

ANALYSIS OF AUDITORY BRAINSTEM RESPONSE  
TO NARROW BAND LEVEL SPECIFIC CE-CHIRP IN  
INFANTS

BY

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International Islamic University Malaysia

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## ABSTRACT

Auditory brainstem response (ABR) is one of the audiological tests used for hearing threshold estimation in infants, especially those under six months of age. The conventional ABR test is considered a time-consuming procedure because of the limitation in the current acoustic stimuli (e.g., click and tone burst) and ABR stimulus parameters that resulted in an extension of the test session. Hence, the present study proposes the latest acoustic stimulus, namely narrow band level specific (NB LS) CE-Chirp and F-test multiple points (Fmp), to address this issue. The combination of frequency specific stimulus and Fmp is foreseen to lessen the ABR assessment period, reduce the number of patients lost to follow up due to miscellaneous factors (i.e., financial and parents' limited annual leave) and decrease the age of audiological diagnosis for early aural rehabilitation management to promote good health, well-being, and quality education opportunities for all ages; as defined in Sustainable Development Goal (SDG) of United Nations Educational, Scientific and Cultural Organization (UNESCO). This study aimed to investigate the ABR findings from NB LS CE-Chirp stimulus in newborn infants in comparison with the ABR elicited from tone burst stimulus in terms of amplitude, absolute latency, hearing threshold estimation, and test time based on two stopping criteria (i.e., signal-to-noise ratio (SNR) objective algorithm; Fmp and visual detection). The current study conducted ABR assessment in 50 infants (27 males and 23 females) aged below 6 months old with normal middle ear conditions and passed the neonatal hearing screening. The ABR using NB LS CE-Chirp and tone burst stimuli were tested at three specific frequencies of 500, 1000, and 4000 Hz at 70 and 40 dBnHL using a 33.33 Hz stimulus rate. The result indicated that the ABR elicited from NB LS CE-Chirp and tone burst stimuli showed similar wave V amplitude across the frequencies and intensity range tested except for 1000 Hz at 70 dBnHL. In contrast, the ABR to NB LS CE-Chirp wave V amplitude was slightly larger than the ABR to tone burst at 40 dBnHL in all frequencies tested. The NB LS CE Chirp has significantly shorter offset absolute latencies and lower hearing threshold estimation than ABR in tone burst stimulus. The ABR to NB LS CE-Chirp also has significantly shortest test time in identifying wave V using  $Fmp \geq 3.1$  and visual detection compared to ABR to tone burst. In conclusion, ABR to NB LS CE-Chirp with SNR objective algorithm detection has the potential for infants' hearing assessment application as it elicits the shortest test time and lower hearing threshold estimations for audiogram prediction. However, the quality of the recording between the ABR to NB LS CE-Chirps was marginal compared to the ABR elicited from tone burst stimulus.

## ملخص البحث

تُعدّ استجابة جذع الدماغ السمعية (ABR) إحدى الاختبارات السمعية المستخدمة لتقدير عتبة السمع عند الأطفال الرضع، وخاصة للأطفال الذين تقل أعمارهم عن ستة أشهر. ومن الشائع أنّ اختبار ABR إجراءً يستغرق وقتاً طويلاً، وذلك لأنّ القيود الموجودة في المحفزات الصوتية الحالية؛ على سبيل المثال، محفز أصوات النقرات أو النغمات، ثمّ معلمات التحفيز ل ABR التي أدّت إلى تمديد دورة الاختبار. ومن أجل معالجة هذه القضية، تعرض هذه الدراسة أحدث المحفز الصوتي وهو محفز NB LS CE-Chirp، وكذلك التحليل الاحصائي لاختبار (ف) لعدة نقاط (Fmp). ومن المتوقع أنّ الجمع بين محفز التردد المحدد و Fmp سيؤدي إلى التقليل في فترة التقييم ل ABR، ثم سيؤدي إلى التقليل في عدد المرضى الذين سقطوا للمتابعة بسبب عوامل متنوعة؛ على سبيل المثال، المال والإجازة السنوية المحدودة للوالدين. وإضافة إلى ذلك، هذا الجمع أيضاً سيؤدي إلى التخفيض في سن التشخيص السمعي لإدارة إعادة التأهيل السمعي المبكر في تعزيز الصحة الجيدة، والرفاهية، وفرص التعليم الجيدة لجميع الأعمار؛ وذلك على النحو المحدد في أهداف التنمية المستدامة (SDG) لمنظمة الأمم المتحدة للتربية والعلم والثقافة (UNESCO). تهدف هذه الدراسة إلى التعرف على نتائج ABR التي حصلت من محفز NB LS CE-Chirp عند الأطفال حديثي الولادة، مقارنةً ب ABR المستنبطة من محفز أصوات النغمات، وذلك من حيث السعة، والخفاء المطلق، وتقدير عتبة السمع، ووقت الاختبار بناءً على معيارين للتوقف؛ وعلى سبيل المثال، الخوارزميات الموضوعية لنسبة الإشارة إلى الضوضاء (SNR)، و Fmp، والكشف البصري. في هذه الدراسة، تقوم الباحثة بإجراء التقييم ل 50 طفلاً رضيعاً (27 ابناً و 23 بنتاً) حيث تقل أعمارهم عن ستة أشهر، وهؤلاء الأطفال لديهم الأذن الوسطى السليم وهم يجتازون فحص السمع للأطفال حديثي الولادة. وإضافة إلى ذلك، تم اختبار ABR باستخدام محفز NB LS CE-Chirp ومحفزات أصوات النغمات بثلاثة ترددات، حيث تنحصر الترددات على 500، و 1000، و 4000 هرتز (Hz) عند 70 و 40 ديسيبل لمستوى السمع العادي (dBnHL) وباستخدام معدل التحفيز 33.33 Hz. وتشير نتيجة الدراسة إلى أنّ ABR المستنبطة من محفز NB LS CE-Chirp ومحفز أصوات النغمات تعرض مدى التردد المماثل للموجة V عبر الترددات ومجموعة من الشدة التي تم اختبارها، باستثناء تردد 1000 Hz عند 70 dBnHL. وإضافة إلى ذلك، تكون ABR إلى مدى التردد للموجة V في NB LS CE-Chirp أكبر بقليل من ABR إلى محفز أصوات النغمات عند 40 dBnHL عبر جميع الترددات التي تم اختبارها. فإنّ محفز NB LS CE-Chirp له أقصر خفاء مطلق الموازن بشكل ملحوظ وأقل تقدير لعتبة السمع، بالمقارنة إلى ABR إلى محفز

أصوات النغمات. وتمتلك ABR إلى NB LS CE-Chirp أيضا أقصر وقت للاختبار في تحديد الموجة  $V$  باستخدام  $F_{mp} \geq 3.1$  والكشف البصري، مقارنةً ب ABR إلى محفز أصوات النغمات. وخلاصة القول، فإنّ ABR إلى NB LS CE-Chirp بالخوارزميات الموضوعية ل SNR لها القدرة على تطبيق تقييم السمع للأطفال الرضع، وذلك لأنها تستنبط أقصر وقت للاختبار وأقل تقديرات لعتبة السمع في تنبؤ تخطيط السمع. وعلى الرغم من ذلك، فإنّ جودة التسجيل بين ABR إلى NB LS CE-Chirp هامشية بالمقارنة إلى ABR المستنبطة من محفز أصوات النغمات.



## APPROVAL PAGE

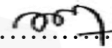
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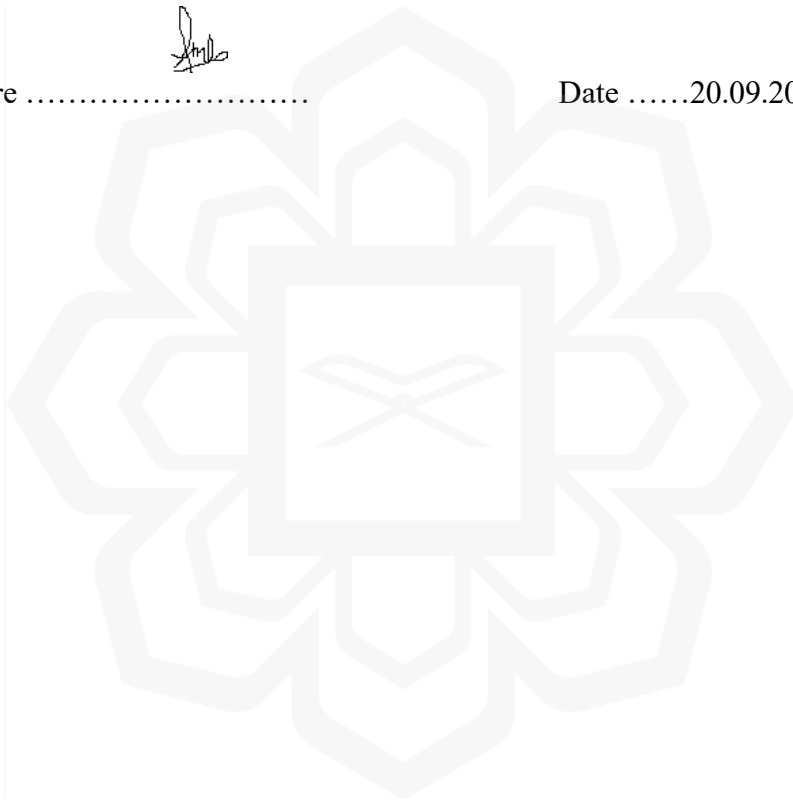
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## DECLARATION

I hereby declare that this dissertation is the result of my investigations, except where otherwise stated. I also declare that it has not been previously or concurrently submitted as a whole for any other degrees at IIUM or other institutions.

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*This thesis is dedicated to my late father, Mr. Mohamad Noor Abdul Jamil, and my mother, Mrs. Rabiah Hamzah, for laying the foundation for what turned out to be my life.*



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## LIST OF SYMBOLS

=	Equal to
$\geq$	Equal or larger than
>	Larger than
<	Smaller than
%	Percent
:	Ratio
$\alpha$	Alpha
$\beta$	Power
d	Effect size
dB	Decibels
dBnHL	Decibels normal hearing level
dBppeSPL	dB peak-equivalent Sound Pressure Level
Hz	Hertz
ms	milliseconds
p	Significant value
RETSPL	Reference Equivalent Threshold Sound Pressure Level.
r	Wilcoxon signed-rank test effect size
Z	Z score
$\chi^2$	Friedman test

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## LIST OF ABBREVIATIONS

ASHA	American Speech-Language-Hearing Association
ABR	Auditory Brainstem response
AABR	Automated Auditory Brainstem response
BSA	British Society of Audiology
CE-Chirp	Claus Elberling Chirp
CPS	Click per second
DPOAE	Distortion product of otoacoustic emission
EEG	Electroencephalogram
Fmp	F test multiple points
IIUM	International Islamic University Malaysia
IQR	Inter quartile range
IREC	IIUM Research Ethics Committee
JCIH	Joint Committee on Infant Hearing
JKTA	Audiologists' Technical Committee
LS CE-Chirp	Level specific CE-Chirp
MOH	Ministry of Health
MREC	Medical Research and Ethics Committee
NB CE-Chirp	Narrow band CE-Chirp
NB LS CE-Chirp	Narrow band level specific CE- Chirp
NHS	Newborn Hearing Screening
NHSP	Newborn Hearing Screening Programme
OAE	Otoacoustic emission
SASMEC	Sultan Ahmad Shah Medical Centre
SNR	Signal-to-noise ratio
SPSS	Statistical Package for the Social Sciences
TEOAE	Transient product of otoacoustic emission
UNHS	Universal Neonatal Hearing Screening
CNVIII	Vestibulocochlear Nerve

# **CHAPTER ONE**

## **INTRODUCTION**

### **1.1 PREFACE**

This chapter provides an overview of the current study. The background of the study comprises the Early Hearing Detection and Intervention (EHDI), the issue surrounding Universal Newborn Hearing Screening (UNHS), and proposed solutions for the current diagnostic ABR procedures for EHDI are discussed. The last part of the chapter discusses the study's novelty, significance, and thesis structure.

### **1.2 BACKGROUND OF THE STUDY**

Hearing is one of the five human senses and the most essential human sensory for developing speech and language knowledge. Hearing is vital to create a healthy lifestyle, good well-being, and quality education opportunities for all ages, aligned with the Sustainable Development Goal (SDG) of the United Nations Educational, Scientific, and Cultural Organization (UNESCO) Number Three: Good Health and Well-being. In Malaysia, one of the initiatives is to identify infants with congenital hearing loss by following the Joint Committee on Infant Hearing (JCIH) guidelines. The JCIH (2019) introduced early hearing detection and intervention (EHDI) program to screen newborns as early as day 1 of life up to 1 month of age, diagnose hearing loss before 2 months old, and for early aural intervention before 3 months. The neonatal hearing screening (NHS) program is a part of the EHDI framework to identify infants with hearing loss as early as possible, and the current standard practice in developing countries is to detect hearing loss among children at a very early age. According to EHDI (2019), the NHS program can be converted into Universal Neonatal Hearing Screening (UNHS) program if the coverage rate of NHS is more than 95%.

