09	0.20	0.06	0.46	0.19
	500Hz	SF	0.39	0.07	0.30	0.22	0.51	0.17
		MF	0.63	0.25	0.35	0.29	0.55	0.21

Paired t-test was carried out to test whether the observed mean differences in amplitude between SFTB and MFTB were statistically significant. This was tested at each test frequency. Results of paired t-test (Table 4.9) showed that there is no significant difference (p>0.05) between the ABRs elicited by the two types of stimuli in wave V of 4000Hz, wave III and V of 2000Hz, wave V of 1000Hz. However, wave I and III of 4000Hz, wave I of 2000Hz, wave III of 1000Hz and wave V of 500Hz elicited by MFTB were significantly different from SFTB in terms of mean amplitude. In these instances where there was statistical significance, the difference in the mean amplitude ranged from 0.03µV (wave I of 2000Hz) to 0.18µV (wave V of 500Hz).

Wilcoxon Signed Rank test showed that there was a significant difference (p>0.05) seen between SFTB and MFTB at wave I of 1000Hz, wave I and III of 500Hz (Table 4.10). The differences in mean amplitude ranged from 0.03µV (wave I of 1000Hz) and 0.08µV (wave I of 500Hz).

Table 4.9: *Results of Paired t-test comparing amplitudes of wave I, III and V between SFABR and MFABR at four different stimulus frequencies in normal hearing group*

Frequency	Wave	't'	p	df
4000Hz	I	2.748	0.010*	30
	III	2.960	0.006*	30
	V	0.566	0.576	30
2000Hz	I	2.128	0.043*	25
	III	0.527	0.603	27
	V	1.279	0.211	30
1000Hz	III	2.616	0.015*	25
	V	0.408	0.686	30
500Hz	V	3.383	0.002*	30

Table 4.10: *Results of Wilcoxon signed rank test comparing amplitudes of wave I and III between SFABR and MFABR at 500Hz and 1000Hz in normal hearing group*

Frequency	Wave	/Z/	p
1000Hz	I	2.127	0.033*
500Hz	I	2.516	0.012*
	III	2.174	0.030*

Table 4.11: *Results of Paired t-test comparing amplitudes of wave III and V between SFABR and MFABR at 1000Hz, 2000Hz and 4000Hz in SNHL group*

Frequency	Wave	't'	p	df
4000Hz	V	0.514	0.618	10
2000Hz	V	0.054	0.958	10
1000Hz	III	0.760	0.469	8
	V	0.752	0.469	10

Table 4.12 : *Results of Wilcoxon signed rank test comparing amplitudes of wave I, III and V between SFABR and MFABR at four different stimulus frequencies in SNHL group*

Frequency	Wave	/Z/	p
4000Hz	I	0.315	0.752
	III	0.140	0.889
2000Hz	I	0.943	0.345
	III	0.297	0.766
1000Hz	I	1.577	0.115
500Hz	I	1.826	0.068
	III	0.031	0.753
	V	0.356	0.722

In *SNHL group*, the lowest mean differences was 0µV (wave V of 2000Hz) while highest mean difference was 0.25µV (wave I of 1000Hz). The mean amplitude decreased as the frequency increased in wave III and V elicited by SFTB.

Results of paired t-test (Table 4.11) showed that there is no significant difference (p>0.05) between the ABRs elicited by the two types of stimuli in wave V of 4000Hz, wave V of 2000Hz and wave III and V of 1000Hz. However, the trend was not followed in wave I of SFABR. Furthermore, particularly there was no trend in which mean amplitude varied between SFABR and MFABR.

Wilcoxon Signed Rank test showed that there was no significant difference (p>0.05) seen between SFTB and MFTB at wave I, III and V of 4000Hz, wave I and III of 2000Hz, wave I of 1000Hz, wave I and V of 500Hz (Table 4.12). Overall the amplitude of the ABRs elicited by two stimulus types were not significantly different in SNHL group.

4.3 Agreement between MFABR Threshold and Puretone Hearing Threshold

Figure 4.2 shows a set of waveforms of a representative participant where in threshold has been tracked using MFABR. Threshold in MFABR was defined as the lowest intensity (dB SPL) at which ABR was present at least at one frequency.

