

Threshold Estimation using Multi-frequency ABR in Infants

Swathy B. L.

(Register No: 15AUD034)

**This dissertation is submitted as part fulfilment for the
Degree of Master of Science in Audiology
University of Mysore**



**ALL INDIA INSTITUTE OF SPEECH AND HEARING
MANASAGANGOTHRI, MYSURU 570006**

May-2017

CERTIFICATE

This is to certify that this dissertation entitled “**Threshold Estimation using Multi-frequency ABR in Infants**” is a bonafide work submitted as a part for the fulfilment for the degree of Master of Science (Audiology) of the student Registration Number: 15AUD034. This has been carried out under the guidance of the faculty of this institute and has not been submitted earlier to any other University for the award of any other Diploma or Degree.

Mysuru
May, 2017

Prof. S. R. Savithri
Director
All India Institute of Speech and Hearing
Manasagangothri, Mysuru-570006

CERTIFICATE

This is to certify that this dissertation entitled “**Threshold Estimation using Multi-Frequency ABR in infants**” 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.

Mysuru
May, 2017

Guide
Dr. Sandeep M.
Reader in Audiology
Department of Audiology

DECLARATION

This is to certify that this dissertation entitled “**Threshold Estimation using Multi-Frequency ABR in infants**” 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, Mysore and has not been submitted earlier to any other University for the award of any other Diploma or Degree.

Mysore
May, 2017

Registration No: 15AUD034

TABLE OF CONTENTS

Chapter no.	Title	Page no.
1	Introduction.....	1-4
2	Review of literature.....	5-16
3	Method.....	17-22
4	Results.....	23-33
5	Discussion.....	34-40
6	Summary and conclusions.....	41-42
	References.....	43-54

LIST OF TABLES

Table no.	Title	Page no.
3.1	Stimulus and acquisition parameters used to record ABRs in the present study	21

LIST OF FIGURES

Figure no.	Title	Page no.
3.1	Waveform of the Multifrequency chain of tone bursts	18
3.2	Spectrum of the Multi frequency chain of tone bursts.	19
4.1	Median of BOA levels and MFABR thresholds at four test frequencies	24
4.2	ABRs recorded using SFABR and MFABR techniques at 80dB SPL in a representative participant	25
4.3	Individual wave V latencies (ms) of MFABRs and SFABRs at 80dB SPL in 500Hz, 1kHz, 2kHz and 4kHz test frequencies	26
4.4	Individual wave V amplitudes (uV) of MFABRs and SFABRs at 80dB SPL in 500Hz, 1kHz, 2kHz and 4kHz test frequencies	28
4.5	Individual wave III latencies (ms) and amplitudes (uV) of MFABRs and SFABRs at 80dB SPL in 500Hz, 1kHz, 2kHz and 4kHz test frequencies	29
4.6	Individual wave I latencies (ms) and amplitudes (μ V) of MFABRs and SFABRs at 80dB SPL in 500Hz, 1kHz, 2kHz and 4kHz test frequencies.	30
4.7	MFABRs of a representative participant where the thresholds have been tracked.	32
4.8	ABR thresholds estimated using MFABR and SFABR techniques (in dB SPL) in participant 2, 3, 4 and 5, at 500Hz, 1kHz, 2kHz and 4kHz.	33

Chapter 1

INTRODUCTION

Auditory Brainstem Response (ABR) is an exogenous evoked potential elicited primarily from the onset of the stimulus and contains a series of five to seven waves arising from the auditory nerve and brainstem. These responses have latencies within 10ms and serve as a potential diagnostic tool for objective estimation of hearing thresholds. (Hecox & Galambos, 1974) showed that ABR could be used for threshold estimation in adults and infants. Since then it is being used for ear specific hearing threshold estimation in difficult to test population, for both screening and diagnostics. ABR being a gold standard test and considering its higher sensitivity and specificity, it becomes imperative that the opportunity of administering the test be available for all the needed cases. One constraint to this is the limited availability of the clinical time, because it consumes lot of time for preparation as well as for recording. This has lead to a reduction in its utility especially for screening.

In the past, several attempts have been made to cut down the time for recording ABRs in its screening as well as diagnostic applications. However all of them have their own significant limitations which compelled researchers and clinicians alike, to retain the conventional methods of recording. For instance, Maximum Length Sequences (Jirsa, 2001) enable the recording at higher repetition rates, which reduces the test duration. But the responses are poorer compared to conventional ABRs (Weber & Roush, 1995). Wave V intensity functions have been shown to be less steep and MLS thresholds are found to be higher than conventional ABRs. Reducing the testing time by increasing the repetition rate, makes the ABR morphology poor. Repetition rates below 25/s are recommended to ensure clear

morphology (American Speech Language and Hearing Association, 2004). Also, increasing the repetition rate leads to neural adaptation. To overcome this, researchers have tried alternate stimuli called chained stimuli (Petoe, Bradley, & Wilson, 2009). With appropriate inter stimulus interval, tone bursts of different frequencies are chained one after the other to generate the chained stimuli.

Another method proposed for rapid and objective assessment of hearing using auditory evoked responses includes recording steady state evoked response. Although they 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; John & Picton, 2000; Small & Stapells, 2004) and therefore have limited clinical utility.

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; 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, and Frey (1994) on humans, they did not use stimulus frequencies below 8kHz, which limits the applicability of the results to study hearing thresholds in human beings.

Mamatha (2016) recorded multifrequency ABR (MFABR) using a stimulus chain sequentially containing tone bursts of 4000Hz, 2000Hz, 1000Hz and 500Hz. The responses recorded were clinically same as that of single frequency tone bursts and the thresholds estimated correlated very well with the behavioral thresholds. However, as clearly stated in the study, inferences drawn in adults can't be generalized to infant population. ABR is used for threshold estimation in all the infants, as an objective cross check. The interval between the consecutive tone bursts ranges from

12ms to 19ms in the Multifrequency chain of tone bursts used in MFABR. Typically, such inter stimulus intervals can lead to neural fatigue in infants in whom neural maturation of the lower brainstem is not complete, thereby leading to poorer responses. However, the responses may not get affected considering that these 4 stimuli involve different neuronal population within the auditory nerve. Therefore, the clinical feasibility of using MFABR for hearing threshold estimation in infants needs to be experimentally verified.

1.2 Aim of the Study

To validate ABRs elicited by MFABR as a clinical tool for recording frequency specific ABRs in infants.

1.3 Objectives of the Study

The three objectives of the present study were,

1. To compare thresholds estimated using MFABR with that of minimum responsive levels of BOA
2. To compare latency and amplitude of ABRs elicited by single frequency tone bursts with that of ABRs elicited by multifrequency chain of tone bursts at 80dB SPL
3. To estimate thresholds using MFABR and compare with that of thresholds using single frequency ABR.

Chapter 2

REVIEW OF LITERATURE

Estimating accurate hearing thresholds plays a significant role in providing appropriate diagnostic and rehabilitative audiological services to an individual. Conventionally, hearing thresholds are estimated using behavioral methods such as puretone audiometry, behavioral observation audiometry, conditioned play audiometry and visual reinforcement audiometry depending on the age of the patient. Considering that hearing deficits of an individual can vary with frequency, frequency specific threshold estimation is crucial in young children and other difficult to test population (Coles, 1977; Stapells & Vancouver, 2000; Hall, 1992) in appropriately rehabilitating thereby preventing delays in the development of speech and language (Yoshinaga-Itano, Sedey, Coulter, & Mehl, 1998; Zielhuis, Heuvelmans-Heinen, Rach, Broek, & Zielhuis, 1989).

Inability to attain accurate hearing thresholds due to immature development or inconsistent responses in infants or other difficult to test population precludes the use of conventional subjective audiometric techniques. Further, in the first few months of infancy, behavioral audiometry tests are unreliable and tend to be elevated compared to adults (Schneider & Trehub, 1992). This necessitates the use of objective methods to estimate auditory thresholds. It is important to estimate frequency specific ABR thresholds to approximate configuration of an audiogram and to provide complete assessment of an individual's hearing sensitivity. Click evoked ABRs are generally used in threshold estimation due to its fast acquisition compared to other techniques. However, click ABR correlates to average threshold in 1k–4k Hz range (Eggermont, 1982; Stapells, 1989) and do not represent accurate measures of hearing thresholds for

any specific frequency, and may completely miss or underestimate/overestimate hearing loss in particular frequency regions (Eggermont & Don, 1980; Stapells et al., 1994). Hence, frequency specific auditory thresholds are essential for accurate diagnosis and precise fitting of hearing aids.

2.1 Different Methods to obtain Frequency Specific Auditory Brainstem Responses

2.1.1 Auditory Brainstem Responses for Tone Bursts and Tone Pips

In infants who cannot be tested behaviorally, it is advised to use tone-evoked ABRs to estimate the audiogram (Stapells, 2002). Tone evoked ABRs in normal infants and young children are studied by several investigators (Stockard, & Coen, 1983; Suzuki et al, 1984; Hyde, 1985; Stockard & Stapells, 1989; Stapells et al., 1994;) and are reported to be variable (Klein, 1984; Sininger, Abdala, & Cone-Wesson, 1997). However, most of them found that responses are similar to adult subjects and strongly correlated with behavioral thresholds (Stapells, Gravel, & Martin, 1995). It has been reported that reasonable estimates of behavioral thresholds can also be done using tone evoked ABR in hearing impaired infants (Kileny & Magathan, 1987; Suzuki et al., 1984).

Stapells (2000) meta analysed data of 32 studies representing results from 1,203 participants (679 infants or young children, 524 adults or older children; 815 individuals with normal hearing; and 388 individuals with sensory neural hearing loss) in order to determine the utility of tone burst ABR for obtaining reliable frequency specific thresholds. Results showed that, individuals with normal hearing have tone evoked ABR thresholds between 10 and 20 dB nHL and participants with SNHL have 5 to 15 dB higher and ± 10 dB ABR thresholds than behavioral thresholds

in adults and infants/young children respectively. Low frequency tones (500Hz) tend to show higher threshold differences than those of mid to high frequency tones (infant show inherent higher ABR thresholds for 4000 Hz stimuli (Sininger et al., 1997). Reportedly, quite consistent threshold results were seen across the studies.

Werner, Folsom, and Mancl (1994) compared behavioral and ABR thresholds for tone pips at 1k Hz, 4k Hz, and 8 kHz in 3 and 6 months old infants and adults. Results indicate that even 3months old infants show adult like ABR thresholds at all the test frequencies. This was true in spite of behavioral thresholds being higher in infants compared to adults. Significant improvement was seen only in 8-kHz behavioral thresholds from 3 months to 6 months. Correlation of behavioral and ABR thresholds was significant at 4 kHz and 8 kHz for 3months old infants and adults respectively. This suggests that variability in sensory function at these frequencies contributes to both behavioral and ABR thresholds.

Hayes and Jerger (1982) showed that there is unacceptably high predictive error at low frequency (especially at 500 Hz) ABRs which resulted in overestimating the hearing loss by 20 dB in 28% of the data. Indicating that there is an inherent difference in our ability to elicit an ABR for lower frequencies when compared to higher frequencies. Since the differences between ABRs and behavioral hearing thresholds for lower frequencies are not constant and are highly variable, it limits the use of tone-burst ABRs to predict behavioral thresholds. However the use of single frequency tone bursts to estimate frequency specific ABRs for all the frequencies in a clinical setup is limited by its excessively long testing time of approximately 2 hours (Karzon & Lieu, 2006; Stueve & O'Rourke, 2003).