EHDI program in Malaysia, unlike in many other countries, as it is crucial for the early identification of hearing loss in infants. With proper audiological follow-up,

they can provide timely interventions (Malaysia Ministry of Health Screening Committee, 2014). Audiological services in Malaysia face challenges such as ensuring access to newborn hearing screening (NHS) programs, especially in rural and remote areas; there may also be issues related to delayed follow up services and coordination between different healthcare workers.

The auditory brainstem response (ABR) assessment is one of the tools used in UNHS to detect hearing loss. ABR is an assessment to estimate hearing threshold level typically in infants from birth to six months. ABR assessment is a crucial tool for hearing threshold estimation in response to the acoustic stimuli (e.g., click, tone burst, chirp, CE-Chirp, NB CE-Chirp, LS CE-Chirp and NB LS CE-Chirp); see Section 2.3.2.3. ABR is an assessment where the patient needs to be calm and relaxed; if possible, the patient needs to sleep. Therefore, there is a need for sedation to complete the ABR assessment; conventional ABR stimuli (e.g. click and tone burst) require extended hours to be completed in a session that leads to more than one session, limited ABR appointment slots in clinical settings, and prolonged waiting time lead to the investigation of the current study.

Malaysia Ministry of Health started the UNHS program with two government hospitals in 2011, and until recently, 48 out of 60 government hospitals provided the UNHS program. However, the coverage rate of UNHS in Malaysia is still below par at 59.86 % (*Jawatankuasa Teknikal Audiologi (JKTA, 2022)* or Audiologist Technical Committee, 2022). The average age of hearing loss detection in Malaysian public hospitals implementing UNHS programs has shown little change since 2013, with 4.4 months. It has been reduced to 4.3 months from 2014 to 2019 (Malaysia Ministry of Health, 2019b, 2014b). From the High-Risk Neonatal Hearing Screening (HRNHS) program, the average detection age for hearing loss between 2013 and 2019 began at 5.3 months, then improved to 4.5 months, and subsequently rose to 6.0 months (Malaysia Ministry of Health, 2019a, 2014a). Previous studies showed earlier hearing loss detection leads to better intervention and prognosis (Ching, 2015; Grey et al., 2018). Without UNHS, late identification of children with hearing impairment may occur, limiting speech, language, and cognitive development.

The audiology field in Malaysia is moving towards an effective and systematic

UNHS program for early diagnosis of hearing loss in infants; which enhanced by the inclusion of ABR test in the UNHS program. As mentioned above, ABR is an assessment that confirms hearing threshold estimations, especially in infants who fail hearing screening. Thus, delayed diagnosis can significantly influence the efficacy of aural rehabilitation. Early identification of hearing loss is a critical factor in optimizing language and speech development outcomes reported significantly higher language quotients in children diagnosed with hearing loss at 6 months of age than those diagnosed later (Yoshinaga-Itano et al. 2017, 2018). Similarly, Ching et al. (2017) reported a more excellent speech development in children who initiated hearing aid use at 3 months or cochlear implantation at 6 months, relative to those who began intervention at 2 years of age. Moreover, Moeller (2000) and Yoshinaga-Itano et al. (2017) found that children who enrolled in early intervention programs before 11 months of age exhibited enhanced vocabulary and verbal reasoning abilities. Consequently, the pursuit of high accuracy and efficiency in ABR testing is essential to facilitate timely diagnosis and intervention in accordance with EHDI guidelines. This unidentified hearing impairment led to a degenerative in auditory development (Graham, et. al, 2021; Yoshinaga-Itano et al., 1998). Lack of early identification and language access for deaf or hard-of-hearing infants can lead to significant delays in communication abilities, cognitive, academic, social-emotional development, and quality of life (JCIH, 2019; Rissman et. al, 2006).

### **1.3 ISSUES SURROUNDING UNIVERSAL NEONATAL HEARING SCREENING (UNHS)**

ABR assessment is one of the assessments for hearing diagnosis to estimate hearing threshold. UNHS program has issues with late diagnosis among the infant population. The conventional frequency specific (FS) ABR which uses tone burst as stimulus to estimate hearing threshold across frequencies needs a longer time to complete ABR assessment. The previous FS ABR using tone burst produced less robust ABR waveform and time-consuming to obtain the ABR true threshold prolonged the ABR testing time. As required by EHDI, infants should undergo FS ABR, which is tone burst stimulus, to get comprehensive information on hearing threshold estimations after failed UNHS before 3 months of age and early intervention by 6 months of age (JCIH, 2000).

This comprises enlightening the multidisciplinary teamwork to create the UNHS as a part of EHDI (Muse et al., 2013; JCIH, 2019). Moreover, ABR recordings using tone burst stimulus need the infant in a quiet or sleep state to entail a complete sweep cycle (e.g., 2000 sweeps) for comprehensive signal averaging of neural responses and to improve signal-to-noise ratio (SNR) in order to obtain the better quality of the ABR; thus, patient need to come for more than one session (i.e., two to three sessions) to complete the ABR assessment (Cain et al., 2020). However, there is limited study on NB LS CE-Chirp and the use of objective algorithm Fmp as stopping criterion in the current clinical practice of ABR, especially in infants. The ABR procedure usually requires 45 minutes to complete the recording process in each ear, not including the time spent on test preparation (Kerneis et al., 2023; Hayes, 2003).

#### **1.4 PROPOSED SOLUTIONS FOR THE CURRENT DIAGNOSTIC ABR PROCEDURES FOR EHDI**

Despite using the routine clinical ABR parameter, the suggestion of ABR parameter for the present study is to improve the ABR testing time by using narrow band level specific (NB LS) CE-Chirp and objective algorithm  $Fmp \geq 3.1$  as stopping criterion in which the ABR signal is expected three times more robust than the noise. Objective methods can improve ABR testing accuracy and sensitivity. As Fmp is a statistical analysis, the ABR results show clinical value when stimuli are presented at intensities above the ABR threshold. For details on the proposed ABR parameter, see Sections 2.3.2.2, 4.2, and 5.2.

The main goal of this study is to improve the performance of ABR using NB LS CE-Chirp stimulus and objective algorithm Fmp for faster ABR recordings in infants. This thesis focuses on detecting Auditory Brainstem Responses (ABR) using Fmp as objective detection methods and facilitating audiologist. The Fmp is a statistical measure of signal -to-noise-ratio (SNR) within a recording, providing a confidence level for ABR waves reproducibility. A higher Fmp value indicates better ABR waveform quality and greater confidence of ABR waves presence or absence which facilitate in shorter testing time and better objectivity of the ABR results. Traditionally, ABR detection relied on visual detection methods. Although this approach can be sensitive,

it is inherently subjective and prone to inter-rater variability, making it challenging to quantify false-positive and false-negative rates (Vidler & Parker, 2004; Don & Elberling, 1996). Consequently, the reliability and objectivity of ABR detection through visual inspection are compromised. The primary goal of these methods is to enhance the inter-rater reliability of visual detection and accelerate the response detection process.

For more than 50 years of ABR in the audiology industry, the development of ABR acoustic stimuli has changed through time to accommodate the information and precision of hearing threshold for better management and intervention for the hearing impaired population. The NB LS CE-Chirp is a frequency specific stimulus with intensity dependent and latency variations. The NB LS CE-Chirp stimulus is developed to compensate for some shortages in tone burst stimulus. NB LS CE-Chirp elicited greater ABRs waveform and improved signal-to-noise ratio (SNR) of the ABR recording; thus, larger amplitude and clearer waveform and shorter test time were observed in adult population (Elberling et al., 2010; Dzulkarnain et al., 2018).

## **1.5 SIGNIFICANCE OF THE STUDY**

The current study aims to investigate the outcome and time efficacy of NB LS CE-Chirp stimulus for auditory brainstem response (ABR) testing in infants. This study explored the ABR parameters using the objective algorithm Fmp of 3.1, which can lessen testing time and improve the quality of ABR recordings (Dzulkarnain et al., 2018; Di Scipio & Mastronardi, 2018; Bal et al., 2022). The impact of the study is foreseen for shorter ABR testing time and more babies tested in a day and decreases the long waiting time for an appointment, especially in clinical settings adapting the EHDI program (Severn et al., 2012).

The shorter the ABR test time, the higher the chance that the ABR test can be done in a single audiology appointment. Thus, ABR follow-up appointments, sedation, and reliable behavioural hearing assessments prior to six months of age necessitates the use of estimated thresholds for early hearing aid fittings. This introduces a significant temporal gap between initial amplification and the verification of hearing levels through

behavioural measures. Moreover, even accurate initial hearing threshold estimation does not guarantee optimal or sufficient hearing aid fittings, as noted by Dillon (2001).

## **1.6 STRUCTURE OF THE THESIS**

This thesis consists of six chapters. The current chapter briefly describes the overall idea of the study, which comprises the background, significance, and structure of the thesis. Chapter two emphasises the literature review on Early Hearing Detection and Intervention (EHDI), Newborn Hearing Screening (NHS), Universal Neonatal Hearing Screening (UNHS), Auditory Brainstem Response (ABR) meticulously including ABR functions, neural generators, detection types, stimulus types, factors affecting the results, and analysis types. Chapter three focuses on the problem statement, research objectives, and hypotheses. Chapter four focuses on experiment one, which studies the NB LS CE-Chirp and tone burst characteristics in terms of the ABR i. amplitude, ii. latency, and iii. hearing threshold estimation. This chapter consists of a detailed methodology, results, and discussion for experiment one. Chapter five discusses experiment two, which explores the ABR acquisition time with numerous combinations of stimulus types and stopping criteria. This chapter comprises detailed methodology, results, and discussion for experiment two. Lastly, chapter six discusses the summary of the thesis, clinical implications, limitations of the study, and recommendations for future research.

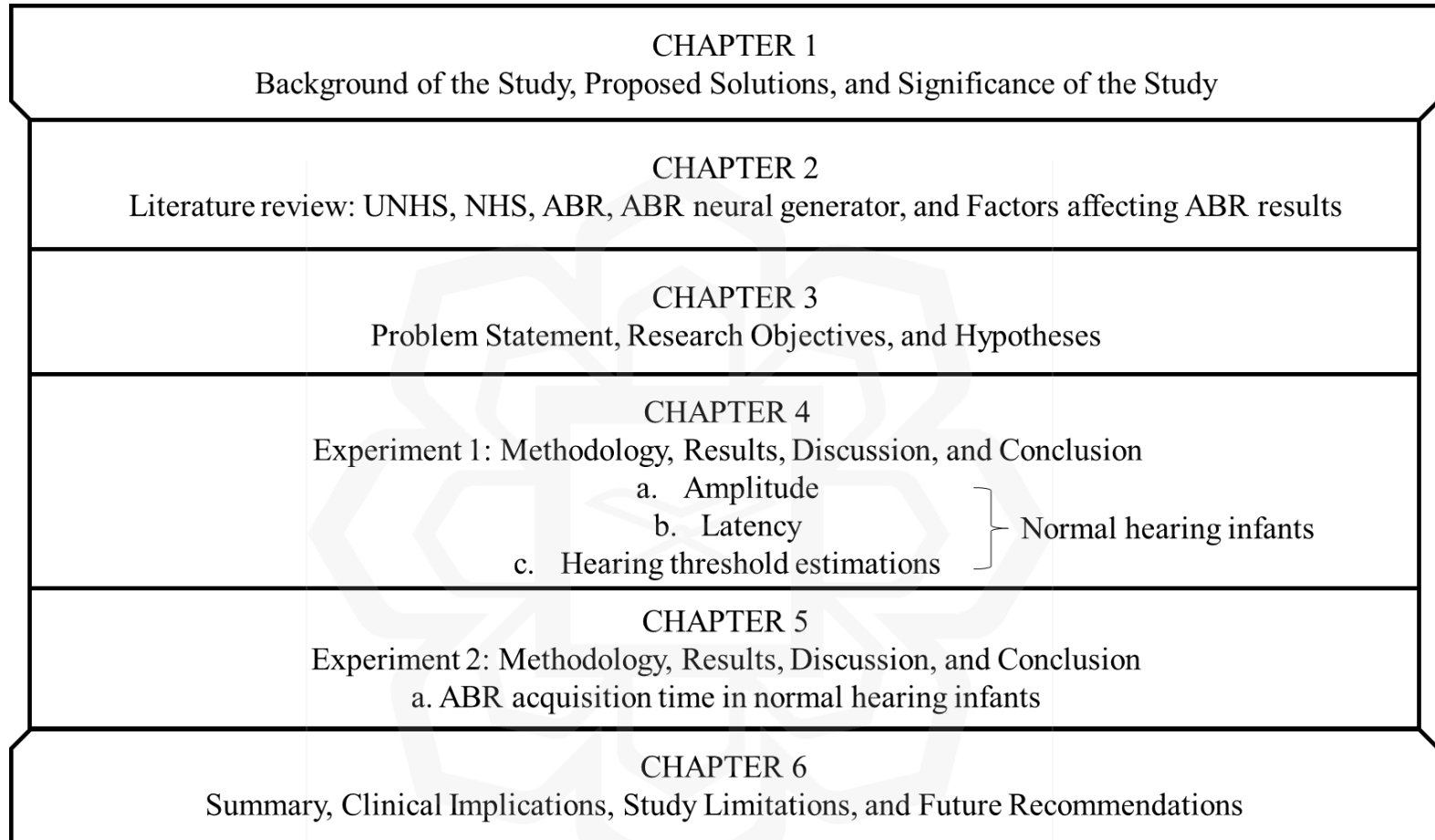


Figure 1.1 Summary of the thesis structure.