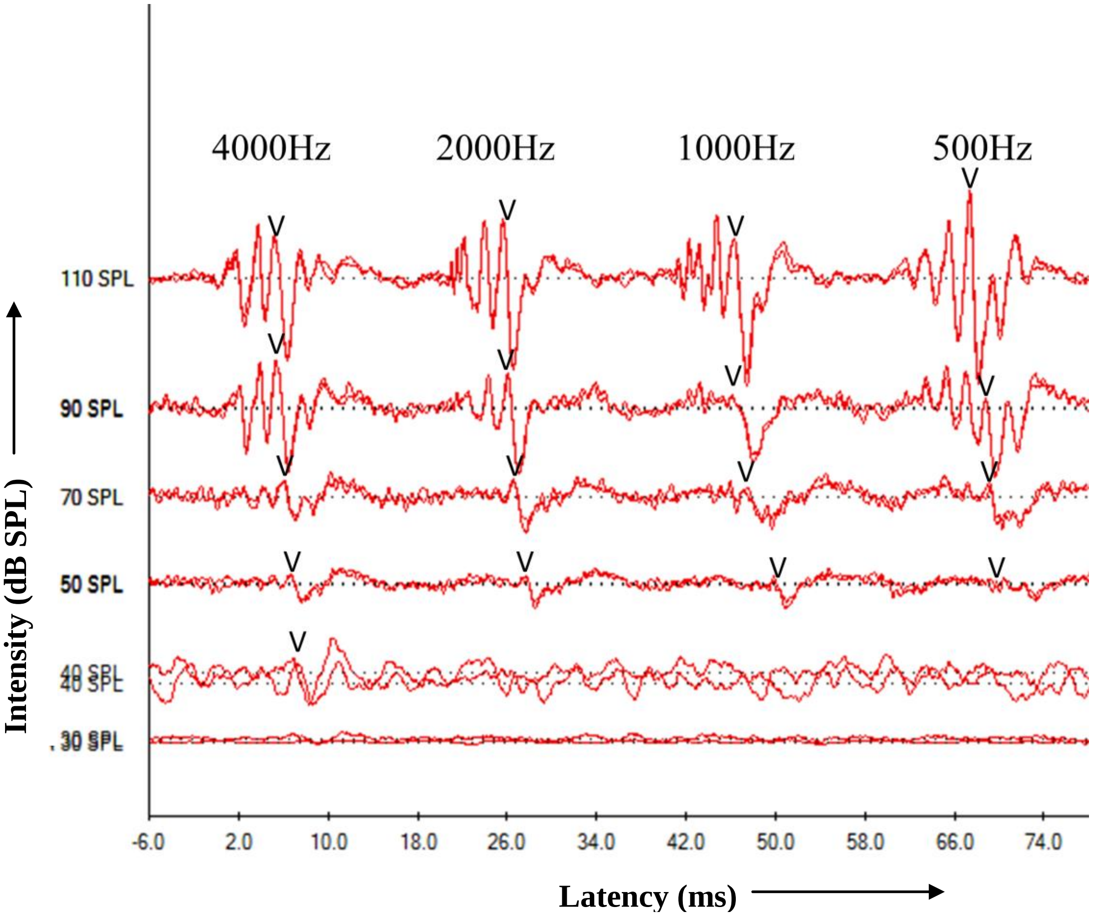

Figure 4.2 A set of waveforms of a representative participant where in threshold has been tracked using MFABR.

The thresholds of MFABR was compared with puretone hearing thresholds to derive the agreement between the two. Prior to this, ABR thresholds estimated in SPL were converted into nHL by subtracting the correction values. These correction values were 29.62dB, 30.62dB, 32.62dB and 43.12dB for 4000Hz, 2000Hz, 1000Hz and 500Hz respectively. The correction values were derived by taking the average hearing thresholds of 20 normal hearing individuals for tone burst of 500Hz, 1000Hz, 2000Hz and 4000Hz. The mean ABR threshold in nHL obtained using MFTB was estimated for each frequency in both the groups. Mean and standard deviation of MFABR thresholds (in nHL) and puretone thresholds (in HL) at the four test frequencies are given in Table 4.11.

As shown in the Table 4.13, mean threshold in MFABR were higher than the mean puretone thresholds at all the test frequencies in both the groups (normal hearing & SNHL group). On comparing across the four frequencies, mean MFABR threshold was highest at 500Hz and successively decreased with increase in frequency in normal hearing group. On contrary in SNHL group, the mean MFABR threshold was highest at 4000Hz and successively decreased with decrease in frequency.

Table 4.13: *Mean and standard deviation (SD) of MFABR threshold and puretone hearing thresholds at the four test frequencies in normal hearing and SNHL group*

Stimulus frequency	Method of Threshold estimation	Normal hearing		SNHL	
		Mean	SD	Mean	SD
4kHz	MFABR (dB nHL)	11.00	3.05	52.73	10.09
	PTA (dB HL)	8.17	2.45	51.36	10.97
2kHz	MFABR (dB nHL)	13.67	4.90	48.18	9.81
	PTA (dB HL)	9.17	2.30	45.00	10.95
1kHz	MFABR (dB nHL)	16.33	4.90	46.36	10.26
	PTA (dB HL)	9.00	2.42	43.18	11.67
500Hz	MFABR (dB nHL)	17.00	5.96	40.00	12.64
	PTA (dB HL)	9.83	2.45	36.82	12.70

Note: MFABR = Multifrequency auditory brainstem response,
PTA = Puretone audiometry

Figure 4.3 shows the scatter plots showing the relation between puretone hearing thresholds and MFABR thresholds at four test frequencies (4000Hz, 2000Hz, 1000Hz and 500Hz). Scatter plots were plotted by combining the data of normal hearing and SNHL group (total N=41). As shown in the Figure 4.3, there is a positive relation between MFABR threshold and puretone thresholds at all the frequencies. That is, as the puretone hearing threshold increases, MFABR threshold increases and this is true at all the frequencies. Furthermore it can also be noticed that there is lot of overlapping data in the scatter plots. For example, in the scatter plot of 4kHz, one can track only 8 individual data although it has data of 41 participants.