2.1.2 Masking Methods in ABRs to Obtain Frequency Specific Hearing

Even though tone burst stimulus seem to be ideal for obtaining ABR thresholds, at higher intensities/low frequency stimuli it causes spectral splatter or spread of acoustic energy to unwanted frequencies due to its brief stimulus onset. In such cases cochlear stimulations in the frequency regions other than the characteristic frequency would reduce the frequency specificity of the recorded tone burst ABR (Hall, 1992; Picton, Ouellette, Hamel, & Smith, 1979; Stapells, Gravel, & Martin, 1995; Stapells & Picton, 1981; Stapells et al., 1994). This necessitates the use of masking to reduce the contributions of off frequency cochlear regions in eliciting frequency specific ABRs. There are several masking methods used to acquire frequency specific ABRs such as, notched noise method, high pass noise masking method and derived band technique. In all the masking methods noise with specific frequency characteristics along with the ABR eliciting stimulus is presented to the test ear.

Stapells, Gravel, and Martin (1995) assessed hearing thresholds in infants and young children with normal hearing or sensorineural hearing loss using ABRs to brief tones of 500, 2k, and 4k Hz presented in notched noise masking. It was compared with behavioral thresholds obtained at follow-up audiological assessments. Results showed that most infants with normal hearing showed ABRs to 30dBnHL tones. In addition, both normal hearing and hearing impaired individuals show high (≥ 0.94) correlation between the ABR and behavioral thresholds. Overall, 80% of the ABR thresholds were within 15 dB of the behavioral thresholds, 93% were within 20 dB, and 98% were within 30 dB. Further, they also found ABR results were unaffected by

age, indicating that ABR is efficient in predicting infant's follow-up behavioral thresholds as it was those of older children.

Studies by Stapells and Picton (1981) and Stapells et al. (1990) showed that there was greater frequency specificity seen in ABR responses to notched noise masking when compared with that of non-masking tone burst ABR especially in individuals with hearing impairment. However, these results were contradicted by Orsini (2004) where he emphasized that there was no significant difference between the two in both normal and hearing impaired individuals.

The earlier studies (Don & Eggermont, 1978; Kileny, 1981; Laukli, 1983; Stapells et al., 1985) have showed different masking methods which uses high pass noise masking methods to obtain frequency specific responses in ABR. They have also reported several advantages of high pass noise masking over notched noise masking, such as larger response amplitudes, requirement of less complex instrumentation. However, frequency specificity of tone burst ABR in high pass noise masking method are reduced relative to responses in notch noise because the stimulus includes all frequencies below the cutoff frequency. However, for frequencies below 1kHz it can still serve to be a good tool to elicit frequency specific information.

Nousak and Stapells (1992) obtained bone conducted ABRs to 500 and 2 kHz tones in quiet and in the presence of high pass noise at 70 (500 and 2kHz) and 46 (2 kHz) dB peak to peak equivalent (re: 1 dyne RMS) from normal-hearing infants and adults. Responses of the non-masked cochlear regions were estimated by derived responses. 500 Hz tone evoked bone conducted ABR show frequency specific responses in infants and adults. For 2000 Hz tones, the results show maximum amplitudes seen in adults and infants were in cochlear regions representing the

nominal frequency of the tone and 1/2 octave of the nominal frequency (1410-2000 Hz) respectively. In both the groups derived response latencies for 2 kHz tones were almost identical in wave V, but shorter in infants for 500 Hz tones, indicating that low frequency bone-conducted stimuli are effectively more intense in infants than adults.

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 (Don & Eggermont, 1978; Eggermont & Don, 1980; Donaldson & Ruth, 1993; Don, 1994, 1997; Eggermont, 1976; Kramer, 1992; Nousak & Stapells, 1992; Oates & Stapells, 1997) or by using pure-tone masking methods (Folsom, 1984; Klein, 1984; Klein & Mills, 1981; Mackersie, 1993; Wu & Stapells, 1994; Pantev, 1985).

Don and Eggermont (1978), described a novel technique called derived band technique to obtain frequency specific ABRs. They recorded click ABRs in quiet and then with high pass noise of different cut off frequencies. Derived band ABRs were obtained by subtracting two ABR responses recorded using high pass noise of 2 adjacent cut off frequencies (for example, 4k Hz and 6k Hz). They also indicate that the subtracted responses are only from the contribution of the limited cochlear region of interest.

The derived band technique is more time consuming and subtraction of ABR responses results in reduced SNR of responses. Furthermore, contribution from the region below 500Hz for ABR elicited by clicks is probably minimal (Don & Eggermont, 1978; Mauldin 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. These findings limit the use of derived band technique in clinical setup even with good experimental validation.

2.1.3 Other Objective Techniques to Obtain Frequency Specific Auditory Thresholds

Estimation of frequency specific hearing threshold can also be acquired using Auditory steady state responses (ASSRs) and Late latency responses (LLRs).

Earlier studies have shown that there is significant correlation between hearing thresholds estimated by LLRs and behavioral audiometric hearing thresholds (Prasher et al., 1993; Hyde, 1997; Tsui et al., 2002; Lightfoot and Kennedy, 2006). However, LLRs are highly affected by state of arousal and drugs, and requires approximately 4 hours to elicit frequency specific responses (Bell, Smith, Allen, & Lutman, 2004). This curtails the use of LLRs in clinical setup especially in infants and children

Rance et al. (2005) established ASSR audiograms using AM and FM tones at octave frequencies from 500 Hz to 4 kHz and compared it with behavioral hearing thresholds in infants [Total of 575 which included infants with normal hearing (285), SNHL (271) and auditory neuropathy (19)]. Outcomes of normal hearing and SNHL infants show high correlation between ASSR and behavioral hearing thresholds at all the test frequencies. However, ASSR thresholds in auditory neuropathy group did not correlate well with the behavioral audiogram. Overall, results indicate that ASSR testing can be useful in estimating frequency specific hearing thresholds in infants.

Rance, Tomlin, and Rickards (2006) showed that in infants, responses to TB-ABR technique were more reliable in predicting hearing thresholds than ASSR assessment, since they are less affected by maturational development in the first few

weeks after the birth and is less variable across subjects. John, Brown, Muir, and Picton (2004) showed that ASSR testing to elicit frequency specific responses will be more appropriate if tested immediately after the neonatal period.

ASSR threshold levels in normal hearing infants are reported to be elevated as compared to adults and mean ASSR threshold levels are found to be around 25 to 45 dB HL (Cone-wesson et al. 2002).

Cone-Wesson, Dowell, Tomlin, Rance, and Ming (2002), studied efficiency of ASSR in predicting frequency specific puretone thresholds of infants and children. ASSR was compared with click and tone burst evoked ABRs. Outcomes showed that the TB ABR thresholds and ASSR thresholds were similar when 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.

Stapells (2004) reported that ASSR responses are highly affected by stimulus related artifacts resulting in high false positives. This restricts the use of ASSR as a clinical tool to estimate frequency specific hearing thresholds, though it is known as the time saving technique to elicit frequency specific responses.

2.2 ABRs for Multi Frequency Chain of Tone Bursts

Importance of eliciting frequency specific ABRs in less acquisition time has lead to initiation of new technique called multi frequency ABR (MFABR). Some researchers have trialed a stimuli called ‘chained stimuli’ to reduce the time of acquisition of frequency specific ABRs.

Fausti, Mitchell, Frey, Henry and O'Connor (1994) recorded ABRs in 10 normal hearing subjects, for four high-frequency tone bursts of 14 kHz, 12 kHz, 10 kHz and 8 kHz and then compared it with the ABRs elicited by multiple stimulus sequence with stimulus onset separated by 10ms. Ten normal hearing subjects participated in the study. 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 statistically significant longer wave V latencies observed in multiple stimulus sequence responses. Test-retest reliability was good between multiple and single conditions. These findings account for use of the proposed technique as time saving method to estimate frequency specific ABRs clinically. Since, the frequencies used in the study are above 8 kHz, and does not cover any of the audiometric frequencies its applicability to estimate hearing thresholds in the audiometric frequencies, needs to be explored.

Mitchell, Fausti and Frey (1994) had also used a similar stimulus paradigm for eliciting frequency specific ABRs in guinea pigs. Multi stimuli sequence included tone bursts at 21 frequencies, from 1 kHz to 32 kHz approximately in 1/4-octave steps. The tone bursts were produced by gating a continuous sine wave from a synthesizer with an electronic switch and had a duration of 2ms, with rise, fall time of 1ms and no plateau. Intensity, intra-pair time and frequency were varied to determine when adaptation measured by a latency delay occurred. Results indicate that adaptation was less if the frequency of the second stimulus in paired stimulus was either above or below that of the first and adaptation effects were minimal when the time separation is 10ms or greater in paired-stimulus. However, the study cannot be

generalized to human population since it has been conducted on guinea pigs for a frequency range of 1 kHz to 32 kHz.

Mitchell, Kempton, Creedon, and Trune (1999) obtained ABR in mice, for single tone burst and multiple stimulus sequence (4k Hz to 32k Hz) of tone bursts. Authors found no significant differences in hearing thresholds, latency and amplitude functions when both the responses were compared. This indicates that responses from multiple stimuli sequences were not adapted or affected in terms of latency and amplitude of responses. The outcomes of the study suggest the use of multiple stimulus sequence to record frequency specific responses as a time saving method. However, stimulus frequencies used are above 4k Hz till 32k Hz and the results are not applicable to lower audiometric frequencies. In addition to this the study was carried out on mice and it restricts the results to be generalized on human population due to structural and functional differences between the two species.

Hoke, Pantev, Ansa, Lutkenhoner, and Herrmann (1991) elicited frequency specific ABRs in adults using a stimulus paradigm which is a series of 7 Gaussian shaped tone pulses with carrier frequencies descending in half-octave steps from 4k to 500 Hz. There was 18ms of inter stimulus interval between the two consecutive pulses and 54ms of pause between consecutive series. So the interval between two of same frequency tone pulses will be 162ms. Simultaneous high pass noise masker is presented to enhance the frequency specificity of the responses recorded. Finding of the study suggest that the described method is efficient in recording frequency specific responses with frequencies as low as 500 Hz and intensities as low as 10dBnHL. They also implicated that, it subsequently reduces the time taken to record

frequency specific ABRs (covering the relevant speech frequency range) when compared to conventional methods.

Petoe, Bradley & Wilson (2009) analyzed the variance in latency of Wave V for ABRs evoked by conventional non chained tone bursts and chained stimuli of tone-pulse series (with frequencies 0.5 kHz, 0.75 kHz, 1 kHz, 1.5 kHz, 2 kHz, 3 kHz, 4 kHz, and 6 kHz in descending order, with rise-plateau-fall envelopes of 2-2-2, 2-2-2, 2-2-2, 3-3-3, 4-4-4, 6-6-6, 8-8-8, 8-8-8 cycles respectively) stimulation with simultaneous Gliding high pass noise Masker (GHINOMA). Results showed that using chained stimuli are similar to conventional tone burst responses. Subsequently, chained stimulus can be used to elicit frequency-specific ABRs in less time and without compromising on the quality of the responses. Test-retest reliability was also reported to be good between chained and single stimulus conditions.