## **CHAPTER TWO**

### **LITERATURE REVIEW**

#### **2.1 INTRODUCTION**

This chapter focuses on the literature review of early hearing detection and intervention (EHDI), newborn hearing screening (NHS), ABR assessment emphasis on the usage, ABR neural generators, and the factors affecting the ABR results. The latter part of this chapter discusses two acoustic stimuli that will be used in this current study which are narrow band level specific (NB LS) CE-Chirp and tone burst.

#### **2.2 EARLY HEARING DETECTION AND INTERVENTION (EHDI)**

Early hearing detection and intervention (EHDI) is an initiative focused on early hearing screening, diagnosis, and intervention to lessen the impact of hearing loss in infants (JCIH, 2007; JCIH, 2019). The EHDI program is guided by two primary objectives. First, as recommended by the JCIH (2007), it advocates for the 1-3-6 benchmark for infants in which all infants should undergo hearing screening by 1 month of age, and all infants who do not pass hearing screening should undergo hearing diagnostic test to confirm the hearing level before the age of 3 months old and given aural intervention by 6 months of old, or as soon as possible for infants in neonatal intensive care unit (NICU). On the latest update of the revised EHDI (JCIH, 2019), the 1-2-3 benchmark recommends hearing screening by 1 month old, diagnosis before 2 months old, and intervention by 3 months old. EHDI aims to optimize language and communication skills, literacy development, and overall psychological well-being of children with hearing impairment (JCIH 2007; JCIH, 2019). Hence, the EHDI (2019) procedures should be readily accessible to families through EHDI services and devices.

### **2.2.1 Newborn Hearing Screening (NHS)**

Newborn Hearing Screening (NHS) is a primary step in the EHDI program and has been applied in several countries, permitting the early identification and management of hearing impairment in infants (Hrncic et al., 2019). For nearly the past two decades, NHS has become the standard protocol in Malaysia, whether it is universal neonatal hearing screening (UNHS) or high-risk hearing screening (HRHS). NHS has significantly minimized the age detection for hearing loss in infants (Ayas & Yaseen, 2021). Previously, the NHS program was a program that screened and diagnosed hearing levels within the first 6 months (JCIH, 2007; Rohfls et al., 2010). However, in 2019 JCIH recommended 1-2-3 benchmarks, see Section 2.2.

The NHS program aims to facilitate the early identification and intervention of neonatal hearing impairment, thereby qualifying adverse effects on speech and language acquisition, educational attainment, and overall pediatric development (Kirkim, et. al, 2008). Newborns who failed hearing screening in the postnatal ward must be reassessed in the next following month at the audiology clinic to confirm the diagnosis. Early hearing loss detection and intervention are crucial for the development in children specifically in terms of linguistic, cognitive, and social skills (Sabo et al., 2016).

#### **2.2.1.1 Universal Newborn Hearing Screening (UNHS)**

Universal Newborn Hearing Screening (UNHS) is a program for early identification of congenital and acquired hearing loss. Early identification of hearing loss is imperative to prevent problems associated with speech, language, social life, and education from falling at a later stage in life (WHO, 2021). In Malaysia, the UNHS program was introduced by the Audiology Services Department at the Malaysia Ministry of Health in 2011. To date, the UNHS program in Malaysia are conducted in 48 government hospitals. The successful UNHS program is influenced by a few factors, which were extra screening equipment, more qualified staff and enhanced screening coverage (Abdullah et al; 2018; Ismail et al., 2018).

The stage of implementation and coverage of the UNHS program differ

significantly across the world. All infants should be screened and assessed to identify hearing loss before 3 months of age. High risk newborns population are probably to miss around 50% of infants with no risk for hearing loss (Wroblewska-Seniuk et al., 2017). The objective of the UNHS program is to detect and identify hearing loss in newborns as early as possible and to proceed with appropriate intervention (WHO, 2021).

## **2.2.2 Equipment used in EHDI**

This section discusses three primary tools used in early hearing detection and intervention (EHDI), which are behavioural observation audiometry (BOA), otoacoustic emissions (OAE), and automated auditory brainstem response (AABR) for hearing screening.

### **2.2.2.1 Otoacoustic emissions (OAE)**

The otoacoustic emissions (OAE) test is a tool to test cochlear function, specifically using a sensitive microphone within a probe that records outer hair cells (OHCs) responses towards acoustic stimuli (Kemp et al., 2002; Kemp et al., 1978; Northern & Downs, 2002). There are two types of OAE which are spontaneous OAE (SOAE) and evoked (EAOE). SOAE recorded the continuous sounds produced by the ear without any external acoustic stimulation. In contrast, for EAOE were generated in response to an acoustic stimulus presented to the ear. For EAOE, there are 3 main types which are transient OAE (TEOAE), distortion product OAE (DPOAE), stimulus-frequency OAE (SFOAE). TEOAE which produced brief and broadband stimuli such as click and tone burst providing a frequency specific of cochlear function and highly sensitive to cochlear pathology which made ideal for NHS (Kemp et al., 2002; Northern & Downs, 2002). SFOAE using continuous pure tone stimuli and making it difficult to distinguish the emission from the stimulus; thus, it rarely used clinically (Kemp et al., 2002).

Previous research indicates that DPOAEs which produced two simultaneous pure tones are widely used in clinical settings for hearing assessment, particularly in

NHS programs and monitoring cochlear function in various populations (Abdala & Visster-Dumont, 2001; Papping et al., 2022). Earlier studies consistently demonstrate the sensitivity and specificity of DPOAEs in detecting cochlear dysfunction, including hearing loss of various degrees and configuration levels (Levit et al., 2015; Reddy et al., 2019). There are particularly effective in identifying mild to moderate sensorineural hearing loss (SNHL), where outer hair cell (OHC) function may be affected. Moreover, DPOAEs have shown efficacy in distinguishing between sensory and neural components of hearing loss, aiding in differential diagnosis (Johnson, 2005).

Challenges highlighted in the literature including variability in DPOAE responses among individuals which can be influenced by factors such as age, ear canal acoustics, and environmental noise (Kemp, 1978). Addressing these challenges involves standardizing testing protocols, establishing normative data for diverse populations, and ensuring adequate training for audiologists and technicians conducting DPOAE measurements (van Dyk et al., 2015). Overall, the literature supports DPOAEs as a valuable tool in audiology practice, offering a non-invasive and objective assessment of cochlear function that complements traditional audiometry (Kemp, 1978; Akinpelu et al., 2014).

#### ***2.2.2.2 Automated auditory brainstem response (AABR)***

Auditory brainstem response (ABR) is an auditory evoked potential that reflects ongoing electrical activity from the vestibulocochlear nerve (CN VIII) up to the brainstem (Jewett & Williston, 1971). Automated auditory brainstem response (AABR) is a screening version of ABR that assesses neural responses from the brainstem, distinguishing it from ABR which is used diagnostically. AABR is noted for its comprehensive assessment of neural hearing pathways, making it more sensitive than OAE screening for detecting neural hearing loss (JCIH, 2000; Sheng et al., 2021). This test is particularly valuable in newborn hearing screening programs, especially in infants who may not be able to participate in behavioural audiometric testing.

### **2.2.2.3 Behavioural observation audiometry (BOA)**

Behavioural observation audiometry (BOA) is an assessment that observes infants' hearing via the reflexes towards the sound given (Downs & Sterritt, 1964). The advantages of BOA are cost-effectiveness, low maintenance, ease of administration, rapid use of specific multi frequency stimuli, and the ability to detect severe to profound bilateral hearing loss (Hall, 1992; Mauk et al., 1993; Morton & Nance, 2006). However, BOA has limitations as it relies on subjective judgment for response detection (Durieux-Smith & Jacobson, 1985; Mauk et al., 1993; Alberti et al., 1983), often underestimates the degree of hearing loss (Karikoski et al., 1998; Parving et al., 1981), struggles with identifying specific hearing loss configurations (Taylor & Mencher, 1972), lacks of ear specific information, and is influenced by the infant's arousal state (Bonino & Leibold; 2017; Northern & Downs, 2002; BSA 2019).

## **2.3 AUDITORY BRAINSTEM RESPONSE (ABR)**

ABR is an assessment of far-field electrophysiology response recorded from the scalp for hearing thresholds estimation via a recording of the transmission times (i.e., latencies) and quantifying the amplitudes (Jewett & Williston, 1971; Young et al., 2022). Jewett and Williston (1971) first described brainstem wave interpretation. The ABR components are generated by neuronal activity in the ear, auditory nerve, brainstem nuclei, and fibre tracts of ascending auditory pathways (Moller, 2006). The labelling of ABR is via Roman numerals (Jewett & Williston, 1971). This labelling component of evoked potential is tracked by a number that gives the normal values of the latency corresponding to the neural generators (Moller, 2006) which will be discussed further in next subsection 2.3.1. Hecox and Galambos (1974) introduced the use of ABR for threshold estimation in infants, thus expanding the range of applications for this technique. In audiology clinics, ABR is widely used for pediatrics population and difficult to test patients (Zhou et al., 2012).

### 2.3.1 ABR Neural Generators

Neurogenic sources of the ABR extend from the distal auditory nerve to potentially the thalamic level (e. g., medial geniculate body). While the early components are relatively well understood, the origins of the later components remain complex and are still under investigation. Besides, the effects of central nervous system pathology on the ABR further solidify its role in diagnosing neurological conditions (Starr & Achor, 1975). The neural generator of ABR is measured from the cochlea up to the auditory brainstem (Moller & Jannetta, 1985). ABR is produced when an acoustic stimulus activates the hair cells in the cochlea and transforms the sound energy into an electrical signal (Moller & Jannetta, 1982a). Then, the electrical signal from the cochlea travels to the cochlear nucleus via the auditory nerve (Moller & Jannetta, 1983). This electrical signal codes the cues to the third order neurons, mostly located in superior olivary complex (SOC) (Moller & Jannetta, 1985). Next, the electrical signal codes the indications that enhance sound dispersion on the source of concurrent binaural ascending inputs to the lateral lemniscus (Hashimoto et al., 1981; Møller and Jannetta, 1982). Subsequently, the lateral lemniscus transmits the sound inputs to brainstem nuclei and eventually to the contralateral lateral lemniscus of the mesencephalon (Hashimoto et al., 1981; Moller & Jannetta, 1982). The inferior colliculus sited on the dorsal surface of the mesencephalon and function to combine ascending and descending information from auditory, i.e., input combination, pitch recognition, and frequency identification (Moller & Janneta 1982; Ito et al., 2016).

Five waves of ABR recordings are attained by signal averaging measurement from abundant runs. The ABR neural generator of wave I originates from the distal portion of the auditory nerve, wave II represents a proximal portion of the auditory nerve, wave III is the response of the cochlear nucleus, wave IV is generated by the nuclei of the SOC, and the most important part of ABR is wave V represents high pons which consists of lateral lemniscus and inferior colliculus (Moller & Jannetta, 1985). ABR wave I in newborns less than three months old resembles adult wave I (Cebulla et al., 2012). In contrast, waves III and V are prolonged in newborns because of incompleteness and constant maturation of the auditory pathway, see subsection 2.3.2.1.1 (Stipdonk et al., 2016). The overview of ABR neural generators is illustrated in Figure 2.1.