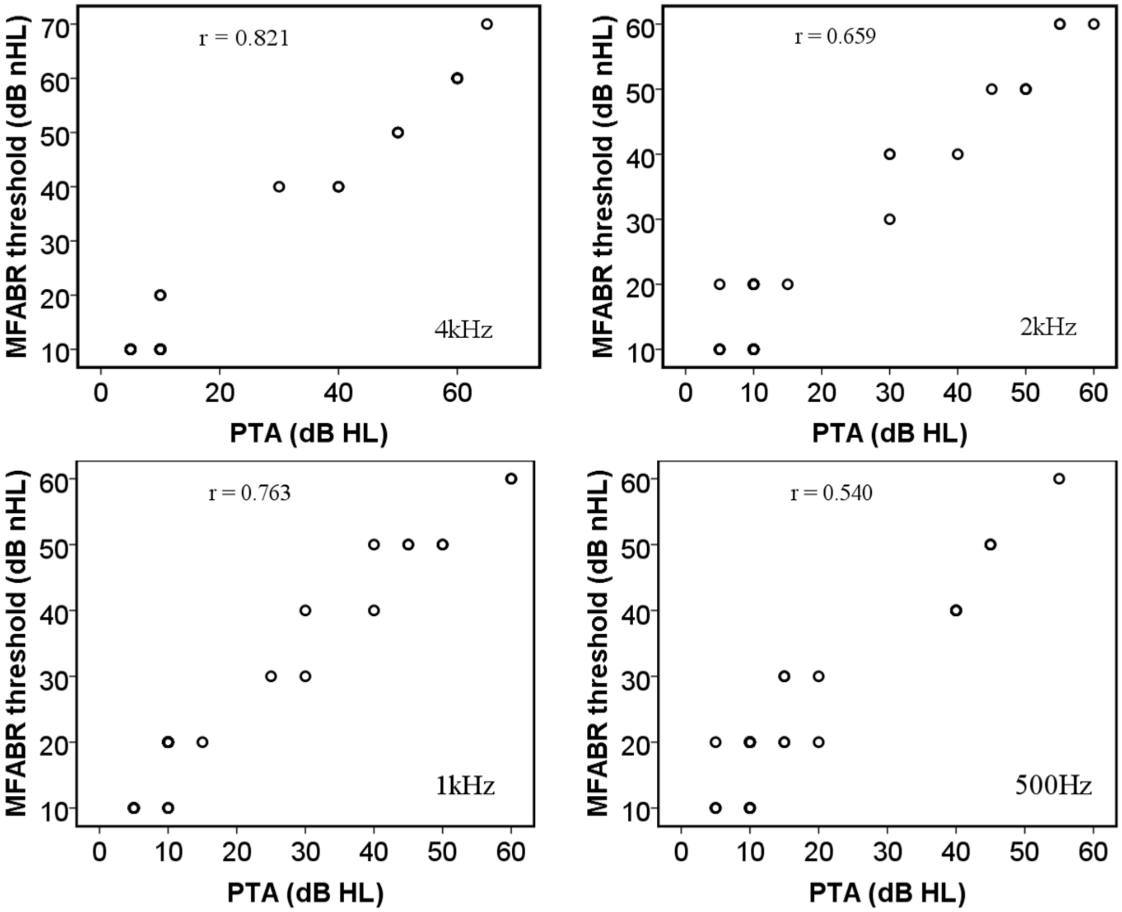

Figure 4.3: *Scatter plots showing the relation between puretone audiometry (PTA) thresholds and multi frequency tone burst auditory brainstem response (MFABR) threshold at four test frequencies (4000Hz, 2000Hz, 1000Hz and 500Hz) N = 41.*

To test whether the observed relationships between the two thresholds is statistically significant, Spearman's rank test was used. The correlation was tested separately at four stimulus frequencies; 4000Hz, 2000Hz, 1000Hz and 500Hz. The data of the two groups was combined for assessing the correlation between the two thresholds.

Results of Spearman's test showed that the correlation coefficients were 0.821, 0.659, 0.763 and 0.540 for 4000Hz, 2000Hz, 1000Hz and 500Hz respectively and all the correlations were significant at 0.01 level (Figure 4.3).

The agreement between the two thresholds was also quantified by taking the difference between puretone thresholds and MFABR thresholds for each individual, at each frequency. The mean and confidence intervals of this difference thresholds in the two groups (Normal hearing & SNHL) is given in Table 4.14.

The mean difference between thresholds of MFABR and PTA are lesser at high frequencies compared to low frequencies in normal hearing group. On comparing the agreement between the two groups it was derived that the SNHL group showed lower difference values compared to normal hearing group at all the frequency. Interestingly, the agreement was same at 2000Hz, 1000Hz and 500Hz in SNHL group.

Table 4.14: *Mean and Confidence Intervals (CI-lower bound & upper bound) of difference in the thresholds of puretone audiometry and MFABR at different stimulus frequencies in normal hearing and SNHL group*

Group	Confidence Interval	4kHz	2kHz	1kHz	500Hz
Normal Hearing	Mean (dB)	2.83	5.33	9	9.83
	Lower Bound	1.46	1.71	4.64	1.37
	Upper Bound	5.81	10.11	12.64	7.72
SNHL	Mean (dB)	1.36	3.18	3.18	3.18
	Lower Bound	0.81	0.46	0.46	0.92
	Upper Bound	3.54	5.90	5.90	5.45

Figure 4.4 shows the mean puretone thresholds and the mean MFABR thresholds plotted against the four test frequencies (500Hz, 1000Hz, 2000Hz & 4000Hz) in an audiogram, in normal hearing (A) and SNHL groups (B).