Mamatha (2016) recorded multifrequency ABR (MFABR) using a stimulus chain sequentially containing tone bursts of 4000Hz, 2000Hz, 1000Hz and 500Hz with onset to onset interval being 20ms. 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 (ranged from 0ms to 0.13ms). However, the amplitudes of the waveforms obtained were not affected. 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. In addition, MFABR thresholds positively correlated with pure tone thresholds. The correlation was better at high frequency compared to low frequencies.

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 difficult to test population seems promising.

Chapter 3

METHOD

The null hypothesis stated was that there is no significant difference in the ABR latency, amplitude and thresholds using multi frequency chain of tone bursts compared to single frequency tone burst. Quasi experimental research design with purposive sampling was used in the present study. The following method was adopted to test the hypothesis.

3.1 Participants

Total of twenty one normal hearing infants of age range 1 month to 1 year (mean age = 7.7months) participated in the study. The normal hearing was confirmed through behavioral observation audiometry (BOA)/Visual reinforcement audiometry (VRA) and click evoked ABRs. Normal middle ear functioning was ensured using immittance evaluation. Only the infants with no significant risk factors for hearing loss, during the pre, peri and postnatal history were considered for the study. It was made sure that they did not have any history of otological/neurological problems and their developmental history (till the date of testing) was normal. Written consent according to AIISH ethical guidelines was taken from each infant's parent/caretaker prior to their participation.

3.2 Test Stimulus

The purpose of the study was to validate MFABRs elicited by chain of multi frequency tone bursts as a clinical tool for recording frequency specific ABRs in infants. Two types of stimuli were used in the present study; single frequency tone

bursts and a chain of multifrequency tone bursts. Single frequency tone bursts of 500Hz, 1kHz, 2kHz and 4kHz were used to obtain frequency specific ABRs.

Multifrequency chained stimulus with total duration of 68ms was generated in the order of frequencies progressing from high to low. The signal was generated using Blackman window with 2-0-2 envelope in the sequence of 4kHz, 2kHz, 1kHz and 500Hz with onset to onset interval of 20ms. The tone bursts have an inter stimulus interval of 19ms, 18ms, 16ms and 12ms respectively as represented (Mamatha, 2016) in Figure 3.1.

Spectrum of the chain of multifrequency tone bursts of 4kHz, 2kHz, 1kHz and 500Hz was compared with that of each single frequency tone burst (4kHz, 2kHz, 1kHz and 500Hz) to assure that the frequency components are similar in both the signals. Figure 3.2 shows the spectrum of the chained stimulus.

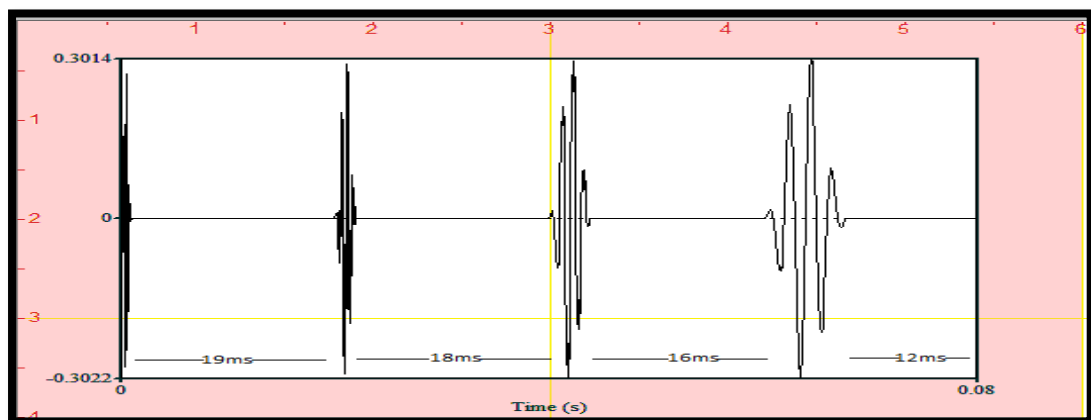


Figure 3.1: *Waveform of the multifrequency chain of tone bursts.*

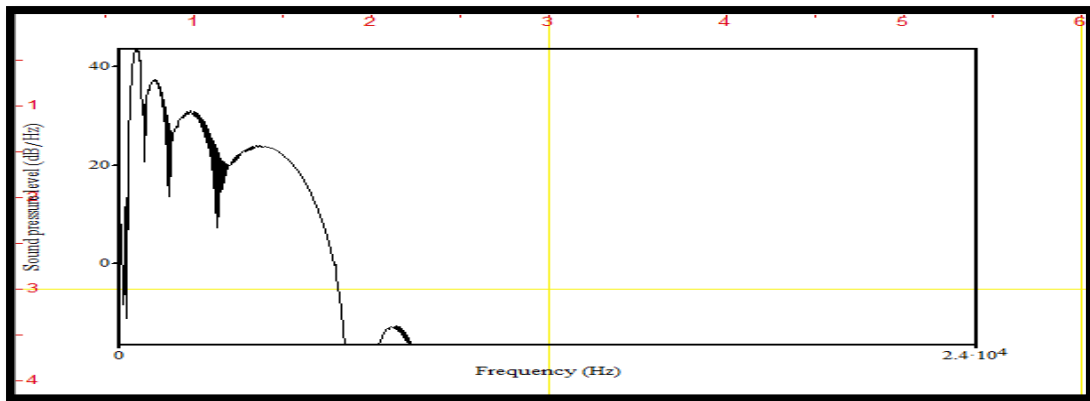


Figure 3.2: *Spectrum of the multi frequency chain of tone bursts.*

3.3 Instrumentation

Behavioural observation audiometry (BOA)/Visual reinforcement audiometry (VRA) was carried out using calibrated diagnostic audiometer (inventis Piano plus VRA) with sound field speakers. Tympanometry and Acoustic Reflex Thresholds were measured using GSI-Tympstar middle ear analyser. A Biologic Navigator Pro with impedance matched transducers was used for acquiring click ABRs, single frequency TBABRs and MFABRs.

3.4 Test Environment

Audiological evaluations were carried out in an air conditioned, electrically shielded and sound treated room where the noise levels were within permissible limits (ANSI S-3, 1991).

3.5 Test Procedure

3.5.1 Preliminary Audiological Evaluations

Preliminary audiological evaluations were done to qualify the infants as participants of the study by ruling out contraindications.

Behavioral observation audiometry was done to estimate hearing thresholds. Additionally, click ABR was recorded to objectively estimate hearing thresholds using conventional settings and parameters. Infants with audiometric thresholds within normal limits were selected for the study.

Conductive component was ruled out by through immittance evaluation. Tympanograms were recorded using 226Hz probe tone and by sweeping the pressure from +200 to -400daPa. Ipsilateral acoustic reflex thresholds (at 500Hz, 1kHz, 2kHz and 4kHz) were also measured. Infants with Type 'A' or 'As' tympanograms with acoustic reflexes being present in both the ears were selected for the study.

3.5.2 Recording of ABR

The participants of the study were made to sleep naturally in the crib or mother's lap and extraneous movements were minimized as much as possible. Only the right ear was tested in all the infants. The target electrode sites were cleaned before placing electrodes to ensure absolute impedance of less than 5k ohms and inter electrode impedance was maintained below 2k ohms. Two sets of averaged ABRs were obtained for each infant. First set consist of tone burst evoked ABRs for each frequency individually at 90dB SPL. The thresholds were also tracked at each test frequency. The second set consisted of ABR for MFTB at 90dB SPL and here again, thresholds were tracked. While tracking the thresholds, ABRs were acquired from

90dB SPL in 20dB steps till 50dB SPL. Below 50dB SPL, thresholds were tracked in 10 dB steps. The threshold for chained stimulus was defined as the lowest intensity at which ABR is present at any one frequency. ABR at each intensity was replicated. The stimulus and recording parameters which was used for recording ABR are given in Table 3.1.

Table 3.1: Stimulus and acquisition parameters used to record ABRs in the present study

Stimulus Parameters	
Transducer	Insert ear phone
Type of stimulus	1) Multi frequency chain of tone bursts. 2) single frequency tone bursts of 500Hz, 1000Hz, 2000Hz, 4000Hz
Polarity	Rarefaction
Repetition rate	9.1/sec
Intensity	90dB SPL and below, till ABR threshold
Mode	Monaural
Acquisition Parameters	
Montage	Vertical FPz – ‘+ve’ Ipsilateral mastoid – ‘-ve’ Contra lateral mastoid – ground
Amplification	1,00,000 times
Analysis time	85ms
Total no. of averages	2000
Filter settings	100-1500 Hz
Artifact rejection	20 μ V
Data points	1024
Test ear	Right ear

3.6 Response Analysis

The recorded data was visually analyzed by 3 senior audiologists with an experience of more than 10years in recording and analyzing ABR. They were blind folded to the purpose of the study and stimulus characteristics. They judged a response to be present or absent and standard response picking criteria was used to mark peaks I, III, V. Peak latency and amplitude of each of these waves were noted down. The minimum intensity at which ABR was present was noted down as the ABR threshold.

3.7 Data Analysis

Group data was analysed to test the significance of difference in the latency and amplitude of ABRs elicited for chained stimulus compared to that of single frequency tone bursts at 80dB SPL. The data was also used to compare the ABR thresholds obtained using single frequency tone bursts with that of multi frequency chain of tone bursts at 500Hz, 1000Hz, 2000Hz and 4000Hz.

Chapter 4

RESULTS

In the present study, a total of twenty one participants were recruited. Of them, in 10 infants, ABRs could not be recorded as the infants woke up right at the beginning of the recording. The total time required for completing threshold estimation using chained stimulus as well as single frequency tone bursts was approximately 2 hours 15 minutes. Among the 11 infants in whom ABRs could be recorded, some of the infants woke up prior to completion of all the recordings. In such a case, attempts were made to reschedule the recording, aiming at completion. However in spite of repeated attempts, not all the recordings could be completed in all the infants.

The data obtained in those 11 infants was analyzed in the present study. Wherever necessary, data was statistically analyzed using Spearman's correlation and Wilcoxon sign rank test in Statistically Package for Social Sciences (SPSS, Version 19). The results obtained is reported under the following headings.

1. Comparison of BOA and MFABR thresholds
2. Comparison between MFABR and SFABR Elicited by 80dB SPL Stimulus
3. Comparison of Thresholds Estimated using MFABRs and SFABRs

4.1 Comparison of BOA Levels and MFABR Thresholds

The minimum level at which behavioral response was observed to each of the frequencies (500Hz, 1kHz, 2kHz & 4kHz) was noted down and was operationally designated as BOA level. The minimum level at which a ABR wave V was observed at each of the frequencies (500Hz, 1kHz, 2kHz & 4kHz) was also noted down and

was designated as MFABR thresholds. Figure 4.1 shows the median BOA levels and MFABR thresholds. It can be seen that the difference in median BOA levels and MFABR thresholds does not exceed more than 10dB. Wilcoxon signed-rank test showed that there was no significant difference between the BOA levels and the MFABR thresholds at 4kHz [$Z(9) = -1.008, p > 0.05$], 2kHz [$Z(9) = -0.654, p > 0.05$] and 1kHz [$Z(9) = -1.368, p > 0.05$]. However, the same was not true for 500 Hz, where the MFABR thresholds were significantly higher than the BOA levels [$Z(9) = -2.677, p < 0.01$]. It is important to note that, though there is a significant difference between the two measures at 500Hz, the median difference was less than 15 dB.