The positive peaks seen in the ABR waveform have been established as indicators of neural activity within the auditory brainstem, as these peaks correspond to the activation of specific neural structures along this auditory brainstem pathway (Rowe III, 1978). The neural generators of the ABR comprise the cochlear nuclei, superior olivary complex (SOC), lateral lemniscus, inferior colliculi, and medial geniculate nuclei, which transmit electrical signals to the auditory cortex collectively form the ascending auditory pathway (Moller, 2003, Felix et al., 2018). Wave I primarily reflects activity in the distal portion of the ipsilateral vestibulocochlear nerve, while wave II is predominantly generated by the proximal portion of the vestibulocochlear nerve, with potential contributions from its distal segment (Moller et al., 1985). Waves III and IV originate from neural activity within the lower brainstem, with wave III primarily generated by neurons in the ipsilateral cochlear nucleus, though small input from auditory nerve fibres. Conversely, other study indicates that wave III represents neural activity within the contralateral superior olivary complex (Moore, 1987) or originates from neural structures in the caudal lateral brainstem, trigeminal nerve (CN V) or between CN V and CN VIII may play an indirect role in the generation of evoked potentials possibly in proximity to the CN V (Moller et al., 1995).

Neural activities from the pons generate waves III and IV (Hashimoto et al., 1981). Moller et al. (1995) reported that wave IV was generated by the bilateral combination of activities in the SOC, cochlear nucleus, and neural activities in the nucleus of the lateral lemniscus. This contradicts with the findings from earlier studies found that wave IV was mainly generated from the inferior colliculus (Jewett, 1970; Lev & Sohmer, 1972). The discrepancy findings and indefinite neural generator for waves III and IV could be attributed to at least three reasons: i) the complexity of the ascending auditory system; thus, waves III and IV might represent neural activities from multiple concurrent neural sources; ii) some anatomical studies conducted on animals, thus, could not be generalized in human at least due to the disparity of anatomical size, and iii) insufficient amount of neural activities to precisely locate the neural generator (Hall et al., 1984; R., Moller Aage et al., 1985). Wave V represents activities at the termination of the contralateral distal lateral lemniscus and as it enters the contralateral inferior colliculus which is the most prominent peak of the ABR (Hamam & Purnami, 2020; Møller et al., 1988, 1995; Møller & Jannetta, 1983a; Moore, 1987). The interpeak latencies (IPL) of waves I-V represent action potentials conduction time from the

peripheral auditory system to the midbrain (Hood, 1998).

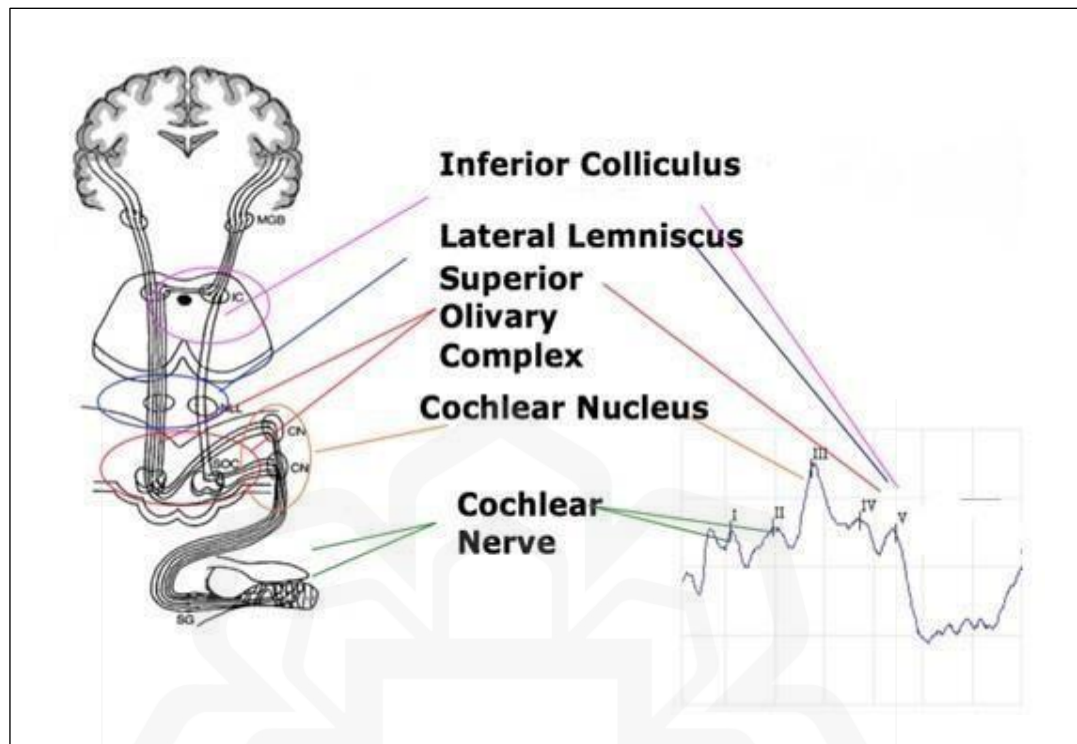


Figure 2.1 Overview of ABR neural generators

<https://www.audiologyonline.com/articles/evoked-potentials-part-1-good-23607>

### 2.3.2 ABR interpretation and analysis

The measurement of ABR recordings are the absolute latencies and amplitudes. The bandwidth of latency and amplitude need to be set appropriately to confirm small waveforms near the threshold are clear. The bandwidth of 0.025 to 0.100 microvolt ( $\mu\text{V}$ ) on the  $y$ -axis (i.e., amplitude) and 1 to 10 milliseconds (ms) on the  $x$ -axis (i.e., latency) is acceptable (Young et al., 2022). Three major peaks are usually observed in the first 10 ms of acoustic stimulation elicited waves I, III, and V as discussed in Section. 2.3.1 (Sloan, 2006). Amplitude is defined by the height of the peak wave to the subsequent trough (Rouillon et al., 2016). This wave amplitude depends on the intensity level and quantity of synchronous neural activity (Verhulst et al., 2016). ABR peak amplitude increases when more neural fibres are simultaneously activated (Rouillon et al., 2016). ABR latency is the duration between the stimulus onset and the peak of a wave

(Rasetshwane et al., 2013). As mentioned in Section 2.3.1, stimulus intensity level and age can influence the wave latencies (Rasetshwane et al., 2013). Wave latencies are found to be prolonged in infants and lessen with age (Rouillon et al., 2016). The ABR waveform response, whether it is clear or purely absent, is recorded at three consecutive levels parted by 5 or 10 dB (Elberling et al., 2010). Absence of ABR waveform is because lack of the myelination and conduction time which leads to auditory signal deprivation with actual temporal relation (Sinclair et al., 2017).

### **2.3.3 Factors Affecting ABR Results**

There are several factors that may affect the wave amplitudes, absolute latencies, and hearing threshold estimation in ABR. These factors are categorized as acquisition variables, stimulus variables, and subject variables.

#### ***2.3.3.1 Non-Pathological Factors***

The non-pathological factors that can influence the ABR results will be discussed in this subsection. Non-pathological factors include age, gender, body temperature, state of arousal, medication, and muscular activities.

##### **2.3.3.1.1 Age**

The maturation of brain and auditory system in infants is age-dependent and the development will last until the age of 6 months (Galambos & Hecox, 1978). ABR showed longer absolute latency in the younger population compared to the adult population (Hecox & Galambos, 1974; Eggermont & Salamy, 1988; Allison, 1983). Neurological maturation facilitates auditory signal transmission efficiently in newborns as the age increases, ABR latencies decrease and in the direction of adult norms (Ponton et al., 1996). Wave I matures early in life, reaching adult-like levels between 3 and 12 years old (Khatoon et al., 2013; Roncagliolo et al., 2000; Sharma et al., 2016). ABR waves III and V develop rapidly in infancy and attain adult-like characteristics between

the age of 12 and 18 months (Hecox & Burkard, 1982; Salamy et al., 1976). However, some studies found that waves II and V mature later at the age of 2 or older (Coenraad et al., 2010; Fria & Doyle, 1984; Gorga et al., 1989; Khatoon et al., 2013; Skoe et al., 2015). These findings were supported by Spitzer et al. (2015), showing that wave V latency is delayed in 3 years old compared to older children suggesting maturation continues beyond 2 years of age and varies among children influenced by differences in the development of the lateral lemniscus and inferior colliculus. Consequently, some children reach adult-like wave V earlier than others (Spitzer et al., 2015).

A study by Sharma et al. (2016) suggested that the brainstem matures around the age of 3 which is the critical period for auditory system development. During this time, the myelination of auditory nerve axons particularly in the inferior colliculus and brainstem pathways are rapidly increases (Johnson et al., 2008). However, cortical maturation begins later between age of 2 and 5 years old, and absolute latency reaches adult levels at the age of 6 to 12 years old (Sharma et al., 2016; Sleifer et al., 2007). ABR in children often elicits shorter amplitude and longer absolute latency compared to adults due to synaptic transmission immaturity, potentially leading to missing of information along the auditory pathway (Sharma et al., 2016). The difference in latency in the elderly is because of central presbycusis in which changes in the cochlear nucleus, SOC, and neuronal propagation within the brainstem and deteriorating of receptor organs (Patterson et al., 1981; Moller, 1985; Starr, 1976).

In adults, ABR latencies for waves I, III, and V generally remain stable as age increases (Beagley & Sheldrake, 1978). However, some studies have reported longer wave III latencies in older adults, particularly those over 50 years of age (Allison et al., 1983; Patterson et al., 1981; Rosenhamer et al., 1980; Rowe III, 1978; Trune et al., 1988). In addition, as amplitude and latency values vary with age, the age adjusted normative data is recommended. As age increases, ABR amplitudes are larger and latencies are shorter; thus, ABR hearing thresholds estimation is lower. There are several studies suggested that the estimated ABR hearing thresholds in infants are often higher than in adults. This is supported by several studies indicating that ABR hearing thresholds estimation in infants are often higher than those of adults (Adelman et al., 1990; Lasky et al., 1987; Mochizuki et al., 1983; Stockard & Curran, 1990).

#### 2.3.3.1.2 Gender

Gender may influence the ABR results in ways other than age-related factors. Frisna (2009) reported that head size influences the ABR results recorded in terms of fibre tract length and the electrode configurations of neural generators. Gender has a major impact on ABR results, such as estrogen hormones will delay the latencies and shorter amplitudes (Ferreira et al., 2019; Zakaria et al., 2022). Previous literature showed that female may have shorter ABR latencies than male (Tafti et al., 2007). This condition is perhaps due to the possibility of shorter conduction times and head size of female (Jerger & Hall, 1980; Aoyagi et al., 1990).

Additionally, shorter absolute latencies occur in female because of female has cochlear duct and the estrogen hormones lead to more stiffness of the basilar membrane; thus, this may elicit earlier ABR latencies than male (Jerger & Hall, 1980). Hormonal and head size influence is connected to the conduction velocity of cochlear travelling wave rises and may cause faster neural synchrony in female (Krizman et al., 2020). Increased levels of estrogen or testosterone can cause longer ABR wave V peak latencies. In female, estrogen levels peak during the menstrual cycle, which can cause ABR wave V peak latencies to elongate (Krizman et al., 2020; Aloufi et al., 2023). In males, testosterone is converted to estrogen in the central auditory pathway, which may also cause increased latency (Aloufi et al., 2023). Hearing sensitivity improves during the late follicular phase, decreases during the luteal phase, and declines rapidly at the onset of menopause (Aloufi et al., 2023; Trott et al., 2019; Caruso et al., 2019). However, estrogen treatment can improve hearing function in postmenopausal women (Aloufi et al., 2023). Pregnancy can cause auditory dysfunction including prolonged ABR interpeak intervals (Aloufi et al., 2023; Dehan, 1990). Other substances that can influence the ABR include progesterone, luteinizing hormone, and follicle-stimulating hormone (Dehan, 1990).

#### 2.3.3.1.3 Body Temperature

Body temperature may affect ABR findings specifically wave I when hypothermia occurs, which is low body temperature (Gulick & Cutt, 1961). Hypothermia may lead

to a reduction of auditory sensitivity for higher frequency signals, as predicted in ABR (Brown et al. 1983). Furthermore, the axon conduction velocity and synaptic transmission are slower (Benita & Conde, 1972). The acoustic nerve and brainstem temperatures are correlated with synaptic transmission and axonal conduction velocity (Kohshi & Konda, 1990).

For hyperthermia, the body temperature is higher than the average normal temperature, which is 37°C. The higher the temperature, the shorter the ABR latency in humans (Kohshi & Konda, 1990). The ABR findings may reduce the latency and amplitude of ABR waves (Barnet, 1980; Brit et al., 1983; Marsh et al., 1984; Gold et al., 1985). It is associated with axonal conduction velocity alteration (Katbamna et al., 1993). Therefore, it is not recommended to conduct ABR assessment in patients with hyperthermia (e.g., high fever).