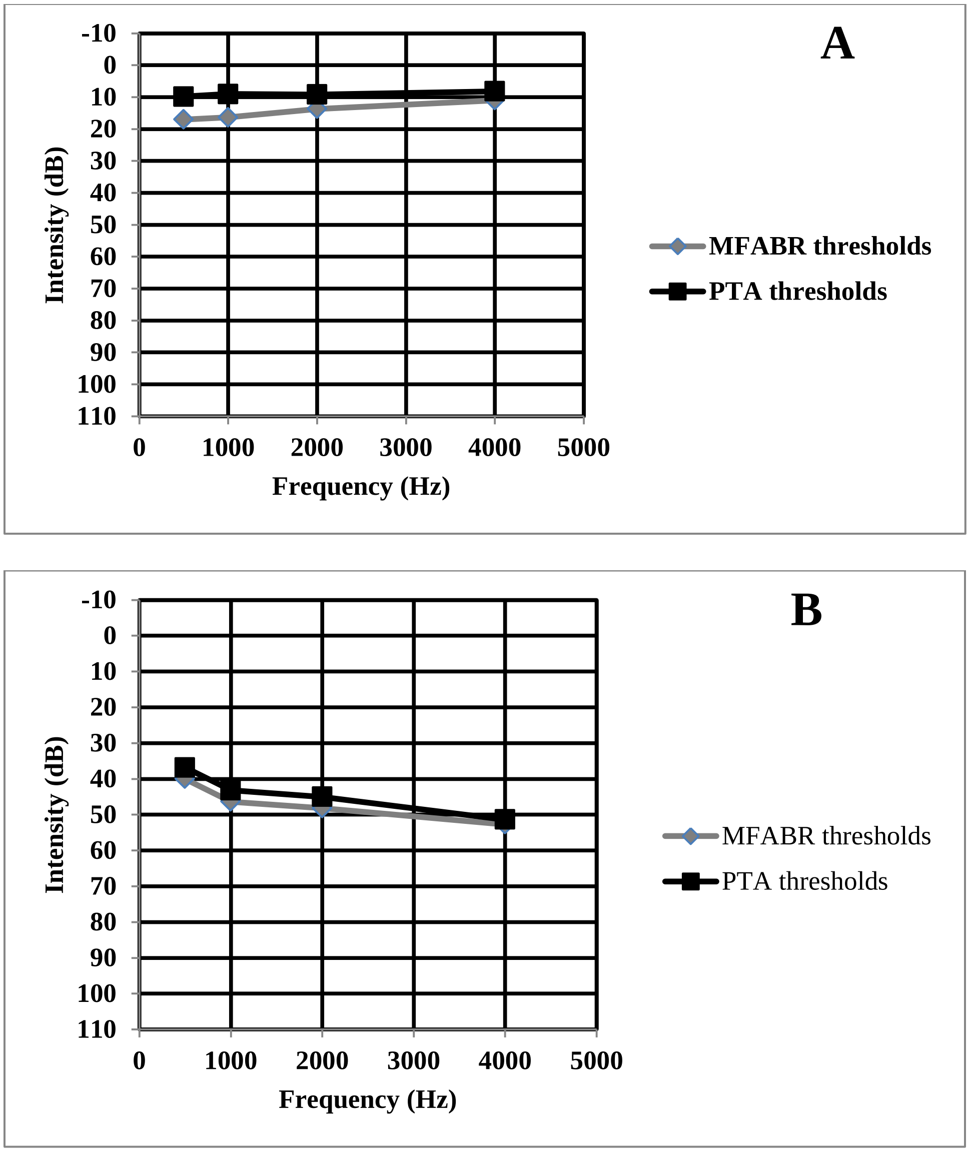

Figure 4.4: *Mean puretone thresholds and mean MFABR thresholds plotted against the four test frequencies in normal hearing(A) and SNHL group(B).*

4.4 Prevalence of Wave I, III and V at Different Intensities at the Four Test Frequencies in MFABR

Prevalence was operationally defined as the number of participants who had responses present out of the total number of participants and it is expressed in percentages. The presence of ABR was judged based on replicability, negative slopes and latency characteristics. Figure 4.5 shows the prevalence of wave I, III and V at different intensities in the 4 test frequencies (500Hz, 1000Hz, 2000Hz & 4000Hz) in MFABR. While estimating threshold using MFABRs, each wave disappeared at different intensities for different frequencies. Of the four frequencies used, ABR of 500Hz disappeared first, followed by 1kHz, 2kHz and 4kHz.

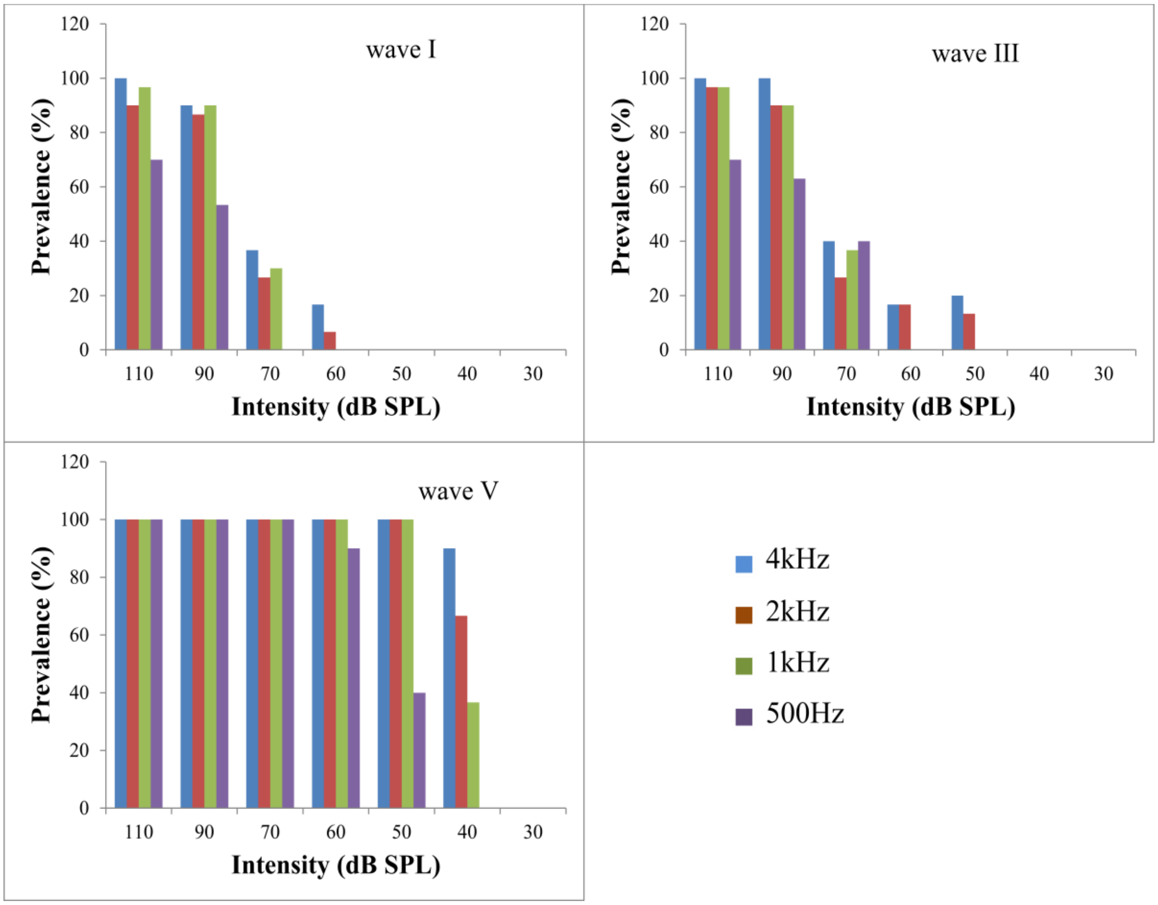

Figure 4.5: *Prevalence of wave I, III and V at different intensities and at the four test frequencies in MFABR.*

Figure 4.5 shows that wave I disappeared (by 60dB SPL), followed by wave III (by 50dB SPL) and wave V disappeared last (by 40dB SPL). Wave V was present till 40dB SPL at 4000Hz, 2000Hz and 1000Hz. However, wave V of 500Hz disappeared by 50dB SPL.

Chapter 5

DISCUSSION

The present study was taken up to validate auditory brainstem responses for multi frequency chain of tone bursts (MFABR) as a clinical tool for recording frequency specific ABRs with relatively lesser time compared to conventional single frequency ABRs (SFABRs). The study also focused on the relation between the MFABR thresholds and the pure tone thresholds. The findings of the present study are discussed under the following headings.