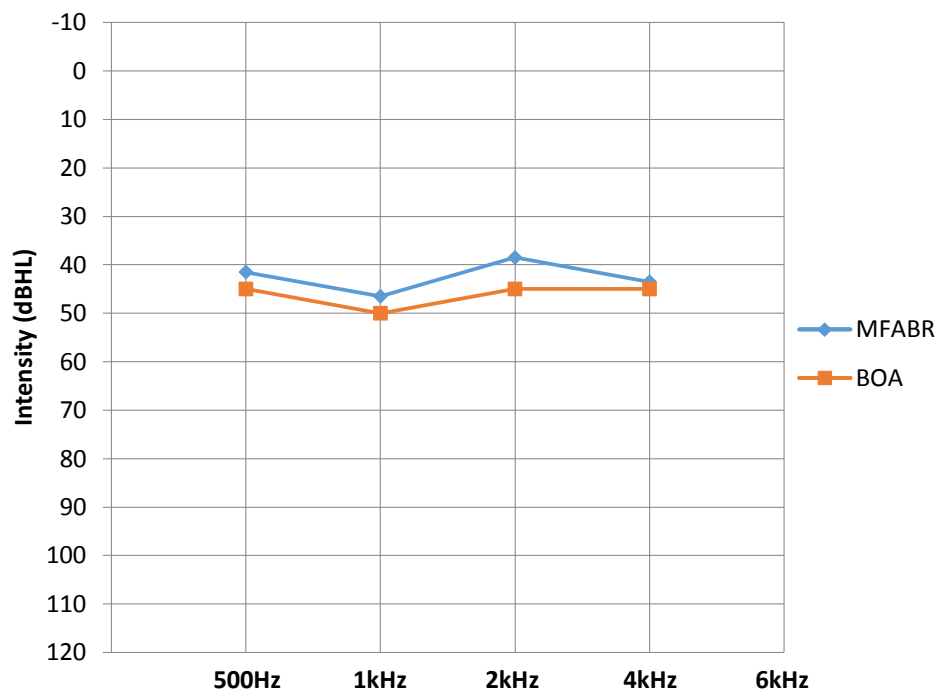


Figure 4.1: Median of BOA levels and MFABR thresholds at four test frequencies.

4.2 Comparison between MFABR and SFABR, Elicited by 80dB SPL Stimulus

In the response recorded for 80dB SPL stimulus, in most instances all the three major waves of ABR, i.e., wave I, III and V were present. The latency and amplitude of these waves, wherever present, were noted down. The group data was analyzed to compare the latency and amplitude of MFABR with that of SFABR. The results are reported separately for the three waves. Figure 4.2 shows ABRs recorded using the two techniques at 80dB SPL in a representative participant.

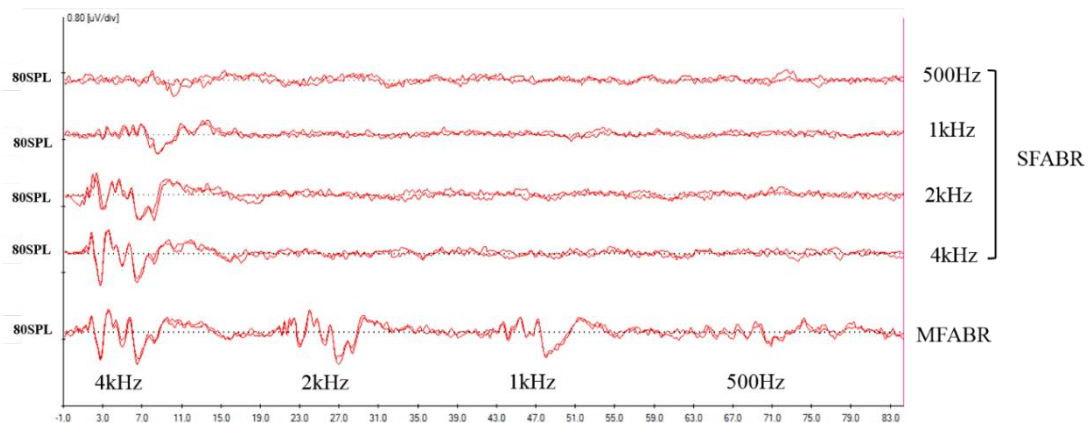


Figure 4.2: ABRs recorded using SFABR and MFABR techniques at 80dB SPL in a representative participant.

4.2.1 Comparison of Latency of Wave V

To test whether MFABR technique is equivalent to the conventional SFABR technique, wave V latencies at the highest intensity tested (80dB SPL) were compared between the two techniques. Comparison was done separately in each of the test frequencies (500Hz, 1kHz, 2kHz & 4kHz). Figure 4.3 shows the individual data of wave V latencies at all the test frequencies using the two techniques. From the figure it can be seen that the latencies at 1kHz, 2kHz and 4kHz are similar in both the

techniques. On the other hand wave V latencies at 500Hz were prolonged when recorded with the MFABR technique.

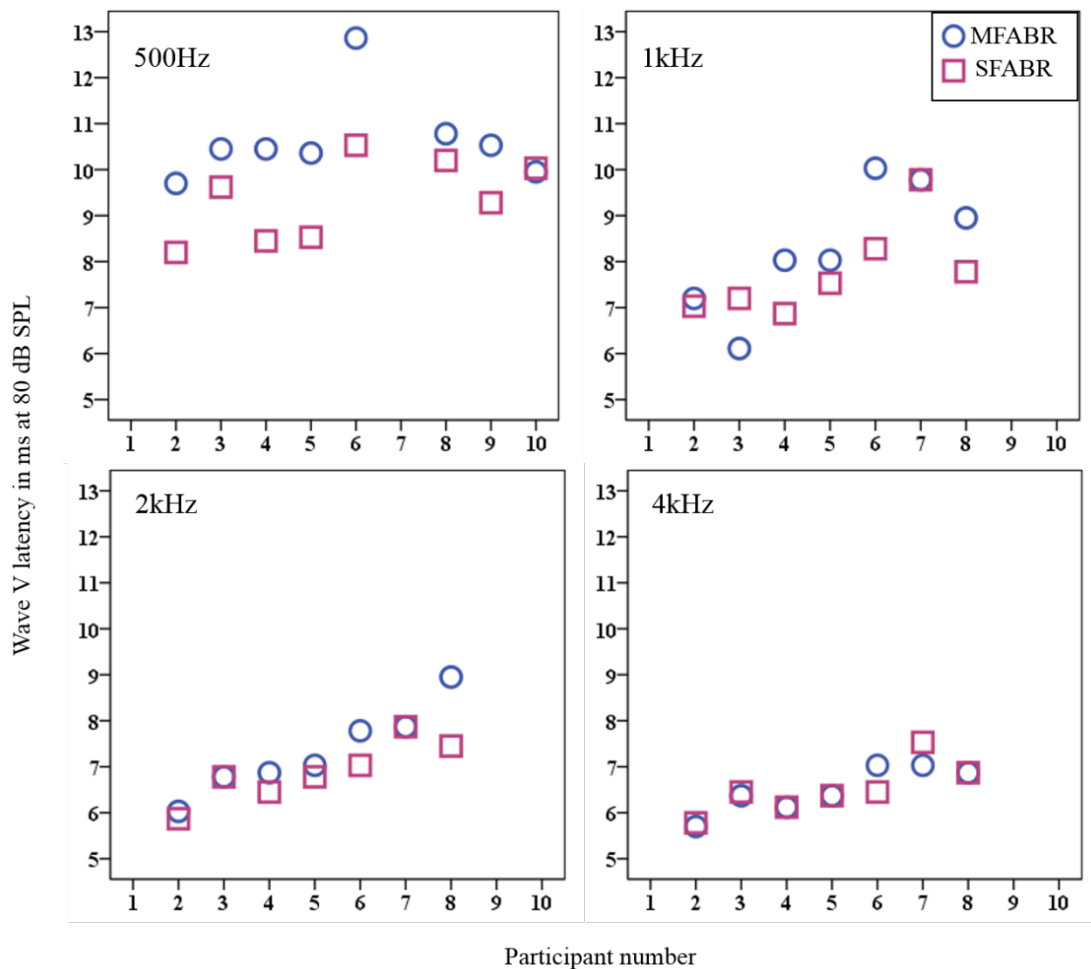


Figure 4.3: Individual wave V latencies (ms) of MFABRs and SFABRs at 80dB SPL in 500Hz, 1kHz, 2kHz and 4kHz test frequencies.

Statistical comparison using Wilcoxon Signed-rank test further confirmed the observation that the wave V latencies at 1kHz [$Z(7) = -1.572, p > 0.05$] and 4kHz [$Z(8) = -0.137, p > 0.05$] did not vary significantly between the two techniques, but at 500Hz [$Z(8) = -2.380, p < 0.05$] and 2kHz [$Z(7) = -2.023, p < 0.05$], the latencies were significantly longer in the MFABR technique than the SFABR technique. The maximum difference in the latencies between MFABR and SFABR at 500 Hz, 1kHz, 2kHz and 4kHz were 2.33, 1.75, 1.5 and 0.5ms respectively. The minimum

differences were 0.08ms at 500Hz and 0ms at 1, 2 and 4kHz. The latency difference in the two techniques increased with decreasing frequency.

4.2.2 Comparison of Amplitude of Wave V

Similar to the results of wave V latency, its amplitudes at 80dB SPL were compared between MFABR and SFABR at each of the test frequencies (500, 1k, 2k, 4kHz). Figure 4.4 shows the single subject wave V amplitudes at all the test frequencies in the two techniques.

It can be seen that the amplitudes in all the frequencies are similar between MFABRs and SFABRs. Statistical comparison using Wilcoxon Signed-rank test further confirmed the observation. Wave V amplitudes at 500Hz [$Z(8) = -1.120, p > 0.05$], 1kHz [$Z(7) = -1.185, p > 0.05$], 2kHz [$Z(7) = -1.183, p > 0.05$] and 4kHz [$Z(8) = -0.351, p > 0.05$] did not differ significantly between the two techniques. The minimum difference between amplitudes in MFABR versus SFABR was 0.01uV at 500 and 2kHz, 0.02uV at 1 and 4kHz. On the other hand, maximum difference in amplitudes at 500 Hz, 1kHz, 2kHz and 4kHz were 0.18, 0.12, 0.15 and 0.16uV respectively. It can be seen that amplitude differences in the two techniques decreased as the frequency increases.