#### 2.3.3.1.4 State of Arousal

Jewett and Willinston (1971) found that no significant difference in ABR waveform was recorded in awake and natural sleep subjects. Robust ABR waveforms are found in deep sleep subjects (Osterhammel et al., 1985). Awake subjects may lead to false positive ABR results. During sleep, ABR elicits robust waveform due to axonal conduction velocity and synaptic transmission increment in the auditory nerve and brainstem (Harvey et al., 2006). The previous studies investigated the effects of sleep on the fast and slow mechanisms of ABR in humans. The ABR was recorded from brainwave activity (EEG), body temperature, and ABR waveforms from one adult male during night sleep (Mokotoff et al., 1977). These results align with the idea that lower body temperature during sleep can lead to slower neural activity in the auditory nerve and brainstem, however, a change that is reversible upon waking. The usage of chloral hydrate is very common in ABR testing for children or difficult to test patients. ABR recordings were obtained from 26 subjects undergoing anesthesia with enflurane halothane, or thalamonal. Under enflurane anesthesia, a prolongation of approximately 0.1 ms in wave III and 0.4 ms in wave V of the ABR was observed (Wilson et al., 2006). However, a dose dependent relationship was not evident suggesting that ABR latencies remained relatively stable within a certain range of anaesthetic dosages. Similar trends

were noted with halothane and thalamonal anesthesia. These findings indicate that ABR is a valuable tool for monitoring brainstem function during surgical procedures under general anesthesia. Given the potential influence of anesthetics on ABR waveforms baseline recordings prior to neurosurgical interventions are crucial (Gundogdu et al., 2022; Kaveh et al., 2021).

#### 2.3.3.1.5 Muscle Activities

Head and neck muscle activities have significant effects on ABR recordings (Maruthy, 2015). The common cause of the noise that may affects ABR results is muscle artifacts. The muscle activities may produce activities with a similar frequency to the ABR; therefore, it cannot be rejected entirely by the recording (Jacobson, 1994; Picton et al., 1974). For instance, eye blinking, teeth grinding, jaw clenching, neck stiffening, or limb movement are known to influence ABR findings and because of that, the patient is always be reminded to relax throughout the recording. However, previous literature found that there was no correlation between ABR recordings and pacifier usage, as the ABR found similar results in whether a pacifier was used or not (Bruhn & Ferraro, 2018).

#### **2.3.3.2 Stimulus Parameter**

The stimulus parameters are stimulus type, stimulus frequency, stimulus intensity, stimulus rate, stimulus polarity, and transducer.

##### 2.3.3.2.1 Intensity

Amplitude and latency of the ABRs are influenced by stimulus intensity, expressed in decibel (dB). At higher intensity levels (e.g., 70 or 80 dBnHL), the ABR amplitude was larger and absolute latency was shorter; as intensity decreases from 80 to 20 dBnHL, it follows with decreases in ABR amplitude and prolongation in absolute latency by 2.0ms or an average of 0.2 ms per 10 dB (Hecox & Galambos, 1974; Picton et al., 1974;

Stockard et al., 1979; Hall III, 2015). ABR latency exhibits a pronounced increase at intensities below 70 dBnHL with minimal or no reduction observed above this level. The latency-intensity function demonstrates a more gradual slope, ranging from 0.10 to 0.20 ms/10 dB between 60 and 95 dBnHL. Beyond this range, wave V latency increases but at a very minimum. Consequently, the average latency-intensity slope is estimated to be an average of 0.38 ms/10 dB (Gorga et al., 1985; Hecox & Galambos, 1974). All ABR waveforms, including waves I to V are visible at high-intensity levels. As stimulus intensity decreases below 50 dB SL, the less prominent waves II and IV become attenuated. A further reduction to 30 dB SL results in the attenuation of waves I and III, while wave V remains detectable due to its comparatively larger amplitude (Hood, 1998).

#### 2.3.3.2.2 Rate

Stimulus repetition rate is number of stimuli presented per second within a given averaging epoch and a critical parameter influencing ABR recording quality and efficiency (Polenenko & Maddox, 2019). Rapid stimulus rate is recommended for use in infant subjects as this faster rate of stimulus allows the test to run rapidly before the subject is awake (Rasetshwane et al., 2013). The stimulus repetition rate denotes the frequency at which stimuli are presented one per second and averaged over the total number of trials. Adjusting this rate can optimize ABR recordings by enhancing signal quality and reducing test duration. A shorter test time increases the likelihood of infants completing ABR tests in a single session, promoting natural sleep, and minimizing the need for sedation. Typically, slower repetition rates are employed for diagnostic purposes, while intermediate rates are suitable for threshold estimation (Hall III, 2015).

Two techniques are employed to decrease ABR acquisition time which are conventional high stimulus repetition rates and maximum length sequences (MLS). The conventional approach utilizes increased repetition rates. For instance, completing 4000 sweeps of somatosensory evoked responses (SSERs) at a slow repetition rate of 11 clicks per second (cps) requires approximately 6 minutes. However, as the rate is increased from 11 cps to 19.1 cps, the time needed for 4000 sweeps is reduced to 3 minutes (Dzulkarnain et al., 2020). Further increases to 61.1 cps and 100 cps yield even

faster completion times of 1 minute and 30 seconds, respectively (Dzulkarnain et al., 2013). However, a critical limitation exists with the conventional method. Increasing the repetition rate beyond 100 cps can introduce distortions and signal overlap during averaging, potentially compromising ABR validity. No significant difference between 11.1 and 31.1 cps was found in ABR recordings (McKnight et al., 2018). However, in another study, there was a significant difference between 9.0 cps and 21.1 cps without influencing the ABR recordings, as the faster rate can decrease the ABR acquisition time (Kerneis, et al., 2023).

From previous literature, Maximum Length Sequences (MLS) were introduced to overcome the limitations of conventional high stimulus repetition rates, enabling the presentation of stimuli at frequencies exceeding 100 cps (Eysholdt & Schreiner, 1982). ABR test using MLS foreseen faster testing time and more efficient because of the longer latency from increased repetition rate (Chiappa et 1970, don et al 1977). The increment of the latency may be due to neural adaptation as refractoriness and decrement of synaptic efficiency. This electrophysiological technique allows for rapid stimulus presentation resulting in overlapping responses between successive stimuli (Eysholdt & Schreiner, 1982; Thornton & Slaven, 1993). Consequently, MLS significantly reduces ABR test duration while maintaining the quality and accuracy of conventional ABR protocols. Previous studies have revealed the efficacy of MLS in both adult and infant populations. ABR waves I, III, and V have been successfully detected at exceptionally high stimulus repetition rates ranging from 856 to 909.1 cps, albeit with varying detection rates (Eysholdt & Schreiner, 1982; Lina-Granade et al., 1994; B. A. Weber & Roush, 1993).

However, in certain situations, both conventional high stimulus repetition rates and MLS can lead to decreased ABR amplitude and prolonged latency because of neural fatigue and auditory system adaptation (April et al., 2007; Cebulla & Stürzebecher, 2013; Don et al., 1977; Fowler & Nofsinger, 1983; Parthasarathy et al., 1998). As the stimulus repetition rate increases, the inter-stimulus interval shortens. This reduced inter-stimulus interval limits the number of neurons capable of responding to subsequent stimuli, as a significant proportion remains in the refractory period. Consequently, the overall neural response diminishes and resulting in reduced ABR amplitude and increased latency (April et al., 2007; Cebulla & Stürzebecher, 2013;

Manuel Don et al., 1977; Fowler & Nofsinger, 1983; Parthasarathy et al., 1998).

#### 2.3.3.2.3 Polarity

There are three stimulus polarities in ABR measurements which are condensation, rarefaction, and alternating. Condensation or positive polarity is characterized by an initial positive pressure phase that induces inward tympanic membrane displacement. Conversely, rarefaction or negative polarity is defined by an initial negative pressure phase resulting in outward tympanic membrane movement. In ABR testing, the stimulus can be presented with either constant (positive or negative) which is also known as alternating polarity (Kumar et al., 2013; De Lima et al., 2008; Jacobson & Hyde, 1985; Stockard et al., 1978). The ABR recordings via modified upward chirp stimuli were obtained from the whole basilar membrane according to the corresponding frequency and position along the membrane (Dzulkarnain et al., 2021). This finding aligns with previous research using ABR elicited by click stimulus (Sand, 1991; Schwartz, 1990; Jiang et al., 2021). To date, there is limited consensus on the impact of stimulus polarity on ABR findings; although several studies reported no significant differences in ABR responses to click and rising chirp stimuli of varying polarities (Fowler, 1992; Balachandra, 1992; Cobb, 2016).

Previous literature reported that alternating stimulus polarity effectively reduced artifact, resulting in a clear, initial, and vertex positive deflection. Rarefaction polarity demonstrated superior synchronizing properties, as evidenced by increased amplitude in waves I until IV and distinct differentiation of waves IV and V (Aurer et al., 1980). In this study, the acoustic stimuli will be presented using alternating polarity to reject the stimulus artifacts (Jacobson & Hyde, 1985; Stockard et al., 1978; Rodrigues et al., 2013).

#### 2.3.3.2.4 Transducer

The acoustic stimulus will be given via ER-3A earphones for comfort purposes and better clinical findings (Muhler et al., 2013). TDH-39 headphones prompt an

electromagnetic shield that results in stimulus artifacts at higher intensity levels. In contrast, earphones have electromagnetic shielding to abolish electromagnetic artifact (Coats et al., 1979). The ER-3A insert earphones decrease the stimulus crossover likelihood from the test ear to the non-test ear.

### ***2.3.3.3 Stimulus Types***

ABR is an assessment to estimate hearing thresholds in infants from birth to six months. There are various stimuli available for ABR assessment, such as click, tone burst, chirp, CE-Chirp, NB CE-Chirp, LS CE-Chirp and NB LS CE-Chirp. For more than 50 years of ABR in the audiology industry, the development of ABR acoustic stimuli has changed through time to accommodate the information and precision of hearing threshold for better management and intervention for the hearing impaired population.

#### ***2.3.3.3.1 Click***

Click is a short duration stimulus with the stimulus energy presented for 0.1 milliseconds (ms) or 100 microseconds ( $\mu$ s) with a broadband frequency spectrum. In click stimulus, due to abrupt onset of the neural responses are dyssynchronous owing to the different travelling times of each of the frequencies that travel along the cochlear (Dau et al., 2000). The ABR elicited from the click stimulus may not be able to identify those with low frequency hearing loss because the click stimulus smeared mainly on the high frequencies region (Cheng et al., 2021). Hearing loss at low frequency might be missed due to normal hearing threshold estimation from the ABR. This normal or delay latencies of ABR results may be because of there is abundant energy in the click between 2000 to 4000 Hz that will elicit presence of an ABR waveform (Hall III, 2013).

As click stimulus with temporal dispersion characteristics which widely spread initially at high frequency regions of the basilar membrane and sooner than towards low frequency regions (Jewett & Williston, 1971). This condition is due to the cochlea travelling wave and the ABR more prominent from HF regions before going further of the cochlear regions. Thus, tone burst stimulus is developed to overcome the limitation

of click stimulus.

#### 2.3.3.3.2 Tone Burst

Tone burst is a frequency specific ABR stimulus that is developed to estimate hearing threshold at a specific octave frequency. It is a short pure tones duration of 5 milliseconds (ms) or less with frequencies specific band from 500 Hz to 4000 Hz (Hecox et al., 1976). The aim was to generate rapid onset to efficiently elicit an ABR waveform while restricting the frequency content of the stimulus. Tone bursts are defined by the rise and fall time of two cycles and a plateau of one cycle (Hecox & Galambos, 1978). The length, the rise fall time and the characteristics in which the stimulus is enveloped to regulate the spectral spread in tone burst stimulus (Gorga et al., 2006). Though tone burst is a FS stimulus which is likely to have a great value for ABR threshold measurements and the usage of these stimuli has been suggested from numerous findings (Stapells & Oates, 1997; ASHA, 2004; JCIH, 2007). However, tone burst stimulus is still underutilized in clinical settings due to several reasons. First, the amplitude elicited from ABR to tone burst is usually 70% smaller than the amplitude of ABR to click as the tone burst is a FS ABR stimulus encompassing a specific frequency range which elicited less robust overall response (Ferm et al., 2013). Secondly, an extended ABR assessment time is required to attain consistent ABR waveforms elicited via tone burst stimulus. Third, audiologists reported indecisiveness regarding the exact procedures and practical difficulties in identifying wave V from ABR to tone burst, specifically at the lower frequency (Windmill & Windmill, 2006).

Tone burst frequencies consist of 500, 1000, 2000, 4000, and 8000 Hz (Shore & Nuttall, 1985; Polonenko & Maddox, 2019). Hall (1992) stated that low frequency tone burst has larger peaks in averaged ABR. Besides, tone burst stimulus is excellent for interpreting the hearing threshold at 500 Hz and 1000 Hz with higher intensity levels only (Dagna et al., 2014). In addition, numerous studies stated that poor quality of ABR was produced by tone burst specifically at 500 Hz in which the waves are complex with unstable responses for visual detection (Pinto & Matas, 2007). The previous study did not suggest that tone bursts should be used as a standardized ABR stimulus for routine audiological assessment (Mobley & Gibson, 2000). This leads to the limitation of ABR

to tone burst findings. Therefore, in the current study, the relationship between NB LS CE-Chirp stimulus and tone burst ABR findings will be further investigated.