1. Comparison between SFABR and MFABR
2. Agreement between MFABR thresholds and the puretone thresholds
3. Utility of the SFABR as a Clinical tool

5.1 Comparison between SFABR and MFABR

The present study compared the latencies and amplitudes obtained from both SFABR and MFABR at 110dB SPL to ensure that MFABR can be used to reliably elicit frequency specific ABRs. This was done in order to assess if the waveforms elicited using the new technique stand up to the gold standard objective method such as frequency specific ABRs, however with lesser testing duration.

5.1.1 Latency of SFABR and MFABR at 110dB SPL

Results of the present study showed that the mean latencies were prolonged as the frequency of the tone burst increases in both single frequency tone burst (SFTB) and multi frequency chain of tone burst (MFTB). This is in congruence with the previous studies on frequency specific ABRs using Tone bursts (Gorga, Kaminski & Jesteadt, 1988; Fausti, Mitchell, Frey, Henry & O’Connor, 1994). The increase in latency with decreasing tone burst frequency represents the time taken for the travelling wave to travel from 4000Hz to 500Hz Gorga et al., (2006). ABRs to tone bursts of different frequencies represent synchronous activity from successive regions across the cochlea. Hence the cochlear travelling wave velocity determines the latency of the tone burst evoked responses. Dau, Wegner, Mellert and Kollmeier, (2000) reported that the apical region is connected by nerve fibers responsible for low frequencies and the basal region is connected by nerve fibers responsible for high frequencies. The traveling wave reaches basal region first and then reaches apical region which would directly correspond to the latencies which were prolonged as the frequency of the tone burst decreases from 4000Hz to 500Hz.

In the current study the average shift in latency was 0.37ms, 0.63ms, and 0.70ms in SFABRs and, 0.43ms, 0.64ms, and 0.66ms in MFABRs, when test frequency shifted from 4000Hz to 2000Hz, 2000Hz to 1000Hz, and 1000Hz to 500Hz respectively.

Sehta (2011) established normative of tone burst ABR for site of lesion testing. The average shift in latency from 4000Hz to 2000Hz, 2000Hz to 1000Hz and 1000Hz to 500Hz were 0.30ms, 0.47ms and 0.34ms in normal hearing group. The average latency shift from 4000Hz to 2000Hz in both normal hearing and SNHL group is in congruence with the above study. However, the difference in average latency shift from 2000Hz to 1000Hz and 1000Hz to 500Hz were different from the present study. The dissimilarity could be due to the differences in the stimulus parameters and acquisition parameters employed in the two studies.

The increase in latency with decreasing frequency is a cardinal property of a frequency specific neural response. The increase in latency observed in the MFABR with decreasing frequency, provides convincing empirical evidence that the responses obtained from MFABR is frequency specific identical to the SFABR. Thus, this served as the proof for MFABR extracting frequency specific ABRs in normal hearing individuals. The shift in latency with increasing frequency was also seen in the SNHL group using both the methods. The average shift in latency in SFABR was 0.23ms, 0.54ms, and 0.89ms. Whereas, the average shift in MFABR was 0.33ms, 0.51ms, and 0.85ms when test frequency shifted from 4000Hz to 2000Hz, 2000Hz to 1000Hz, and 1000Hz to 500Hz respectively.

The primary aim of the present study was to compare between SFABR and MFABR. The peak latencies were marked and the obtained latencies from SFABR and MFABR were compared. Results showed that the latencies in MFABR were prolonged when compared to SFABR except for wave I of 500Hz. The mean latency differences between two stimulus types were more at 500Hz and 1000Hz. The mean latency difference ranged from 0ms to 0.13ms. Though there were statistically significant differences in the latency, it can be inferred from the mean latency differences that the difference in latency will not be clinically significant. this is particularly true when ABR is recorded with the purpose of estimating thresholds.

Similarly, in SNHL group the ABRs were prolonged when elicited by MFTB compared to that of SFTB in wave V of 500Hz and wave III of 2000Hz. The mean prolongation in latency was 0.07 ms for the wave V of 500Hz and wave III of 2000Hz. Though the difference was statistically significant, this difference is often miniscule to be considered of any clinical significance when ABR is used for threshold estimation. This very small difference obtained could also be attributed to a possible margin of the subjective judgment involved in marking the waves.

Support for the differences between ABRs elicited with SFTB and MFTB can be drawn from Fausti, Mitchell, Frey, Henry and O’Connor (1994). They acquired ABRs using single stimulus and multiple stimulus sequence and the test frequencies ranged from 8kHz to 14kHz. The mean latency difference between single stimulus and multiple stimulus sequence was higher at 8kHz and there was no latency difference in mean at 14kHz. In congruence with the present study, the latencies of multiple stimulus sequence was longer than the single stimulus. However, the findings of the study showed that there was no statistically significant difference between ABRs elicited by single stimulus and multiple stimulus at 10kHz, 12kHz and 14kHz. At 8kHz, there was a significant difference between the latencies obtained from single stimulus and multiple stimulus sequence. Intersession variability was also checked in the above study and the results revealed that the highest mean difference between two separate sessions were 0.05ms in single stimulus and 0.09ms in multi stimulus sequence.

5.1.2 Amplitude of SFABR and MFABR at 110dB SPL

In the present study, mean amplitudes were higher in ABRs obtained from SFTB compared to MFTB in normal hearing group. The differences ranged from 0.5 to 0.44µV. These differences might be due to the possible spread of excitation in the SFTB condition which might have lead to greater amplitude of adjacent neural firings. However, the differences in amplitude between two stimulus types (SFTB & MFTB) in SNHL group did not show statistically significant difference. This implies that neural synchrony is not compromised by using MFABR. Other studies comparing the amplitude differences between SFTB and MFTB are not available to the best of knowledge. The findings suggest that the possible confounding factors such as spread of excitation, refractory period etc. are not different between the ABRs elicited by two stimulus types (SFTB & MFTB). This further lends support to the use of MFTB for eliciting frequency specific ABRs as viable alternative to SFTB as it does not affect the amplitude of the waveforms obtained.

The results elicited from clinical population such as SNHL aided in providing stronger evidence that the MFABR can give reliable frequency specific information in a compromised auditory system as well. Thus, this exercise served to ***validate*** the MFABR as a viable clinical tool for recording frequency specific ABRs.