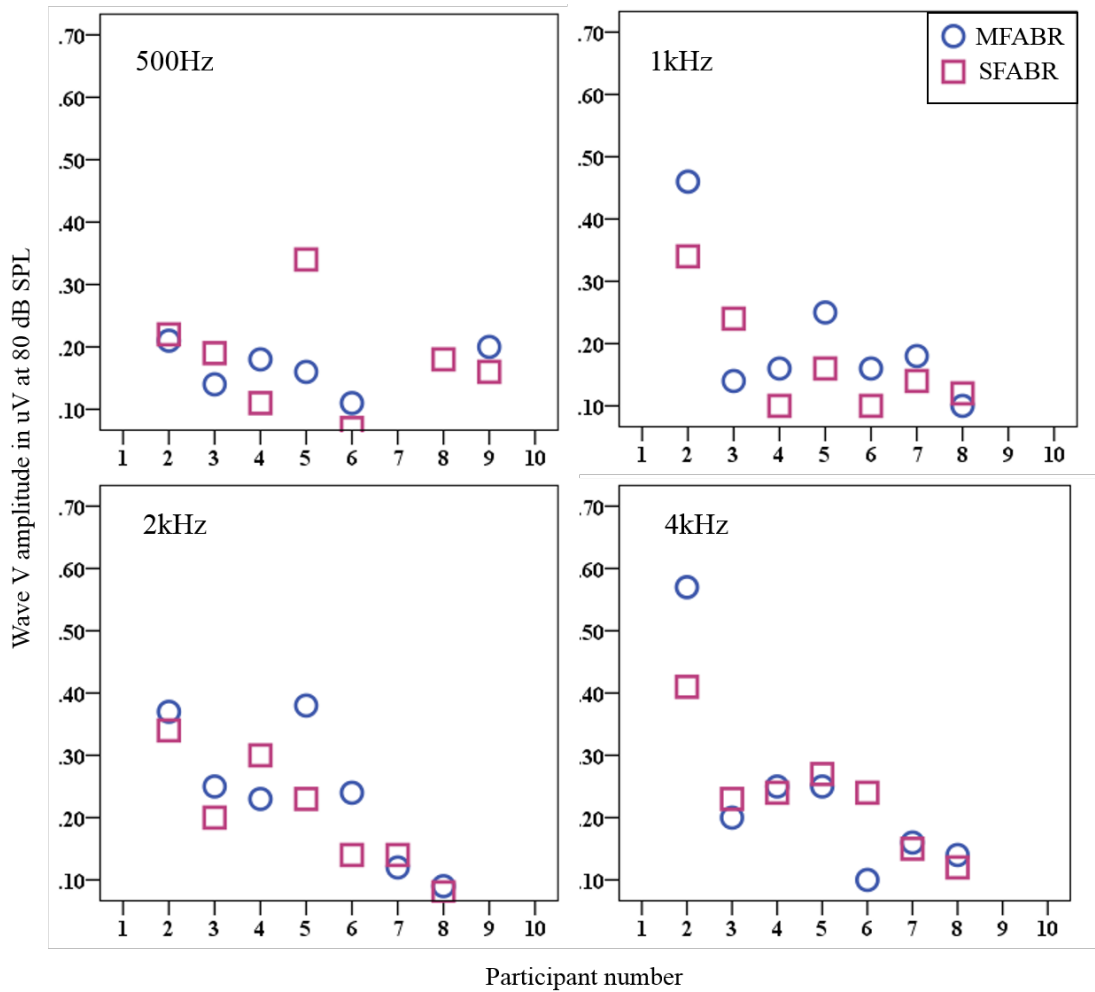


Figure 4.4: Individual wave V amplitudes (uV) of MFABRs and SFABRs at 80dB SPL in 500Hz, 1kHz, 2kHz and 4kHz test frequencies.

4.2.3 Comparison of Latency of Wave III

Figure 4.5 shows the individual wave III latencies at the highest intensity tested (80dB SPL) using the two techniques. It can be seen that the latencies at 1kHz, 2kHz and 4kHz are similar in both the techniques. Statistical comparison using Wilcoxon Signed-rank test, further confirmed the observation that the wave V latencies at 1kHz [$Z(5) = -1.214, p > 0.05$], 2kHz [$Z(7) = -0.631, p < 0.05$] and 4kHz [$Z(8) = -0.1826, p > 0.05$] did not differ significantly between the two techniques. The maximum difference in the latencies between MFABR and SFABR at 1kHz, 2kHz

and 4kHz were 2.33, 0.5 and 1.17 ms respectively. The lowest differences were 0ms at 2 and 4kHz, and 0.17 at 1kHz. On the other hand, latencies at 500Hz were not compared since wave III could not be reliably identified at this frequency.

4.2.4 Comparison of Amplitude of Wave III

Figure 4.5 shows the single subject wave III amplitudes at each of the test frequencies, SFABR and MFABR techniques. It can be seen that the amplitudes in all the frequencies are similar between MFABRs and SFABRs.

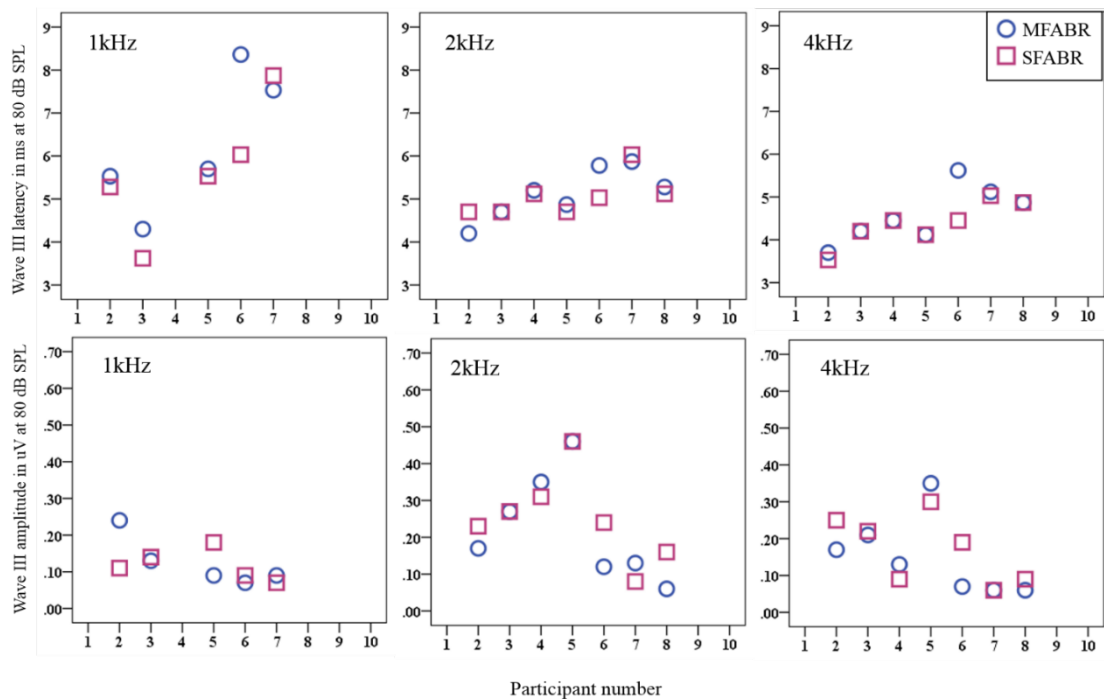


Figure 4.5: Individual wave III latencies (ms) and amplitudes (uV) of MFABRs and SFABRs at 80dB SPL in 500Hz, 1kHz, 2kHz and 4kHz test frequencies.

Statistical comparison using Wilcoxon Signed-rank test showed that Wave III amplitudes at 1kHz [$Z(5) = 0.00, p > 0.05$], 2kHz [$Z(7) = -214, p > 0.05$] and 4kHz [$Z(8) = -0.339, p > 0.05$] did not differ significantly between the two techniques. The minimum difference between amplitudes in MFABR versus SFABR was 0 at 2kHz

and 4kHz, 0.01uV at 1kHz. On the other hand, maximum difference in amplitudes at 1kHz, 2kHz and 4kHz were 0.13, 0.14 and 0.08uV respectively. It can be seen that amplitude differences in the two techniques decreased as the frequency increases. Latencies at 500Hz were not compared since wave III could not be reliably identified.

4.2.5 Comparison of Latency of Wave I

Figure 4.6 shows the individual wave I latencies at the highest intensity tested (80dB SPL) using the two techniques. It can be seen that the latencies are strikingly similar at 4kHz, fairly similar at 2kHz in both the techniques. MFABR latencies in 1kHz were longer when compared to SFABR latencies and statistical comparison was not done as it could be reliably identified only in two participants.

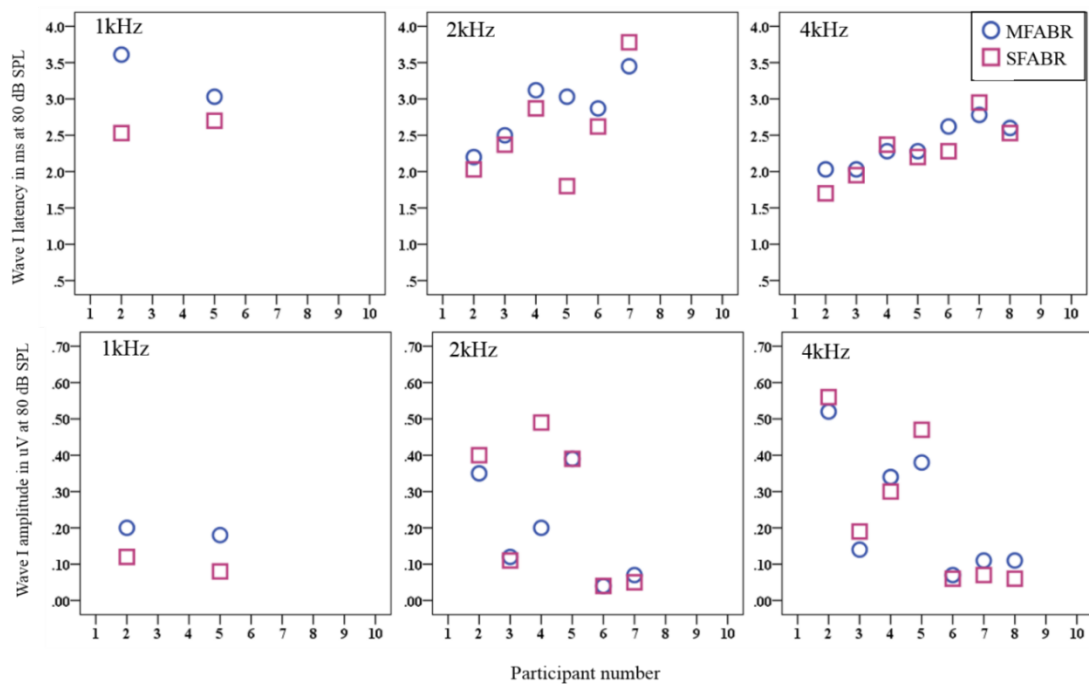


Figure 4.6: Individual wave I latencies (ms) and amplitudes (μV) of MFABRs and SFABRs at 80dB SPL in 500Hz, 1kHz, 2kHz and 4kHz test frequencies.

Statistical comparison using Wilcoxon Signed-rank test showed that wave I latencies at 2kHz [$Z(6) = -1.156$, $p < 0.05$] and 4kHz [$Z(8) = -0.847$, $p > 0.05$] did not differ significantly between the two techniques. The maximum difference in the latencies between MFABR and SFABR at 1kHz, 2kHz and 4kHz were 1.08 and 1.23, 0.33ms respectively. The lowest differences were 0.03, 0.13 and 0.08 at 1k, 2k and 4kHz respectively. Latencies at 500Hz were not compared since wave I could not be reliably identified at this frequency.

4.2.6 Comparison of Amplitude of Wave I

Figure 4.6 shows the single subject wave I amplitudes at all the test frequencies using both the techniques. It can be seen that the amplitudes in all 2kHz and 4kHz are similar between MFABRs and SFABRs. Statistical comparison using Wilcoxon Signed-rank test showed that wave I amplitudes at 2kHz [$Z(6) = -0.730$, $p > 0.05$] and 4kHz [$Z(8) = -0.211$, $p > 0.05$] did not differ significantly between the two techniques. The minimum difference between amplitudes in MFABR versus SFABR was 0.08uV at 1kHz, 0 at 2kHz and 0.01 at 4kHz,. On the other hand, maximum difference in amplitudes at 1kHz, 2kHz and 4kHz were 0.09, 0.29 and 0.09uV respectively.