#### 2.3.3.3.3 Chirp

Dau et al. (2000) first introduced chirp stimulus as a significant innovation in auditory research inspired by the linear cochlear model (de Boer, 1980) and expanding upon the concept of frequency-swept stimuli used by Shore and Nuttall (1985) in compound action potential recordings. The development of a chirp stimulus compensates for the delay of the cochlear wave travelling in ABR by stimulating different neural units along the basilar membrane (Elberling & Don, 2000). The chirp stimulus arrives at a low frequency about five milliseconds (5 ms) earlier than the high frequencies (Hall III, 2013). ABR to chirp is twice as robust as ABR to click and less averaging is needed (Hall III, 2013). Chirp stimulus is easily distinguishable specifically at near threshold level and refining ABR waves leads to extra accurate hearing threshold estimation (Xu et al., 2014). ABR to chirp produces a similar signal-to-noise ratio (SNR) that can lessen ABR testing time for newborns (Ferm et al., 2013). This chirp has limitations as the ABR findings showed wave distortion at higher intensity stimulation levels that produce lower amplitude and longer latency (Maloff & Hood, 2014).

Claus Elberling (CE) improved the chirp stimulus to overcome the limitation of conventional chirp. This modified chirp stimulus is a family of short duration with broadband spectrum of 12 ms (Elberling et al., 2008; Elberling et al., 2010). CE-Chirp with five octave band oscillating from 350 to 11 3000 Hz and has better responses towards the temporal distribution in the normal cochlea by introducing energy to the low frequency part first before the high frequency in order the acoustic stimuli arrive at the same time (Elberling, 2007; Elberling & Don, 2008; Suleman, 2021). This condition is called the cochlear travelling wave delay model which has a latency frequency function that is fixed with the stimulation level. However, joint dataset analysis reported there were small differences in latency for different stimulation levels (i.e., ranging from 10 to 70 dBnHL) (Don et al., 1998; 2005). Thus, the differences were small to consider the latency delay to be persistent across all stimulus levels (Elberling et al., 2010).

The ABR to chirp results in enhanced neural synchrony activities that lead to

larger ABR amplitudes and earlier ABR latencies (Morimoto et al., 2019; van Dyk, 2019). However, ABR to CE-Chirp findings are deficient at higher intensity stimulation levels. This condition happens because the chirp duration is too short to excite the fast component of ABRs (Kristensen & Elberling, 2012).

#### 2.3.3.3.4 Level specific CE-Chirp

Level specific (LS) CE-Chirp was introduced to elevate the amplitude saturation of broadband (BBN) chirp (Cargnelutti et al., 2017). The LS CE-Chirp is characterized via the stimulus intensity level (i.e., 0 to 100 dBnHL) with a five dBnHL step (Di Scipio & Mastronardi, 2015). The purpose of the LS CE-Chirp is to overcome all wave amplitude for all intensities especially higher intensity to elicit larger amplitude (Elberling et al., 2008; Elberling et al., 2010). This stimulus produces longer latency at a higher intensity level (i.e., at 80 dB or 60 dB) than in click stimulus and has a direct method for delay compensation. At higher intensity levels, LS CE-Chirp widens the upward spread of excitation (Elberling et al., 2010). This is because LS CE-Chirp has a wider range of frequency components and will excite along the basilar membrane, resulting in a consecutive smeared signal and desynchronization of neuronal firing. Hence, this LS CE-Chirp stimulus is a broadband spectrum and is inconclusive for frequency specifics.

#### 2.3.3.3.5 Narrowband (NB) CE-Chirp

The narrow band (NB) CE-Chirp stimulus is developed to compensate for some shortages in tone burst stimulus. NB CE-Chirp consists of a set of frequency specific stimuli centred which are around 500 Hz (360 to 720 Hz), 1000 Hz (720 to 1440 Hz), 2000 Hz (1440 to 2880 Hz), and 4000 Hz (2880 to 5760 Hz) (Ocal et al., 2021). The stimulated range of the NB CE-Chirp stimulus is broader than the tone burst stimulus and allows different synchronous neural firing along the basal part to the apical end of the cochlea. ABR to NB CE-chirp generates shorter latencies than the ABR to tone burst especially at low frequencies (Rodrigues et al., 2013). Higher amplitudes were found with ABR to NB CE-Chirp for all frequencies tested except at high intensity levels

which are more than 60 dBnHL (Xu et al., 2014; Rodrigues et al., 2016). The larger spectral spread of the NB CE-Chirp leads to increased neural synchrony across a larger number of nerve fibres resulting in an increased description of wave V. Therefore, the ABR findings are found that larger amplitude and lower threshold level are obtained using NB CE-Chirp than tone burst (Ferm et al., 2013; 2015).

As known, CE-Chirp acoustic stimuli produce bigger wave V amplitudes by eliciting ideal stimulation to the basilar membrane. The stimulation by CE-Chirp contributes to greater neural synchronization across the frequency range initially to the low frequency energy and followed by high frequency energy. Ferm et al. (2013) studies showed that NB CE-Chirp stimulus is more effective than tone burst in newborn hearing screening (NHS) programs. Following the original idea of broadband LS CE Chirp, NB LS CE-Chirp was then used for infant hearing assessment. This NB LS CE-Chirp offers various stimuli for each 5 dBnHL step from 0 to 100 dBnHL with four specific frequencies (Maslin, 2017).

#### 2.3.3.3.6 Narrowband level specific (NB LS) CE-Chirp

The NB LS CE-Chirp is a frequency specific ABR stimulus based on non-monotonous level-dependent and latency variations. NB LS CE-Chirp is precisely timed to account for cochlear traveling wave delays at central frequencies of 500, 1000, 2000, and 4000 Hz. This timing coupled with the latency reference (0 ms) which results in significantly shorter ABR latencies for low frequency stimulus (500 and 1000 Hz) compared to those elicited by tone burst stimulus (Cebulla & Elberling, 2020). In the present study, two types of acoustic stimuli will be used which are NB LS CE-Chirp and tone burst. Furthermore, in the previous study, ABR findings using NB LS CE-Chirp produced larger wave V amplitude and shorter latency than tone burst in adults (Bal et al., 2022) and no effect of different electrode montages among adults (Dzulkarnain et al., 2018). From other literature, the present study suggests comparing NB LS CE-Chirp and tone burst because there is limited literature on ABR findings between NB LS CE-Chirp and tone burst especially among the infant population.

## 2.4 ACQUISITION FACTORS

The acquisition variables are electrode montages, amplification, filters, analysis time, and signal averaging.

### 2.4.1 Electrode Montages

The electrode montage placement is the arrangement of ABR recording electrodes that significantly influences the ABR waveforms. The four electrode montages are ipsilateral, contralateral, vertical, and horizontal. The frequent montage used in clinical settings is an ipsilateral montage and is commonly used in paediatrics and adult populations (Hall, 1992). For ipsilateral montage, the inverting electrode is located on the earlobes (A1/ A2) or mastoid areas (M1/ M2), the non-inverting electrode is located at the midline of the head either on the vertex (Cz) or in the centre of the high forehead (Fz), and the common or ground electrode is positioned on the lower forehead. Previous literature stated that the placement of the non-inverting electrode on the vertex (Cz) elicited a larger amplitude of waves V in adults; however, the placement of the non-inverting electrode on Fz elicited a larger amplitude of waves III and V (Starr & Squires, 1982). Moreover, the skin preparation for non-inverting electrode placement on Fz is easier compared to Cz placement, in which the Cz is covered by hair. Electrode placement at the Cz location may be contraindicated in certain pediatric populations, including neonates with a soft fontanelle and those with brain injuries. The inverting electrode near the cochlea can enhance the amplitude of wave I in ABR. This is attributed to the proximity of the recording electrode to the neural generator of wave I, which originates from neural activity within the ipsilateral distal portion of the vestibulocochlear nerve (Durrant, 1977; Dzulkarnain et al., 2017; Ferraro et al., 1986).

Other electrode montages, such as contralateral, vertical, and horizontal configurations, offer distinct advantages for ABR recordings (Hall et al., 1984; Møller & Jannetta, 1983b; Aage et al., 1985). Contralateral montage is characterized by inverting electrodes placed on opposite ear lobes or mastoids typically results in larger amplitudes of waves II and IV, albeit with longer absolute latencies compared to ipsilateral recordings (Hughes et al., 1981; Kato et al., 1998). Vertical montage,

the electrodes are positioned outside the scalp, such as on the nape of the neck, can effectively separate waves IV and V (Hall et al., 1984; Hughes et al., 1981). This enhancement in wave separation is attributed to several factors: i) improved definition of wave V, ii) increased stability of wave IV and V in the contralateral montage, leading to greater waveform reproducibility with a narrower inter-peak latency variability (0.08 ms) compared to ipsilateral recordings (0.3 ms), iii) improved overall recording reliability: Contralateral recordings generally provide more reliable recordings of waves I-V. Furthermore, contralateral recordings demonstrate reduced variability within the ABR waves IV/V complex and exhibit higher reproducibility compared to ipsilateral recordings (Hall III, 2015; Mizrahi et al., 1983).

In the vertical electrode montage, the non-cephalic electrode, typically positioned outside the scalp, acts as a relatively inactive electrode, minimizing its contribution to the recorded auditory brainstem response (ABR) peaks. Consequently, the observed ABR waveforms primarily originate from the cephalic electrode. This significant electrical difference between the active cephalic electrode and the relatively inactive reference electrode results in reduced common mode rejection (CMR) of the ABR signals. As a result, waves IV and V are more clearly identified and distinguishable within the recorded waveforms.

In the horizontal electrode montage, the non-inverting electrode is positioned opposite to the inverting electrodes located on the earlobes or mastoids. This configuration enhances the distinctiveness of wave I because of the parallel orientation of the horizontal electrode array with the dipole generated by wave III; this montage typically produces larger amplitudes of waves I and III compared to the ipsilateral array (Ruth et al., 1982). However, this configuration generally results in longer latencies for these waves compared to vertical and ipsilateral montages. Waves IV and V are often used, and exhibit reduced amplitudes in the horizontal montage. This attenuation is likely attributed to the increased distance between the active electrode at the mastoid and the neural generators of waves IV and V located in the cephalic regions. Furthermore, the close proximity and horizontal orientation of the electrodes may influence the activity of neurons with different orientations, potentially reducing the contribution to the recorded ABR waveforms (Hall III., 2015).

### 2.4.2 Filters

The acoustic stimuli filters function to preserve the slow negative wave components in the subjects while eliminating any artifacts or muscle activities unrelated to the ABR recordings. Mathematical parameter analysis with a skimming association window, a 20 Hz filter was identified as the parameter that maximizes ABR detection performance at thresholds approaching the limit of audibility (Mason et al., 1984). Reducing the high pass filter (e.g., 30 Hz) cut off frequency enhanced the visibility of wave V (Kumar et al., 2016). ABR filter used in infants is 30 to 3000 Hz, as recommended by Hall III (2013) and Sininger et al. (1995); and in other studies, the filter used is 300 to 1500 Hz (Ormundo et al., 2024; Diao et al., 2022); ABR to click in infants, the filter is between 30 to 1500 Hz whilst ABR filter using tone burst stimulus in infants is between 30 to 3000 Hz. As 30 Hz is a high filter pass, less noise was diminished by at least 30%, and ABR amplitude was reduced (Reichmuth et al., 2007). On the other hand, ABR filters in adults are typically set between 100 to 3000 Hz (Mason et al., 1984).

### 2.4.3 Analysis Time

Analysis time, also known as time window, is the time calculated immediately after stimulus presentation until the ABR waveforms are elicited (Epoch size) (Eggorment et al., 1979). Analysis time of 10 to 12 milliseconds (ms) is adequate enough to capture the ABR waves, especially wave V, as it arises in normal hearing person within 5 to 6 ms at high intensities and around 8 to 9 ms for the intensities near the hearing threshold (Hall, 1992). The illustration of ABR waveform (Epoch size) with multiple intensities range with various latencies is shown in Figure 2.2. The ABR window analysis time for tone burst is suggested to be longer as it may include the temporal spectrum of the stimulus, and the wave V may be presence a bit later, especially for low frequency stimulus (Lewis et al., 2015; Gorga et al., 2006). Therefore, the time window for tone burst is typically set between 15-25 ms. For stimulus elicited from NB LS CE-Chirp, most of the manufacturers temporally adjusted the onset of the response in accordance with the broadband LS CE Chirp (Elberling & Don, 2008; Spiedel et al., 2016). Because of that, a standard time window as per broadband stimulus can be employed.