5.2 Agreement between MFABR Thresholds and the Puretone Thresholds

Comparison between thresholds obtained from MFABR and PTA were done to ensure that MFABR is equally capable of providing accurate thresholds as PTA. An objective measure is especially important to estimate frequency specific hearing thresholds in whom reliable behavioral thresholds cannot be elicited (for eg. infants, individuals with intellectual disability, cerebral palsy, functional hearing loss etc.).

ABRs were elicited in MFABR and thresholds were tracked at test frequencies of 4000Hz, 2000Hz, 1000Hz and 500Hz , and behavioral hearing thresholds were also obtained using puretone audiometry at the given test frequencies.

SFABR thresholds at low frequencies were elevated than those at high frequencies. This trend is seen in all previous studies (Suzuki & Horiuchi, 1977; Klein & Teas, 1978; Kodera, Yamada, Yamane & Suzuki, 1978; Folsom, 1984) estimating hearing threshold with tone burst ABR. The rise/fall time for the low frequencies are larger than those at the high frequencies. Sharp rise/fall times lead to better neural synchrony and in turn greater amplitude and better detectable responses (Gorga et al., 1988). The low frequency tone-bursts by virtue of their longer rise/fall time may lead to relatively lesser neural synchrony and less detectable responses especially at low intensities. This might have led to lower thresholds at high frequencies compared to the low frequencies.

Comparison between thresholds obtained using MFABR and PTA showed that, thresholds obtained by MFABR were relatively higher than those obtained using puretone audiometry in both individuals with normal hearing and SNHL (Suzuki & Horiuchi, 1977; Dündar et al., 2014). Gorga, Kaminski and Jesteadt (1988) acquired ABRs for 20 normal hearing subjects using tone-burst stimuli. ABRs were obtained for frequencies from 250Hz to 8000Hz at intensities from 20 to 100dB SPL. Similar to the findings of the current study, they found that thresholds were higher in tone burst ABR compared to puretone audiometry at all frequencies. They attributed these differences to the rise/fall time, duration of the tone and cochlear organization, all of which might adversely affect the signal-to-noise ratio for ABR measurements.

The highest mean difference of threshold between MFABR and PTA for obtaining threshold was 9.83dB at 500Hz and least mean difference obtained was 2.83dB at 4000Hz in normal hearing individuals (Figure 4.4). In the SNHL group however, the highest mean difference was 3.18dB at 500Hz and least mean differences was 1.36dB (Figure 4.4). That is, the mean difference between MFABR threshold and PTA threshold were higher at low frequencies compared to high frequencies. This finding is common across most studies on tone burst ABR (Dündar et al., 2014; Gorga et al., 2006). Gorga, Kaminski and Jesteadt (1988) found that ABR thresholds were higher than pure tone thresholds at all frequencies and the differences between the two estimates were higher for lower frequencies. This difference across frequencies can again be attributed to the differences in rise/fall time and eventual difference in neural synchrony across frequencies.

In the present study, results of correlation between thresholds of MFABR (in nHL) and pure-tone threshold (in HL) at stimulus frequencies 4000Hz, 2000Hz, 1000Hz and 500Hz was also analyzed. Results showed that MFABR thresholds positively correlated with puretone thresholds. The correlation was better at high frequency compared to low frequencies.

Akin to the results in our study, Dündar et al. (2014) found strong correlation between tone burst ABR thresholds and puretone thresholds i.e., 0.945, 0.962, 0.985at 500 Hz, 2000 Hz and 4000 Hz respectively in individuals with SNHL. This suggests that the MFABR thresholds varied as the pure thresholds varied. This provides a good evidence that the MFABR thresholds can aid in scaling the frequency specific hearing levels.

The agreement between the thresholds obtained through MFABR and PTA were analyzed between the two groups. The difference between the mean thresholds obtained from MFABR and PTA threshold are 7.17dB, 7.33dB, 4.50dB and 2.83dB for 500Hz, 1000Hz, 2000Hz and 4000Hz respectively in normal hearing group. Whereas in the SNHL group, it was 3.18dB, 3.18dB, 3.18dB and 1.33dB. This suggests that there was a better agreement between the pure tone thresholds and the MFABR thresholds in SNHL compared to the normal hearing individuals. The findings are in concordance with Durgut et al. (2014). They studied eighty patients with advanced and very advanced SNHL. Comparison of pure-tone air conduction thresholds of advanced, and very advanced SNHL patients with tone-burst ABR thresholds were made at 500, 2000 and 4000 Hz. They found the differences between tone-burst ABR thresholds and pure-tone thresholds in normal hearing group to be 13dB, 7dB, 8dB for 500, 2000, and 4000 Hz respectively, while the corresponding differences in patients with SNHL were 4.75dB, 6.25dB, and 4.87dB respectively. The better agreement between tone burst ABR thresholds and pure tone thresholds in SNHL group has been often attributed to the steeper loudness growth and larger spread of excitation in SNHL (Dündar et al., 2014).

An additional evidence for the similarity in the conventional tone burst ABR and the MFABR can be drawn from the results of prevalence of waves at different intensities across frequencies. It can be seen in Figure 4.5 that the earlier waves disappeared first followed by the later ones. The prevalence of waves was higher for the wave V across all intensities. This further strengthens the evidence that the MFABR is a tool for hearing threshold estimation that follows similar trend as the conventional tone burst ABR.

5.3 Utility of the MFABR as a Clinical Tool

The most common use of objective measures of hearing levels are in infant hearing assessment and hearing aid fitting. Conventional click evoked ABRs do not provide frequency specific hearing information, which impedes empirically guided hearing aid amplification fittings. The recommended hearing aid fitting process for individuals with hearing impairment is by using real ear insertion gain measurements. The pre-requisite for which is frequency specific hearing thresholds. This is not a problem with most children and adults who can cooperate for behavioral threshold estimation. However in very young children and non-cooperative adults, obtaining reliable behavioral thresholds is difficult. Thus an objective measure of frequency specific hearing threshold is paramount for diagnosis and successful rehabilitation. However, obtaining objective threshold using the conventional tone burst ABR is time consuming, and clinicians often tend to compromise frequency specificity by just using a click ABR supplemented by a 500 Hz tone-burst ABR. This is done usually to cut down the time taken for diagnosis.