4.3 Comparison of Thresholds Estimated using MFABRs and SFABRs

Among the twenty-one participants of the study, the thresholds in both MFABRs and SFABRs at 500, 1k, 2k and 4kHz could be tracked in only four. Figure 4.7 shows MF ABRs in a representative participant wherein threshold was tracked till 30dB SPL. The MFABR and SFABR thresholds of each of these participants were compared individually to see the similarities between the thresholds at all the test

frequencies. Figure 4.8 shows the comparison of MFABR and SFABR thresholds at each of the test frequencies in participant 2, 3, 4 and 5.

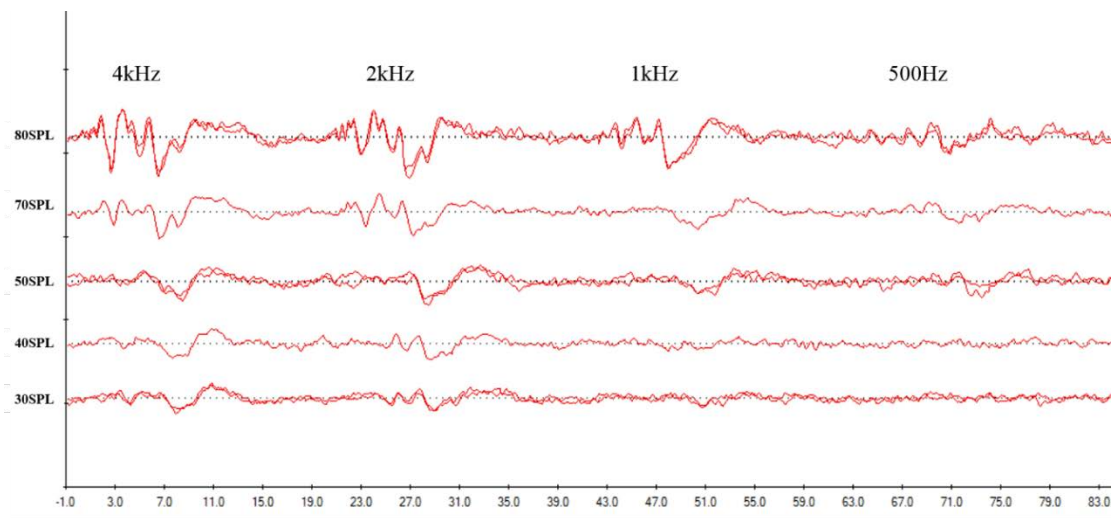


Figure 4.7: MFABRs of a representative participant where the thresholds have been tracked.

Participant 2 had similar thresholds at 500, 2k and 4kHz, while at 1kHz, MFABR threshold was higher by 10dB when compared to that of SFABR threshold. Participant 3 had similar thresholds at 500Hz, 20dB higher MFABR thresholds at 1 and 4 kHz, and 10 dB higher MFABR thresholds at 2kHz when compared to that of SFABR thresholds. In participant 4, MFABR thresholds were higher than SFABR thresholds by 10 dB at 500, 1k and 2kHz. However, at 4kHz MFABR threshold was 10 dB lower than SFABR thresholds. Participant 5 had similar thresholds in both the techniques at 1 and 2kHz. On the other hand, MFABR thresholds were 10dB higher at 500Hz and 10 dB lower at 4kHz compared to SFABR. Overall, comparison of thresholds in the two techniques among different participants indicate that MFABR thresholds were just higher or similar to SFABR thresholds at 500, 1k and 2kHz. On the other hand MFABR thresholds were similar or lower at 4kHz when compared to that of SFABR. It is important to note that the difference between MFABR and

SFABR thresholds did not exceed more than 10dB in 3 participants and 20dB in one participant among the 4 participants.

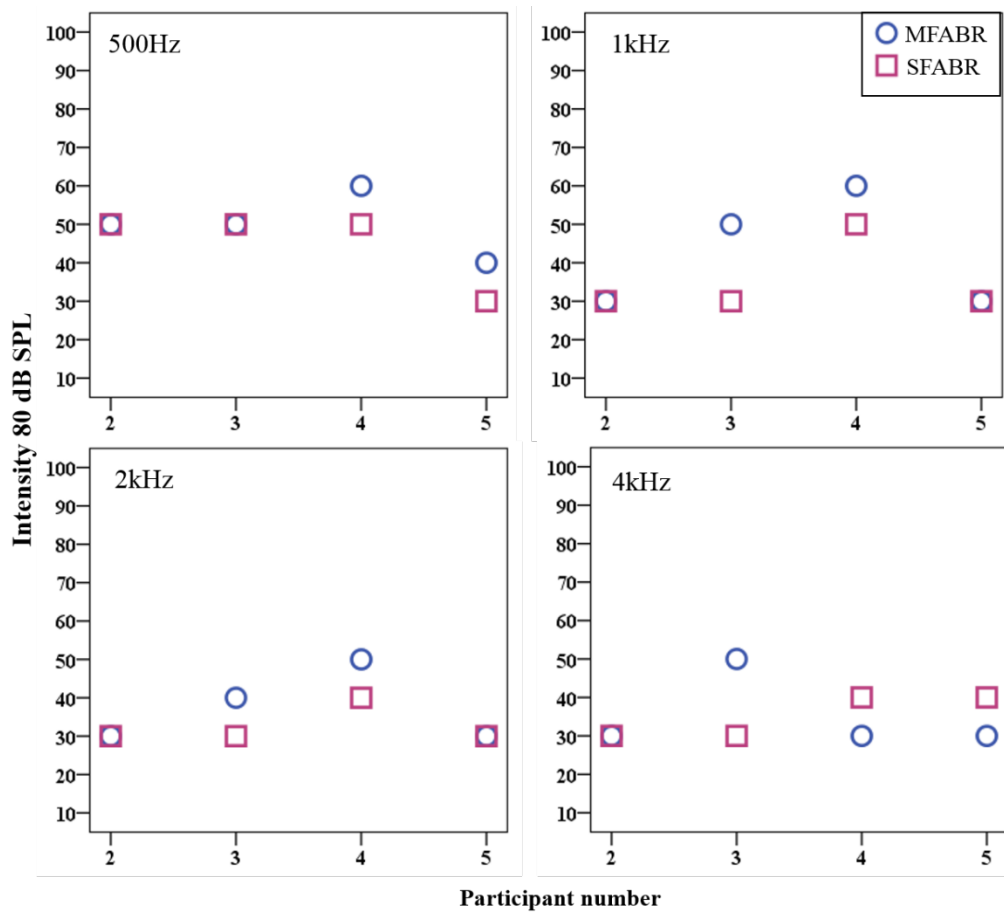


Figure 4.8: ABR thresholds estimated using MFABR and SFABR techniques (in dB SPL) in participant 2, 3, 4 and 5, at 500Hz, 1kHz, 2kHz and 4kHz.

Chapter 5

DISCUSSION

Primary aim of the study was to validate the MFABR technique as a time saving technique in recording frequency specific ABRs in infants. ABRs recorded using multi frequency chain of tone bursts are likely to give frequency specific information at four frequencies within the same time as that of conventional click ABRs, which lacks frequency specific information. Any new technique has to be extensively evaluated and validated against the existing gold standards before introducing into clinical practice. The utility of this technique has been established in adults by Mamatha (2016). Obtaining frequency specific thresholds are more important in infants for effective early identification and rehabilitation. Considering the time efficiency of new MFABR technique, we sought to validate the technique against the conventional single frequency tone-burst ABRs and behavioral observation audiometry. The results of the study show encouraging evidence towards the clinical use of MFABR for time-efficient frequency-specific hearing threshold estimation in infants. The results are discussed in detail in the following sub-sections.

1. Agreement between BOA and MFABR thresholds
2. Similarity in the characteristics of SFABR and MFABR elicited at high Intensity
3. Similarity in thresholds between MFABRs and SFABRs
4. Clinical utility of MFABR

5.1 Agreement between BOA and MFABR thresholds

In an audiological test battery, ABR is used as a test for crosschecking the results of behavioral test. Therefore it was important to assess the correlation between behavioral and MFABR responses. Considering the wide range of age of the infants in this study, behavioral observation audiometry was used a common test among all for uniformity. Results showed that median MFABR thresholds correlated with median BOA levels and there was no significant difference found at 1, 2 and 4kHz. This indicates that the estimates of MFABR thresholds can be clinically used as crosscheck similar to click evoked ABRs.

Typically behavioral thresholds are expected to be better than tone burst ABR thresholds. However, in the present study MFABR thresholds were better than the BOA responses. This could be because, BOA responses does not give an accurate measure of hearing and are at least 20dB behavioral thresholds depending on the age of the infant. On the other hand MFABR must be eliciting thresholds close to the behavioral thresholds

It is also important to note that the age of the infants in the present study ranged between 5 months and 12 months. Earlier studies have proposed that responses at 60 to 70 dB SPL can be interpreted as normal hearing for very young infants (McConnell & Ward, 1996; Northern & Downs, 1984). Since BOA is a measure of responsiveness to the auditory stimuli rather than a measure to estimate accurate hearing thresholds BOA responses tend to be elevated in infants.

Olsho et al. (1988) has reported that the audibility curve of younger infants may differ in shape compared with the curve of older infants and adults. It was assumed that this audibility curve difference was at least in part due to the

characteristics of the external and middle ears in infants. Arlington (2000) and Olsho et al. (1988) suggested that some of the threshold differences can be related to sensory immaturity in infants compared to adults. Hence, objective measures like ABRs can be used in reliable estimation of hearing thresholds in both the ears separately. MFABR can be used to estimate more reliable frequency specific thresholds in infants. However, in the present study MFABR responses at 500Hz are significantly higher than BOA levels but the median difference remained within 15 dB.

5.2 Similarity in the Characteristics of SFABR and MFABR Elicited at High Intensity

Single frequency tone burst ABRs (SFABRs) are known to be gold standard techniques for estimating frequency specific hearing thresholds for clinical purposes. Therefore it was important in the present study to assess how the findings in MFABRs relate to that in SFABRs. This was assessed by comparing the latency and amplitude at the highest intensity tested and also by comparing the thresholds. The results showed that latency and amplitude at the highest intensity tested (80dB SPL) were comparable between SFABR and MFABR. In the present study, all the three prominent waves; wave I, III and V were compared with that of SFABRs in order to assess the extent of similarity.

Results of the present study showed that the latencies were prolonged as the frequency of the tone burst decreases in both SFABR and MFABR. The time taken for the travelling wave to travel from 4000Hz to 500Hz is represented by the increase in latency with decreasing frequency (Gorga et al., 2006). ABRs to tone bursts of different frequencies represent synchronous activity from successive regions in 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 and the basal regions of the cochlea are connected to nerve fibers responsible for low frequencies and high frequencies respectively. The traveling wave reaches the basal region of the cochlea before the apical region. This would directly correspond to the differences in latencies from 4kHz to 500Hz.

Latencies predominantly indicate the neural conduction time of the pathway although cochlear transport time, cochlear filter build up time and synaptic delay cells do play their role (Don, Ponton, Eggermont, & Kwong, 1998). Comparable latencies between SFABR and MFABR would indicate that all the physiological processes remained same irrespective of whether single tone burst is presented versus multiple tone bursts of different frequencies are presented. Although, during threshold estimation, latencies are not really given importance, it was important to understand whether the underlying mechanism remained same.