The epoch duration in ABR recordings can vary depending on the stimulus type, specifically between tone bursts, NB LS CE-chirp, and clicks. This variation is primarily due to the different temporal characteristics of these stimuli and the resulting neural responses. Tone burst has a longer epoch, and slower onset compared to click. This results in a longer neural response requiring a longer epoch to capture the complete ABR waveform. LS CE-chirps have a longer duration than clicks but a shorter duration than tone bursts (Bal et al., 2022). This results in an intermediate epoch length, capturing the neural response to the chirp stimulus. By understanding the factors that influence epoch duration in ABR recordings, clinicians can optimize the recording parameters to obtain high quality data and accurately assess auditory function.

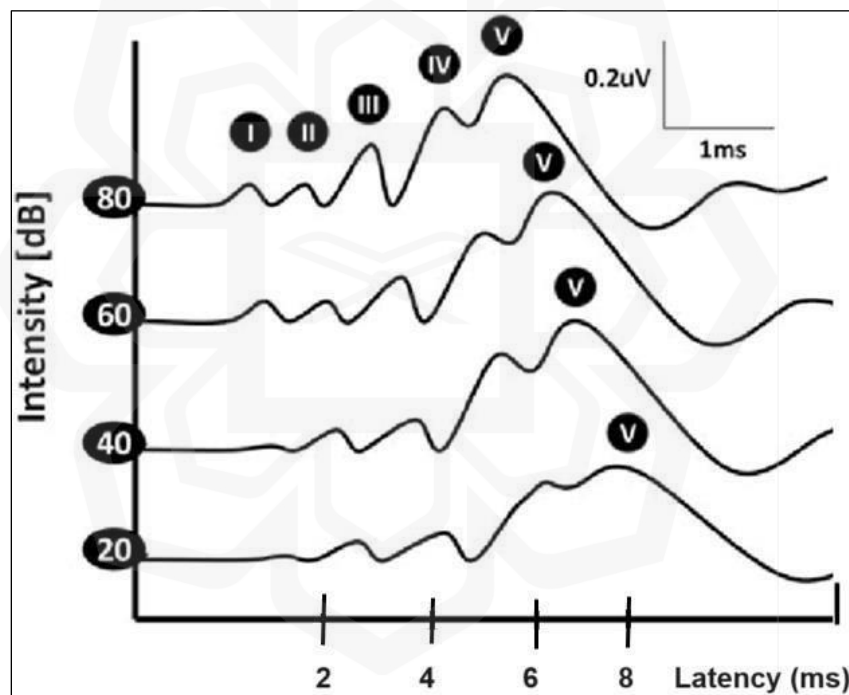


Figure 2.2 ABR waveform with multiple intensities range with various latency  
<https://www.researchgate.net/profile/Syed-Habib-6/publication/354950448/figure/fig4/AS:1076707423465476@1633718462458/Figure-4-Normal-auditory-brain-stem-response-ABR-waves-recorded-at-80-60-40-and-20.png>

#### **2.4.4 Signal Averaging**

Signal averaging is a procedure to distinguish accurate electrophysiological responses from noise. In other words, a process to lessen noise and boost the acoustic signal (Hassan & Anwar, 2010). The usage of ABR signal averaging is to excerpt meaningful acoustic signals in background noise. ABR presentations of signal and noise bands always overlap (Leski, 2014). Cross and autocorrelation functions (Bershad & Rockmore, 1974), Fourier transformation, baseline correction, pink noise, Gaussian noise, and Bayesian interference are the examples of signal averaging process. The latest technology, signal averaging was recommended to improve the estimation of ABR signals. A novel Bayesian approach is a new method to estimate ABRs from non-stationary electrophysiological data. This method downweighs noisy recording segments to improve ABR estimation accuracy (Elberling & Wahlgreen, 1985). Bayesian averaging with block weighing improves SNR better than artifact rejection. Previous study showed 8-block of 2000 sweep significantly improved detection in 30% of cases (Elberling et al., 1994). These improvements resulted in a substantial reduction (approximately 50%) in the variance of parameter estimates (e.g., latency and amplitude) (Elberling et al., 1994).

#### **2.5 ABR RECORDINGS USING NARROW BAND LEVEL SPECIFIC (NB LS) CE-CHIRP**

Anatomically, the cochlea is a tonotopical structure starting with the basal part in which the high frequencies are perceived and then low frequencies are perceived at the apical end, as shown in Figure 2.3 (Sasmal et al., 2019). As the high frequency at the basilar membrane of the cochlear first, the NB LS CE-Chirp was developed to overcome the other chirps by the low frequency was designed to be five milliseconds (5 ms) earlier than the high frequencies (Hall III, 2013). As a result, all cochlear regions are concurrently depolarized by chirp stimulus, which results in a higher amplitude of ABR waves (Megha et al., 2019). The decrement in ABR testing time elicited via NB CE-Chirp stimulus because the onset time positioning of separate frequency fundamental in the stimulus to its place of upward spread of excitation along the basilar membrane (Megha et al., 2019). As mentioned in subsection 2.3.2.3.6, NB LS CE-Chirp is a

frequency-specific stimulus.

In the previous study, it is proven that the ABR to CE-Chirp is up to 1.5 to 2.0 times greater in amplitude recording than the corresponding ABR to click in normal hearing subjects (Elberling & Don, 2008; El-Mously et al., 2020); larger amplitude produced by BBN CE-Chirp is to allow lesser ABR acquisition time compared to tone burst among infants (Muhler et al., 2013). Rodrigues et al. (2013) studied the fact that ABR to NB CE-Chirp elicits shorter latency and higher amplitude of wave V compared to tone burst in young infants. There are limited studies on ABR to NB LS CE-Chirp and limited literature on comparison between NB LS CE-Chirp and tone burst in infants. Therefore, the present study is conducted to explore the benefits of NB LS CE-Chirp in infants.

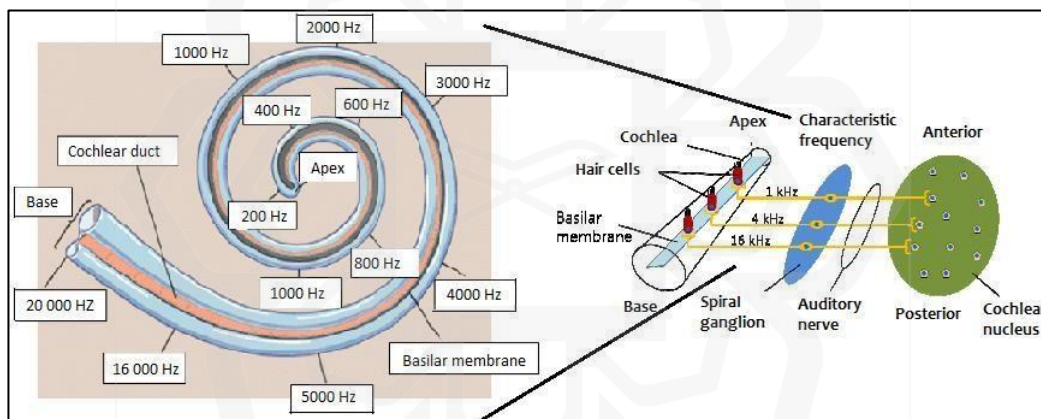


Figure 2.3 Tonotopical structure of basilar membrane and cochlear nucleus (Lee et al., 2013).

## 2.6 ABR ANALYSIS

### 2.6.1 Visual Detection

Visual detection is an initial method for ABR detection, crucial for ABR waveform identification, and the quality of the ABR peaks. This detection was found to be more sensitive to detect ABR presence (Arnold, 1985). This ABR analysis using visual observation is based on human judgement (i.e., clinical audiologist). The audiologist is required to identify the ABR waveform manually (i.e., amplitude and latency of waves

peak I, III, and V) based on ABR guidelines according to the norms, replication, and consistency of the ABR waveform. Subject factors like age, hearing status, and medical history can influence ABR waveforms and the interpretation of Fsp and Fmp (Arnold, 1985). Advanced techniques like peak picking algorithms and waveform recognition can help improve the accuracy of Fsp and Fmp measurements especially in noisy or ambiguous waveforms. By cautiously considering these notes and following best practices, clinicians can make accurate and reliable interpretations of ABR waveform leading to better diagnosis and management of auditory disorders (BSA, 2019).

Most ABR sessions used visual detection technique as it is easier to do in clinical settings, especially in normal hearing cases. However, in the cases of hearing loss patients, poor ABR findings and junior audiologists; this technique is grim for clinical application (Weber, 1983). The visual detection technique has a few advantages that need i) elongated time for the audiologist to confirm the ABR waveform, ii) audiologists feel demotivated especially in poor ABR recordings and error in ABR interpretation, iii) tester bias (i.e., the audiologist well versed in the history or condition of the patients) (Weber, 1983; Jacobson, 1985). Thus, Fmp is used to supplement the ABR findings.

According to BSA (2018), visual detection by an audiologist is the main methods to accept or rejecting an ABR results. When objective measurements are available, these can be an additional valuable information in facilitating the interpretation with confidence and in deciding when to stop averaging. Replication of waveforms contributing to the reported result is essential if a correct visual interpretation is to be made. Replication is not needed at other stimulus levels. For example, if the first stimulus level is 40 dBnHL and a flat trace is obtained, then the best use of time may not be to replicate until a response is observed at higher stimulus levels and it is clear which levels need to be replicated to determine the threshold. ABR threshold has been defined in the NHSP early assessment guidelines as the lowest level at which a clear response (CR) is present, with a response absent (RA) recording at a level 5 or 10dB below the threshold, obtained under good recording conditions. Hence, the current study focused to investigate the objective analysis (i.e., Fmp).

## 2.6.2 Objective Algorithm $F$ Multiple Point Test (Fmp)

Objective measurement is aimed to facilitate the subjective measurement (i.e., visual detection), further delicate technique of ABR detection than visual detection, and abrupt findings of the ABR for the audiologists in clinical practice. The objective technique uses the averaged evoked potentials to assess auditory function. Objective technique is unlike the conventional audiometric tests. However, in most clinical applications, evoked potential methods require a human observer to interpret visually the averaged recordings.

Objective measurement for assessing ABR quality include the Fsp (Elberling & Don, 1984) and Fmp (Martin et al., 1994) indices, both of which compare the variance of the averaged signal to the estimated noise variance (BSA, 2019). There are numerous stopping criteria for ABR recording, such as i)  $F=$  statistical analysis, single point test (Fsp), ii)  $F=$  statistical analysis, multiple point test (Fmp), and iii) residual noise. However, in the present study, the Fmp stopping criteria will be used.

Fmp is a statistical analysis of multiple points of ABR recording (i.e., ABR signal and noise) based on statistical confidence of the repeated detection of a response (Lv et al., 2007). The Fmp is an objective and consistent response. Fmp is measured with 5 points/sweep for noise estimation (Elberling & Don, 1984). For instance, Fmp which is equal to 3.1, indicates 99% confidence that the ABR is present above the noise floor. The Fmp of 3.1 is considered a conservative SNR estimation stopping criterion and the ratio can be adjusted to a 95% or 90% confidence level with a less conservative SNR estimation (Elberling & Don, 1987). Automated detection of response criterion (i.e.,  $Fmp \geq 3.1$ ) with 800 sweeps and tester-judgemental response by qualified audiologists are among the criteria that are used for ABR waveforms presence or absent confirmation (Interacoustics, 2010). Previous literature concludes that Fmp values and amplitudes of ABR recordings using chirp are larger than tone burst (Ferm et al., 2015). In addition, Fmp is linked with the ABR findings, which are 1.8 to 3.0 times higher in NB chirp stimulus than tone burst stimulus due to the larger amplitude elicited (Sininger, 2016). Thus, the present study will be focused on the ABR recordings that apply the Fmp stopping criterion.

British Society of Audiology (2019) recommended using Fmp indices to confirm a SNR of at least 3:1 for a 'clear response' determination. However, the determination of other "clear response" characteristics, including ABR morphology and waveform reproducibility, still requires visual analysis. Furthermore, the absence of a response cannot be confirmed solely using Fmp, necessitating continued reliance on visual analysis. A primary benefit of objective methods over visual detection lies in the superior reliability. Unlike human judgement, which is susceptible to inter-rater variability, objective methods provide consistent results.

The ABR with a maximum amplitude of  $0.5 \mu\text{V}$  is often obscured by background noise fluctuations of  $\pm 15 \mu\text{V}$  or more. Consequently, the SNR of ABR within the continuous EEG is extremely low, ranging from approximately -35 to -23 dB, depending on stimulus intensity (Chesnaye et al., 2018). Clinical ABR detection primarily relies on visual interpretation (Vidler & Parker, 2004; BSA, 2019c). Clinicians typically assess pairs or single averaged waveforms across a stimulus level range. Reproducibility of latency, amplitude, and morphology are from the waveform and then analyzed to estimate individual ABR thresholds (BSA, 2019c).