The MFABR method was proposed to provide a potential time-efficient objective tool for hearing threshold estimation. The time taken to complete the MFABR is 1/4th of that of conventional tone burst ABR. With such drastic reduction in testing time, clinicians can efficiently estimate hearing thresholds in their patients and also provide evidence based hearing aid fitting solutions. The results of the current study successfully validate the use of MFABR as a viable tool for hearing threshold estimation and is comparable with conventional tone burst ABR in results.

An added advantage of the new technique was that the response identification was easier. This was because of the readily comparable ABR waveforms of different frequencies. The responses at the different frequencies served as good reference points to mark the peaks in the other frequencies.

An important methodological feature which could have been a possible confounding variable is the time resolution. The time resolution in the MFABR and SFABR were kept constant by using the same long analysis time window for both recordings (85ms). Thus the results obtained in the study are not affected by differences in the analysis epochs.

Despite all the advantages listed above, one specific disadvantage was that, because of the chained nature of the stimulus, it could not be calibrated in dB nHL, and therefore were calibrated in dB SPL. This however does not downplay the use of MFABR, because an appropriate correction can always be applied and valid hearing thresholds can be estimated easily.

Chapter 6

SUMMARY AND CONCLUSIONS

In an audiological clinic, estimating reliable behavioral thresholds in infants and non-cooperative (malingering) adults is always a challenge. In such instances, audiologists invariably depend on objective techniques to estimate the hearing threshold and auditory brainstem responses (ABRs) happen to be the universal choice. Although frequency specific hearing thresholds can be obtained using ABRs elicited by tone bursts and some of the masking based techniques, most often it is avoided due to prolonged testing time. As a substitute, click ABRs are utilized and the frequency specific information is compromised. In other words, considering the practical issue with testing time, audiologists deviate from the best practices of clinical audiology. Therefore, the aim of the present study was to propose and validate a novel technique called ABR for multi frequency chain of tone bursts (MFABR), which is likely to take 1/4th of the time taken by conventional tone burst ABR, for testing at 4 octave frequencies.

Single frequency tone burst ABR (SFABR) and MFABR were recorded in 30 normal hearing adults and 11 adults with SNHL. The participants were in the age range of 20 to 50 years. SFABRs were recorded for tone bursts of 4000Hz, 2000Hz, 1000Hz and 500Hz at 110dBSPL, while MFABR was recorded using same tone bursts aligned as a single chain with appropriate inter-stimulus intervals. ABRs for the two types of stimuli were recorded with exactly the same recording parameters within a single session. Additionally, thresholds were tracked in MFABR and compared with that of puretone hearing thresholds.

The resultant ABRs were analyzed to identify wave I, III and V. The peak latency and peak to peak amplitude of each of the waves present was noted down. Additionally in MFABR, thresholds were tracked and the ABR threshold (in dB SPL) at each of the test frequencies were noted down.

The data were subjected to statistical analysis using IBM SPSS version 21. To begin with, Shapiro-Wilk test of normality was carried out and based on its results, either paired t-test or Wilcoxon signed rank test was used for within group comparisons. Spearman's rank correlation was used to analyze the relation between MFABR thresholds and puretone thresholds.

The results showed that the amplitudes did not differ significantly between MFABR and SFABR. However, the latencies of MFABR were prolonged compared to SFABR which was in congruence with the earlier studies in literature. A close inspection of the mean differences in latency revealed that, the differences were meagre enough to be considered as clinically significant, particularly while recording ABR for threshold estimation.

MFABR thresholds could be tracked up to 40dB SPL at 4000Hz. However, as frequency decreased thresholds elevated. The correlation of MFABR thresholds and puretone thresholds showed a significant positive relationship at all the 4 test frequencies. That is, as the hearing thresholds got elevated ABR thresholds were also elevated. The correlation was stronger at higher frequencies compared to lower frequencies.

The agreement between the MFABR thresholds and the behavioral thresholds was further tested by taking the difference between the two. Results showed that there was better agreement at higher frequencies compared to lower frequencies. Additionally, it was also observed that the agreement was better in SNHL group compared to the normal hearing group.

The findings of the present study are in strong agreement with the reports in literature. Overall, MFABR gave similar results as that of SFABR but within 1/4th of the testing time required for SFABR. The MFABR was found to be valid in terms of all the response parameters analyzed in the present study and is in close agreement with the behavioral thresholds (within 10 dB) both in normal hearing and SNHL individuals. Therefore, based on the present study it is strongly recommended to use MFABR as a routine audiological test to estimate frequency specific hearing thresholds objectively.

REFERENCES

American Speech Language-Hearing Association (1987). Short latency auditory evoked potentials. Retrieved from www.asha.org/policy on 16.08.2015.

Cone-wesson, B., Dowel, R. C., Tomlin, D., & Rance, G. (2002). The Auditory Steady-State Response : Comparisons with the Auditory Brainstem Response. *Journal of the American Academy of Audiology, 13*(4), 173-187.

Burkard, R., Shi, Y., & Hecox, K. E. (1990). A comparison of maximum length and Legendre sequences for the derivation of brain-stem auditory-evoked responses at rapid rates of stimulation. *Journal of the Acoustical Society of America*, *87*, 1656-1664.

Burkard, R., Shi, Y., & Hecox, K. E. (1990). Brain-stem auditory-evoked responses elicited by maximum length sequences: effect of simultaneous masking noise. *Journal of the Acoustical Society of America*, *87*(4), 1665-1671.

Campbell, K., & Abbas, P.J. (1987). The effect of stimulus repetition rate on the auditory brainstem response in tumor and nontumor patients. *Journal of Speech, Language and Hearing Research*, *30*(4), 494.

Coles, R. R. A. (1977). Objective audiometry: A general and historical review. *The Journal of Laryngology and Otology*, *91*(8), 639–654.

Dau, T., Wegner, O., Mellert, V., & Kollmeier, B. (2000). Auditory brainstem responses with optimized chirp signals compensating basilar-membrane dispersion.*Journal of the Acoustical Society of America*, *107*(3), 1530–1540.