Comparison of MFABR in terms of latencies of wave I and III with that of SFABR showed that there is no significant difference between the latencies at 500,1k, 4kHz. Similarly with reference to latency of wave V at 1k and 4kHz, the two techniques did not differ. These findings show that the chaining of the multi frequency tone burst does not affect the latencies at the mentioned peaks and are equivalent to that of the conventional tone burst ABRs. This means that the underlying physiology does not differ between the two techniques. The finding supported the use of MFABR technique in infants for obtaining frequency specific responses. The objective techniques in hearing aid prescription such as real ear measurements warrant frequency specific hearing thresholds. Therefore MFABR can

be highly useful in estimating the frequency specific hearing and thereby contribute in early rehabilitation.

On the other hand, the results showed significant prolongation of wave V at 500Hz and 2kHz in MFABR compared to SFABR. Although this indicates the presence of neural fatigue, one needs to duplicate the finding in a larger population, before conclusive remarks.

Earlier studies also have shown differences between SFABRs and MFABRs in their latencies (Fausti, Mitchell, Frey, Henry, & O'Connor, 1994). They recorded ABRs using single and multiple stimulus sequence. The test frequencies were from 8kHz to 14kHz. The mean latency difference was higher at 8kHz while there was no mean latency difference at 14kHz. Similar to the present study, the latencies of multiple stimulus sequence were prolonged compared to single stimulus. Intersession variability was also assessed in their study and the results showed the highest mean difference between two sessions to be 0.05ms for single stimulus and 0.09ms for multi stimulus sequence.

Amplitudes of ABRs represent the synchronous firing of the neurons involved in the respective generator site. This also accounts for neural integrity in auditory system. Results of the study showed that there is no significant difference between the MFABR and SFABR amplitudes of the wave I, III and V indicating that MFABR can be used to measure neural integrity reliably. The finding implies that there is no compromise of neural synchrony in MFABR technique. Mamatha (2016) had reported similar findings in adults. The finding suggests that the possible confounding factors such as refractory period, spread of excitation, etc. are not very different between the two techniques. This further supports the use of MFABR for eliciting frequency

specific ABRs as an alternative to SFABR. No compromise in the amplitude also indicates that the thresholds could be similar between the two techniques.

5.3 Similarity in Thresholds between MFABRs and SFABRs

In the previous section we learnt that the MFABR has characteristics similar to that of SFABR at higher intensity. However, for this technique to be a viable alternative to SFABR, it had to provide same estimated thresholds in the infants. Results of the present study showed that MFABR thresholds were similar to that of SFABR thresholds. The MFABR thresholds were higher by 10dB in 500, 1k and 2kHz, and lower by 10dB in 4kHz compared to that of SFABR. That is, the threshold obtained in MFABR fell within 10dB of that in SFABR. This again supports the use of MFABR technique in estimating frequency specific hearing thresholds with time efficiency compared to that of SFABR. However one must note that the step size used in the present study for estimating threshold was 10dB. Therefore agreement better than 10dB, if any, has been missed.

The findings of the present study, wherein individual data was represented and analyzed, is similar to that of Mamatha (2016) wherein group data was represented. In mamatha's study, agreement of 10dB or lesser was found in both normal hearing individuals and individuals with Sensorineural hearing loss. Taking the findings of both the studies into account, it can be concluded that MFABR estimates hearing thresholds same as that of SFABR.

In infants, the use of tone burst ABR has been advised to estimate frequency specific hearing thresholds (Stapells, 2002). Use of conventional single frequency ABRs to estimate frequency specific ABRs takes longer time of approximately 2 hours (Karzon & Lieu, 2006; Stueve & O'Rourke, 2003). Whereas MFABR estimates

frequency specific hearing thresholds approximately in the same time as that of ABR. In other words it cuts down the recording time by a factor equal to the number of frequencies being tested. Therefore, it is a time efficient and appropriate technique in estimating frequency specific ABRs in infants and other difficult to test population.

5.4 Clinical Utility of MFABR

Subjective methods used in estimating hearing thresholds in infants are less reliable and most of the time overestimates the hearing thresholds of an infant. Objective measures such as click ABRs are used in clinical setups to estimate hearing thresholds reliably. However, the click ABRs are not frequency specific since they use broader spectral stimuli. It is important to elicit frequency specific ABRs in infants for early identification and intervention of hearing impairment. Fitting of hearing aids with appropriate amplification requires objective techniques to elicit frequency specific thresholds in infants and difficult to test population where subjective measures to obtain frequency specific ABRs are not reliable. Even though there are many methods to obtain frequency specific ABRs, longer test duration taken in those methods curtails the use of those techniques in a clinical setup.

Results of the study validate the use of MFABR as a clinical tool in estimating frequency specific responses in infants in remarkably less time compared to that of SFABR. MFABRs are highly reliable as that of conventional ABRs. This validates and recommends the use of MFABR technique as a clinical tool to estimate frequency specific responses in infants.

Chapter 6

SUMMARY AND CONCLUSIONS

In spite of availability of different objective measures to elicit frequency specific responses, the click auditory brainstem responses (ABRs) are used to estimate hearing thresholds due to their time efficiency. The importance and need of the frequency specific thresholds is shown time and again in diagnosis as well as rehabilitation of infants with hearing impairment. Therefore in the present study, it was attempted to explore the feasibility of multifrequency auditory brainstem responses (MFABR) as a clinical tool in estimating frequency specific hearing, in a time efficient manner. Specifically, the findings in MFABR were compared with that of conventional single frequency ABR (SFABR) and behavioral estimates of hearing to draw the inferences.

A total of 21 infants in the age range of one month to one year participated in the study. Behavioral observation audiometry (BOA) was used to estimate the minimum responsive levels, which was followed by estimating ABR thresholds using MFABR and SFABR techniques. Thresholds were estimated at 4 frequencies; 500Hz, 1kHz, 2kHz, and 4kHz. Each recording of MFABR took 4 times lesser time than the SFABRs for the same 4 frequencies. ABRs were analyzed to identify wave I, III and V to note down their latency, peak to peak amplitude and the thresholds. ABRs recorded using the two techniques were compared in terms of their latency, amplitude and the thresholds. The MFABR thresholds were also analyzed for its relation with the BOA levels. Further, the data were subjected to statistical analysis using Wilcoxon signed rank test and Spearman correlations.

The results of the study showed that there is no significant difference between MFABR thresholds and BOA levels at all the test frequencies except at 500Hz. However, at this frequency, the median difference was less than 15dB. MFABR thresholds were lower than the BOA levels and the agreement between the two was less than 10dB at most frequencies. Latencies and amplitudes of wave I, III and V were comparable between MFABR and SFABR, except for few instances. The thresholds estimated using the two techniques also was similar.

In the present study, individual data are represented and analyzed which is unique compared to previous studies wherein in group data was analysed. However, the findings in the present study are in strong agreement with the reports in the literature.

Overall, results of the present study indicate similarity between SFABR and MFABR. MFABRs were found to be in agreement with conventional SFABRs in all the response parameters analysed in the present study and is also in close agreement with the behavioral responses. Considering that the time taken by MFABR is 1/4th of the time taken by SFABR for estimating frequency specific hearing at 500Hz, 1000Hz, 2000Hz and 4000Hz, outcomes of the present study strongly recommend the use of MFABR in clinical setup as a routine audiological test to estimate frequency specific hearing thresholds.

REFERENCES

- American Speech Language and Hearing Association. (2004). *Guidelines for the Audiologic Assessment of Children From Birth to 5 Years of Age* (No. GL2004-00002). Rockville, MD: American Speech-Language-Hearing Association. Retrieved from <http://www.asha.org/policy/GL2004-00002/>
- Beattie, R. C., Franzone, D. L., & Thielen, K. M. (1992). Effects of notch noise bandwidth on the auditory brainstem response to clicks. *Journal of the American Academy of Audiology*, 3(4), 269–274.
- Bell, S., Smith, D., Allen, R., & Lutman, M. (2004). Recording the middle latency response of the auditory evoked potential as a measure of depth of anaesthesia. A technical note. *British journal of anaesthesia*, 92(3), 442-445
- Carhart, R., & Jerger, J. F. (1959). Preferred Method For Clinical Determination Of Pure-Tone Thresholds. *Journal of Speech and Hearing Disorders*, 24(4), 330–345. <https://doi.org/10.1044/jshd.2404.330>
- Coles, R. R. (1977). Objective audiometry: a general and historical review. *The Journal of Laryngology and Otology*, 91(8), 639–54.
- Cone-Wesson, B., Dowell, R. C., Tomlin, D., Rance, G., & Ming, W. J. (2002). The auditory steady-state response: comparisons with the auditory brainstem response. *Journal of the American Academy of Audiology*, 13(4), 173-187-226.
- Donaldson, G. S., & Rubel, E. W. (1990). Effects of stimulus repetition rate on ABR threshold, amplitude and latency in neonatal and adult Mongolian gerbils. *Electroencephalography and Clinical Neurophysiology/Evoked Potentials Section*, 77(6), 458–470. [https://doi.org/10.1016/0168-5597\(90\)90006-Y](https://doi.org/10.1016/0168-5597(90)90006-Y)

- Donaldson, G. S., & Ruth, R. A. (1993). Derived band auditory brain-stem response estimates of traveling wave velocity in humans. I: Normal-hearing subjects. *The Journal of the Acoustical Society of America*, *93*(2), 940-951.
- Don, M., & Eggermont, J. J. (1978a). Analysis of the click-evoked brainstem potentials in man using high-pass noise masking. *The Journal of the Acoustical Society of America*, *63*(4), 1084. <https://doi.org/10.1121/1.381816>
- Don, M., & Eggermont, J. J. (1978b). Analysis of the click-evoked brainstem potentials in man using high-pass noise masking. *The Journal of the Acoustical Society of America*, *63*(4), 1084–1092. <https://doi.org/10.1121/1.381816>
- Don, M., Ponton, C. W., Eggermont, J. J., & Masuda, A. (1994). Auditory brainstem response (ABR) peak amplitude variability reflects individual differences in cochlear response times. *The Journal of the Acoustical Society of America*, *96*(6), 3476-3491.
- Don, M., Masuda, A., Nelson, R., & Brackmann, D. (1997). Successful detection of small acoustic tumors using the stacked derived-band auditory brain stem response amplitude: LWW.
- Don, M., Ponton, C. W., Eggermont, J. J., & Kwong, B. (1998). The effects of sensory hearing loss on cochlear filter times estimated from auditory brainstem response latencies.
- Eggermont, J. J., Spoor, A., & Odenthal, D. W. (1976). Frequency specificity of tone-burst electrocochleography. *Electrocochleography*, *215*, 246
- Eggermont, J. J., & Don, M. (1980). Analysis of the click-evoked brainstem potentials in humans using high-pass noise masking. II. Effect of click intensity. *Journal of*

the Acoustical Society of America, 68(6), 1671–1675.

- Eggermont, J. J. (1982). The inadequacy of click-evoked auditory brainstem responses in audiological applications. *Annals of the New York Academy of Sciences*, 388(1), 707-709.
- 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. *The Journal of the Acoustical Society of America*, 75(3), 919–24. <https://doi.org/10.1121/1.390538>
- Gorga, M. P., Neely, S. T., Hoover, B. M., Dierking, D. M., Beauchaine, K. L., & Manning, C. (2004). Determining the Upper Limits of Stimulation for Auditory Steady-State Response Measurements: *Ear and Hearing*, 25(3), 302–307. <https://doi.org/10.1097/01.AUD.0000130801.96611.6B>
- Gorga, M. P., Kaminski, J. R., Beauchaine, K. A., & Jesteadt, W. (1988). Auditory brainstem responses to tone bursts in normally hearing subjects. *Journal of speech, language, and hearing research*, 31(1), 87-97.
- Hayes, D., & Jerger, J. (1982). Auditory Brainstem Response (ABR) to Tone-Pips: Results in Normal and Hearing-Impaired Subjects. *Scandinavian Audiology*, 11(October), 133–142. <https://doi.org/10.3109/01050398209076210>
- Hecox, K., & Galambos, R. (1974). Brain Stem Auditory Evoked Responses in Human Infants and Adults. *Archives of Otolaryngology - Head and Neck*

Surgery, 99(1), 30–33. <https://doi.org/10.1001/archotol.1974.00780030034006>

Hoke, M., Pantev, C., Ansa, L., Lutkenhoner, B., & Herrmann, E. (1991). A timesaving BERA technique for frequency-specific assessment of the auditory threshold through tone-pulse series stimulation (TOPSTIM) with simultaneous gliding high-pass noise masking (GHINOMA). *Acta Otolaryngol Suppl*, 482(August 2016), 45–56.

Hyde, M. (1997). The N1 response and its applications. *Audiology and Neurotology*, 2(5), 281-307.

Jerger, J. F., & Hayes, D. (1976). The Cross-Check Principle in Pediatric Audiometry. *Archives of Otolaryngology*, 102(10), 614–620.

Jirsa, R. E. (2001). Maximum length sequences-auditory brainstem responses from children with auditory processing disorders. *Journal of the American Academy of Audiology*, 12(3), 155–164.

John, M. S., Brown, D. K., Muir, P. J., & Picton, T. W. (2004). Recording auditory steady-state responses in young infants. *Ear and Hearing*, 25(6), 539–553. <https://doi.org/10.1097/01.AUD.0000148050.80749.AC>

John, M. S., & Picton, T. W. (2000). MASTER: a Windows program for recording multiple auditory steady-state responses. *Computer Methods and Programs in Biomedicine*, 61(2), 125–150. [https://doi.org/10.1016/S0169-2607\(99\)00035-8](https://doi.org/10.1016/S0169-2607(99)00035-8)

Karzon, R. K., & Lieu, J. E. C. (2006). Initial audiologic assessment of infants referred from well baby, special care, and neonatal intensive care unit nurseries. *American Journal of Audiology*, 15(1), 14-24

- Kileny, P. (1981). The Frequency Specificity of Tone-Pip Evoked Auditory Brain Stem Responses. *Ear and Hearing*, 2(6), 270–275.
- Kileny, P. R., & Magathan, M. G. (1987). Predictive value of ABR in infants and children with moderate to profound hearing impairment. *Ear and hearing*, 8(4), 217-221.
- Klein, A. J. (1984). Frequency and age-dependent auditory evoked potential thresholds in infants. *Hearing Research*, 16(3), 291–297.
- Laukli, E. (1983). High-pass and notch noise masking in suprathreshold brainstem response audiometry. *Scandinavian Audiology*, 12(2), 109–115.
<https://doi.org/10.3109/01050398309076233>
- Laukli, E., Fjermedal, O., & Mair, I. W. S. (1988). Low-frequency auditory brainstem response threshold. *Scandinavian audiology*, 17(3), 171-178.
- Lightfoot, G., & Kennedy, V. (2006). Cortical electric response audiometry hearing threshold estimation: accuracy, speed, and the effects of stimulus presentation features. *Ear and Hearing*, 27(5), 443–56.
- Luck, S. J. (2005). *An Introduction to the Event-Related Potential Technique*. Cambridge, Mass: MIT Press.
- Mauldin, L., Jerger, J., N, Y., Galambos R, H. K., Yamada O, Y. T. Y. H. et al, Suzuki M, S. J., Schulman-Galambos C, G. R. (1979). Auditory Brain Stem Evoked Responses to Bone-Conducted Signals. *Archives of Otolaryngology - Head and Neck Surgery*, 105(11), 656–661.

- Mackersie, C., Down, K. E., & Stapells, D. R. (1993). Pure-tone masking profiles for human auditory brainstem and middle latency responses. *Hearing research*, 65(1), 61-68.
- McConnell, F. E. |Ward. P. H. . E. (1967). Deafness in Childhood. Vanderbilt University Press, Nashville, Tennessee 37203.
- 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., Kempton, J. B., Creedon, T., & Trune, D. (1996). Rapid acquisition of auditory brainstem responses with multiple frequency and intensity tone-bursts. *Hearing Research*, 99 (1996) 38-46
- Mitchell, C. R., Kempton, B., Creedon, T. A., & Trune, D. R. (1999). The Use of a 56-Stimulus Train for the Rapid Acquisition of Auditory Brainstem Responses, 97207, 80–87.
- Nousak, J. M., & Stapells, D. R. (1992). Frequency specificity of the auditory brain stem response to bone-conducted tones in infants and adults. *Ear and Hearing*, 13(2), 87–95.
- Oates, P., & Stapells, D. R. (1997). Frequency specificity of the human auditory brainstem and middle latency responses to brief tones. I. High-pass noise masking. *The Journal of the Acoustical Society of America*, 102(6), 3597–3608. <https://doi.org/10.1121/1.420148>
- Olsho, L. W., Koch, E. G., Carter, E. A., Halpin, C. F., & Spetner, N. B. (1986).

- Pure-tone sensitivity of human infants. *The Journal of the Acoustical Society of America*, 80(S1), S123-S123.
- Orsini, R. M. (2004). A comparison of tone burst auditory brainstem response (ABR) latencies elicited with and without notched noise masking, 21.
- Pantev, C., Lagidze, S., Pantev, M., & Kevanishvili, Z. (1985). Frequency-specific contributions to the auditory brain stem response derived by means of pure-tone masking. *Audiology*, 24(4), 275-287.
- Parthasarathy, T. K., Borgsmiller, P., & Cohlman, B. (1998). Effects of repetition rate, phase, and frequency on the auditory brainstem response in neonates and adults. *Journal-American Academy Of Audiology*, 9, 134–140.
- 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. <https://doi.org/10.1375/audi.31.2.80>
- Picton, T. W., Ouellette, J., Hamel, G., & Smith, A. D. (1979). Brainstem evoked potentials to tonepips in notched noise. *The Journal of otolaryngology*, 8(4), 289.
- Picton, T. W. & John, M. S. (2004). Avoiding electromagnetic artifacts when recording auditory steady-state responses. *Journal of the American Academy of Audiology*.
- Prasher, D, Mula, M., & Luxon, L. (1993). Cortical evoked potential criteria in the objective assessment of auditory threshold: a comparison of noise induced hearing loss with Meniere's disease. *Journal of Laryngology and Otology*, 107, 780–786

- Rance, G., Roper, R., Symons, L., Moody, L.-J., Poulis, C., Dourlay, M., & Kelly, T. (2005). Hearing threshold estimation in infants using auditory steady-state responses. *Journal of the American Academy of Audiology, 16*(5), 291–300. <https://doi.org/10.3766/jaaa.16.5.4>
- Rance, G., Tomlin, D., & Rickards, F. W. (2006). Comparison of Auditory Steady-State Responses and Tone-Burst Auditory Brainstem Responses in Normal Babies. *Ear and Hearing, 27*(6), 751–762.
- Schmullian, D., Swanepoel, D., & Hugo, R. (2005). Predicting pure-tone thresholds with dichotic multiple frequency auditory steady state responses. *Journal of the American Academy of Audiology, 16*(1), 5-17.
- Sininger, Y. S., Abdala, C., & Cone-Wesson, B. (1997). Auditory threshold sensitivity of the human neonate as measured by the auditory brainstem response. *Hearing research, 104*(1), 27-38.
- Small, S. A., & Stapells, D. R. (2004). Artifactual responses when recording auditory steady-state responses. *Ear and Hearing, 25*(6), 611–623.
- Stapells, D. R., Picton, T. W., Perez-Abalo, M., Read, D., & Smith, A. (1985). Frequency specificity in evoked potential audiometry. *The auditory brainstem response, 147-177*.
- Stapells, D. R. (1989). Auditory brainstem response assessment of infants and children. In *Seminars in Hearing* (Vol. 10, No. 3, pp. 229-251).
- Stapells, D. R., Picton, T. W., Durieux-Smith, A., Edwards, C. G., & Moran, L. M. (1990). Thresholds for short-latency auditory-evoked potentials to tones in

notched noise in normal-hearing and hearing-impaired subjects. *Audiology*, 29(5), 262-274.

Stapells, D. R. (2000). Threshold Estimation by the Tone-Evoked Auditory Brainstem Response: A Literature Meta-Analysis. *Journal of Speech-Language Pathology and Audiology*, 24(2), 74–83.

Stapells, D. R. (2002). The tone-evoked ABR : Why it's the measure of choice for young infants. *The Hearing Journal*, 55(11), 14–18.

Stapells, D., Picton, T., & Durieux-Smith, A. (1994). Electrophysiologic measures of frequency-specific auditory function. *Principles and applications in auditory evoked potentials*, 251-283.

Stapells, D. R., Gravel, J. S., & Martin, B. a. (1995). Thresholds for auditory brain stem responses to tones in notched noise from infants and young children with normal hearing or sensorineural hearing loss. *Ear and Hearing*, 16(January), 361–371. <https://doi.org/10.1097/00003446-199508000-00003>

Stockard, J. E., Stockard, J. J., & Coen, R. W. (1983). Auditory Brain Stem Response Variability in Infants. *Ear and Hearing*, 4(1), 11–23.

Stueve, M. P., & O'Rourke, C. (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), 125-136.

Suzuki, J. I., Kodera, K., & Yamada, O. (1984). Brainstem response audiometry in newborns and hearing-impaired infants. *Sensory evoked potentials*, 1, 85-93.

- Tsui, B., Wong, L. L., & Wong, E. C. (2002). Accuracy of cortical evoked response audiometry in the identification of non-organic hearing loss. *International journal of audiology*, 41(6), 330-333.
- Weber, B. A., & Roush, P. A. (1995). Use of maximum length sequence analysis in newborn hearing testing. *Journal of the American Academy of Audiology*, 6(2), 187–190.
- Werner, L. A., Folsom, R. C., & Mancl, L. R. (1994). The relationship between auditory brainstem response latencies and behavioral thresholds in normal hearing infants and adults. *Hearing Research*, 77(1–2), 88–98. [https://doi.org/10.1016/0378-5955\(94\)90256-9](https://doi.org/10.1016/0378-5955(94)90256-9)
- Wu, C. Y., & Stapells, D. R. (1994). Pure-tone masking profiles for human auditory brainstem and middle latency responses to 500-Hz tones. *Hearing research*, 78(2), 169-174.
- Yoshinaga-Itano, C., Sedey, A. L., Coulter, D. K., & Mehl, A. L. (1998). Language of early- and later-identified children with hearing loss. *Pediatrics*, 102(5), 1161–71.
- Zielhuis, D. A., Heuvelmans-Heinen, E. W., Rach, D. H., Broek, P., & Zielhuis, G. A. (1989). Environmental Risk Factors for Otitis Media with Effusion in Preschool Children. *Scand J Prim Health Care*, 7, 33–8.