Davis, H., Hirsh, S. K., Turpin, L. L., & Peacock, M. E. (1985). Threshold sensitivity and frequency specificity in auditory brainstem response audiometry. *Audiology, 24*(1), 54–70.

Don, M., Allen, A.R., & Start, A. (1977). Effect of click rate of the latency of auditory brain stem responses in humans. *Annals of Otology, Rhinology and Laryngology, 86*(2), 186-195.

Dündar, R., Kulduk, E., Soy, F. K., Kilavuz, A. E., Sakarya, E. U., Yazici, H., & Eren, A. (2014). Comparison of hearing thresholds of patients with advanced , and very advanced sensorineural type hearing loss using tone-evoked ABR. *Journal of Medical Updates*, *4*(2), 52–55.

Emanuel, D. C. (2002). The auditory processing battery: survey of common practices. *Journal of the American Academy of Audiology*, *13*(2), 93–117.

Fausti, S. A., Mitchell, C. R., Frey, R. H., Henry, J. A, & O’Connor, J. L. (1994). Multiple-stimulus method for rapid collection of auditory brainstem responses using high-frequency (> or = 8 kHz) tone bursts. *Journal of the American Academy of Audiology*, *5*(2), 119–126.

Folsom, R. C. (1984). Frequency specificity of human auditory brainstem responses as revealed by pure-tone masking profiles. *Journal of the Acoustical Society of America*, *75*(3), 919–24.

Fowler, C. G., & Noffsinger, D. (1983). Effects of stimulus repetition rate and frequency on the auditory brainstem response in normal, cochlear-impaired, and VIII nerve/brainstem impaired participants. *Journal of Speech, Language and Hearing Research, 26*(4), 560.

Gorga, M. P., Kaminski, J. A. N. R., & Jesteadt, W. (1988) Auditory brainstem responses to tone bursts in normally hearing subjects. *Journal of Speech and Hearing Research, 31*(1), 87–97.

Gorga, M. P., Johnson, T. A., Kaminski, J. K., Beachaine, K. L., Garner, C. A. et al. (2006). Using combination of click and tone burst evoked auditory evoked potentials to estimate of pure tone thresholds. *Ear and Hearing, 27*(1), 60-74.

Hayes, D. & Jerger, J. (1982). Auditory brainstem responses (ABR) to tone pips: Results in normal and hearing-impaired subjects. *Scandinavian Audiology, 11,* 133-144.

Kileny, P. (1981). The frequency specificity of tone-pip evoked auditory brainstem responses. *Ear and Hearing, 2,* 270-275.

Laukli, E. (1983). High-pass and notch noise masking in suprathreshold brainstem response audiometry. *Scandinavian Audiology, 12,* 109-115.

Laukli, E. (1986). Low frequency hearing loss: Auditory brainstem responses using derived band technique. *Audiology, 25*(3), 184-190.

Lightfoot, G. & Kennedy, V. (2006). Cortical electrical response audiometry hearing threshold estimation: accuracy, speed, and the effects of stimulus presentation features. *Ear and Hearing, 27*(5), 443-456.

Mitchell, C., Kempton, J. B., Creedon, T., & Trune, D. (1996). Rapid acquisition of auditory brainstem responses with multiple frequency and intensity tone-bursts. *Hearing research, 99*(1), 38-46.

Mitchell, C. R., Fausti, S. a, & Frey, R. H. (1994). Paired tone-burst study of auditory brainstem response adaptation in guinea pigs: implications for development of multiple-stimulus methods. *Journal of the American Academy of Audiology, 5*(2), 110-118.

Mitchell, C. R., Kempton, J. B., Creedon, T. A., & Trune, D. R. (1999). The use of a 56-stimulus train for the rapid acquisition of auditory brainstem responses. *Audiology and Neurotology*, *4*(2), 119-126.

Orsini, R. M. (2004). A comparison of tone burst auditory brainstem response (ABR) latencies elicited with and without notched noise masking. *Doctoral dissertation submitted to the university of South Florida,Tampa.*

Petoe, M., Bradley, A., & Wilson, W. J. (2009). On The Benefits of Using Chained Stimuli for Frequency Specific ABR Acquisition. *Australian and New Zealand Journal of Audiology, 31*(2), 80-95.

Sehta, A. (2011). Normative of tone burst ABR for site of lesion testing, *Independent project*, *Submitted to University of Mysuru*, *Mysuru.*

Smith, R. L., & Brachman, M. L. (1982). Adaptation in auditory-nerve fibers: A revised model. *Biological Cybernetics, 44*(2), 107-120.

Spoendlin, H. (1972). Innervation densities of the cochlea. *Acta Otolaryngologica, 73,* 235-248.

Stapells, D. R., & Picton, T. W. (1981). Technical aspects of brain-stem evoked-potential audiometry using tones. *Ear and Hearing, 2*(1), 20-29.

Stapells, D. R., & Vancouver, B. C. (2000). Threshold estimation by the tone-evoked ABR: A literature meta-analysis. *Journal of Speech-Language Pathology and Audiology*, *24*(2), 74-83.

Stueve, M. P., & O’Rourke, C. A. (2003). Estimation of hearing loss in children: comparison of auditory steady-state response, auditory brainstem response, and behavioral test methods. *American Journal of Audiology, 12*(2), 121-125.

Suzuki, T., & Horiuchi, K. (1977). Effect of high-pass filter on auditory brain stem responses to tone pips. *Scandinavian Audiology, 6*(3), 123-126

Teas, D. C., Eldredge, D. H., & Davis, H. (1982). Cochlear responses to acoustic transients: An interpretation of whole nerve action potentials. *Journal of the Acoustical Society of America, 34,* 1438-1459.

Terkildsen, K., Osterhammel, P., & Huis in't Veld, F. (1975). Far field electrocochleography. Frequency specificity of the response. *Scandinavian Audiology*, *4*(3), 167-172.

Vander Werff, K. R., Brown, C. J., Gienapp, B. A., & Schmidt Clay, K. M. S. (2002). Comparison of Auditory Steady-State Response and Auditory Brainstem Response Thresholds in Children, *23*(5), 227-235.