In addition, it is assumed that the repeated ABR run with the same constant number of sweeps has an output signal-to-noise ratio (SNR) sufficiently similar to the first run to permit the comparison in ABR to the common assumption that the ABR is a deterministic signal. The judgement by the observer of either waveform imitations have been sufficiently elicit independent plotting variabilities. The Fmp metric estimates the variance of EEG background noise by averaging multiple single-sweep variances, calculated as the variance of individual data columns within the dataset. The Fmp is computed according to the formula presented by Martin et al. (1994):

$$\text{SNR} = \frac{\text{Variance}[\text{ABR}]}{\text{Variance}[\text{Noise}]} \quad (2.1)$$

$$F_{sp} = N \times \frac{\text{VAR}(\bar{E})}{\text{VAR}(SP)} \quad (2.2)$$

$$F_{mp} = N \times \frac{\text{VAR}(\bar{E})}{\left(\frac{1}{M} \sum_{i=1}^M \text{VAR}(SP_i)\right)} \quad (2.3)$$

## 2.7 EFFECTS OF INTENSITY LEVELS ON THE ABR RECORDINGS

The different stimulus intensity levels can affect the ABR recordings in several ways including; i. reducing the intensity of the stimulus which can reduce the amplitude of the waves, ii. increase the absolute latencies, and iii. the threshold estimation is determined by the stimulus intensity at which the ABR is no longer present. As the stimulus intensity decreases, it can become difficult to detect waves. For example, wave I may become undetectable at lower intensities. There are several factors affecting ABR recordings such as age, intensity, and frequency. According to Bargaen (2015), chirp stimulus levels of 10 to 40 dB SL produce higher wave V amplitude than 50 dB SL and above. In addition, short duration chirp at low intensity levels produces higher amplitude and shorter latency (Zirn et al., 2014). NB LS CE-Chirp stimulus is intended to compensate for temporal distribution in the cochlea and to astound the cochlea travelling wave delay (Elberling & Don, 2008). Additionally, NB CE-Chirp at lower stimulation levels (i. e., 20 and 40 dBnHL) elicited larger amplitude compared to tone burst in young infants (Rodrigues et al., 2013).

ABR to tone burst at higher intensity levels elicits various ABR waves throughout the multiple frequencies (see Section 2.6.1). This condition is due to the action potential, larger tuning curve of the auditory nerve, and spatial extension beyond two octaves along the cochlea, shifting the basal of the cochlea for the low frequency region to the apical end of the cochlea for the high frequency region (Ota et al., 2020). Physiologically, cochlea travelling wave theory is the cochlea response towards ABR

stimulus comprised of a dispersion wave which spreads along the basilar membrane from the basal part to the apical end (Junius & Dau, 2005). At present, there is limited study on NB LS CE-Chirp with different intensity levels, specifically in infants. Hence, the present study aims to discover the influence of different intensity levels in ABR findings using NB LS CE-Chirp and tone burst in the infant population.

## **2.8 ABR IN NEWBORNS**

Accurate audiological diagnosis permits early intervention by the first 3 months of life (Kenna, 2003). Because of that, ABR is used for NHS program and estimation of hearing loss (Paludetti et al., 2012). Hearing loss in newborns is usually caused by congenital factors, i.e., hyperbilirubinemia requiring exchange transfusion, craniofacial anomalies, syndromes associated with hearing loss, and so on; see Appendix O (JCIH, 2019). The two important measurements in ABR results which are amplitude and latency are age-dependent (Konrad-Martin et al., 2012). The ABR amplitude significantly increases with age due to the maturation of the brainstem, mainly on synchronization of synaptic transmission, myelination density of the auditory pathway, and conduction velocity of axonal parts (Cebulla et al., 2014). The synaptic transmission duration which determines the latency of the ABR continues to shorten until the age of 3 years old (Moore et al., 1996). In addition, the myelination density increases in the auditory pathway and moves rapidly in neural conduction velocity of the auditory pathway until the age of 1 year old (Moller & Jannetta, 1983). Hence, this situation leads to decrease in latencies of wave II to V in infants between birth and the age of three.

## CHAPTER THREE

### PROBLEM STATEMENT, RESEARCH OBJECTIVES, AND HYPOTHESES

#### 3.1 INTRODUCTION

This chapter deliberates the problem statement of the thesis based on the current issues in audiology and the research gaps found in the literature. The latter part of this chapter discusses general objectives, specific objectives, and hypotheses of the current study.

#### 3.2 PROBLEM STATEMENT

This thesis identified several problems that require the present study to address them accordingly. In general, this research is undertaken because of the following reasons:

##### 3.2.1 Issues with the ABR test time

1. Conventional ABR stimuli are time-consuming (Cone & Norrix, 2015; Dzulkarnain et al., 2023; Hall III, 2013) and this has led to limited appointments being offered to patients in audiology clinics. The ABR elicited from click stimulus takes about 45 to 60 minutes to complete (Ness, 2009), whereas the ABR to NB LS CE-Chirp acquisition time in adults takes  $14.57 \pm 3.83$  minutes, and for ABR tone burst takes approximately  $28.2 \pm 4.5$  minutes (Ceylan et al., 2020). The improvement of test time given by NB LS CE-Chirp in adults indicates the same time efficacy of ABR to NB LS CE-Chirp could possibly be obtained in infants for the betterment and efficiency of audiology clinical sessions. Therefore, there is a need to further investigate the use of ABR elicited by NB LS CE-Chirp stimulus in infants.
2. Moreover, the lengthy waiting list can be up to six months and in the worst case scenario, it will be up to 1 year old if postponed. These conditions may lead to late detection of hearing impairment among infants, postponement of hearing intervention and developmental consequences. The impact of late

diagnosis of hearing impairment in infants is different from that in adults, as newborns have yet to acquire speech and language. Late hearing diagnosis in infants can lead to significant delays in speech development, besides existing with illnesses in psychological behaviour, which can have a huge impact on the child's social, quality of life and academic skills (Wroblewska-Seniuk et al., 2017; Pathak & Deshpande, 2021). Therefore, there is an urgency to conduct ABR in infants who fail the NHS program at birth. It is essential to study ABR to NB LS CE- Chirp usage as it is frequency specific ABR that can provide complete hearing threshold information to estimate the behavioural audiogram. Given the potential of ABR to NB LS CE-Chirp to reduce the testing time and provide comprehensive audiological threshold information, it may indirectly reduce the long waiting list in audiology clinics around the world.

### **3.2.2 Limited studies investigating the ABR to NB LS CE- Chirp in Infants**

As highlighted in section 2.3.2.3.1, ABR elicited from click stimulus prone to the effect from phase dispersion due to its rapid onset with poor frequency specificity to estimate comprehensive hearing threshold level. In contrast, the ABR to tone burst has better frequency specificity than ABR to click stimulus however the waveforms morphology is poorer due to the limited contributions of the ABR fast components and subsequently might interfere with the detection of ABR waves. Tone burst does not have robust ABR waveform, especially at low and middle frequencies, due to the phase dispersion (Peteo et al., 2009; Gorga et al., 2006). Previous studies on ABR to NB LS CE-Chirp were mostly conducted in adult population with the attention centered towards understanding the effects of different stimulus polarities (Klaassen et al., 2016) and different electrode montages (Dzulkarnain et al., 2018) see Section 2.4.1. Most of the studies in infants using broadband level specific CE-Chirp (Kaynakoğlu & Ceyhan, 2023; Chahed et al., 2023; da Silva Ormundo & Lewis, 2021).

Whilst the results of the ABR elicited by NB LS CE Chirp are promising in the adult population, to our knowledge, there is still a lack of studies investigating the ABR to NB LS CE-Chirp among infants and comparing it with tone burst to date. Previous

studies were from an adult population that NB LS CE-Chirp elicited larger amplitude than tone burst (Dzulakrnain et al., 2018) and NB CE-Chirp produced larger amplitude than tone burst in paediatric population (Talaat et al., 2020). Moreover, Talaat et al. (2020) found that ABR to NB CE-Chirp has a higher correlation with pure tone audiometry (PTA) threshold than the PTA threshold versus ABR to tone burst. Hence, the findings are incomparable to the infant population. The brain structures of adults and infants are different and brain maturation of infants usually occurs up to two years of age, see Section 2.3.2.1.1 (Holland et al., 1985; Hayakawa et al., 1989; Khan et al., 2024). In the course of understanding NB LS CE-Chirp usage in infants, a study to systematically investigate this niche is extremely crucial.

### **3.3 RESEARCH OBJECTIVES**

The objectives of this study are as follows:

#### **3.3.1 General objective**

To investigate the use of ABR elicited from NB LS CE-Chirp stimulus in the infant population.

#### **3.3.2 Specific objectives**

1. To compare the ABR amplitude (waves I, III, and V) in infants between NB LS CE-Chirp and tone burst using frequency specific of 500, 1000, and 4000 Hz at 70 and 40 dBnHL.
2. To compare the ABR latency (waves I, III, and V) in infants between NB LS CE-Chirp and tone burst using frequency specific of 500, 1000, and 4000 Hz at 70 and 40 dBnHL.
3. To compare ABR threshold estimations between NB LS CE-Chirp and tone burst in infants using frequency specific of 500, 1000, and 4000 Hz.
4. To compare the ABR acquisition time in infants via NB LS CE-Chirp and

tone burst at frequency specific of 500, 1000, and 4000 Hz using two stopping criteria (visual detection and  $F_{mp} \leq 3.1$ ) at 70 and 40 dBnHL.

### **3.4 RESEARCH HYPOTHESES**

1. ABR to NB LS CE-Chirp elicits larger amplitude (waves I, III, and V) in infants compared to ABR to tone burst using frequencies of 500, 1000, and 4000 Hz at 70 and 40 dBnHL.
2. ABR to NB LS CE-Chirp produces shorter latency (waves I, III, and V) in infants compared to ABR to tone burst using frequencies of 500, 1000, and 4000 Hz at 70 and 40 dBnHL.
3. ABR to NB LS CE-Chirp using frequencies specific to 500, 1000, and 4000 Hz yield lower ABR hearing threshold estimations in infants compared to ABR to tone burst.
4. ABR to NB LS CE-Chirp using frequencies specific to 500, 1000, and 4000 Hz has lesser acquisition time in infants using  $F_{mp} \leq 3.1$  compared with ABR to tone burst using visual detection.

### **3.5 SUMMARY**

This chapter has described the limitations of ABR in terms of time-consuming procedures that lead to restrictions for ABR patients daily. This situation made it difficult to identify infants with hearing loss younger than three months old due to the extensive hours of ABR assessment and ABR appointments waiting list. Besides the clinical issues, there is lacking ABR to NB LS CE-Chirp literature, especially in the infant population, in terms of time efficacy and results accuracy. These limitations motivate the development of the current study and lead to the research objectives and hypotheses.

Table 3.1 Research Questions, Research Objectives and Hypotheses

RESEARCH QUESTIONS	RESEARCH OBJECTIVES	HYPOTHESES
i. Does ABR in infants using NB LS CE-Chirp elicit larger amplitude (wave I, III, and V) than tone burst using frequencies specific to 500, 1000, and 4000 Hz at 70 and 40 dBnHL?	i. To compare the ABR amplitude (wave I, III, and V) in infants between NB LS CE-Chirp and tone burst using frequency specific of 500, 1000, and 4000 Hz at 70 and 40 dBnHL.	i. ABR to NB LS CE-Chirp elicits larger amplitude (wave I, III, and V) in infants compared to ABR to tone burst using frequencies of 500, 1000, and 4000 Hz at 70 and 40 dBnHL.
ii. Does ABR in infants using NB LS CE-Chirp elicit shorter latency (wave I, III, and V) than tone burst using frequencies specific of 500, 1000, and 4000 Hz at 70 and 40 dBnHL?	ii. To compare the ABR absolute latency (wave I, III, and V) in infants between NB LS CE-Chirp and tone burst using frequency specific of 500, 1000, and 4000 Hz at 70 and 40 dBnHL.	ii. ABR to NB LS CE-Chirp elicits shorter latency (wave I, III, and V) in infants compared to ABR to tone burst using frequencies of 500, 1000, and 4000 Hz at 70 and 40 dBnHL.
iii. Does ABR to NB LS CE-Chirp produces lower ABRs threshold compared to tone burst at frequencies specific of 500, 1000, and 4000 Hz?	iii. To compare ABR thresholds between NB LS CE-Chirp and tone burst in infants using frequency specific of 500, 1000, and 4000 Hz.	iii. ABR to NB LS CE-Chirp using frequencies specific of 500, 1000, and 4000 Hz yield lower ABR hearing threshold estimations in infants compared to ABR to tone burst.
iv. Does ABR via NB LS CE-Chirp in infants using $F_{mp} \leq 3.1$ for frequency specific of 500, 1000, and 4000 Hz require lesser acquisition time compared to ABR to tone burst using visual detection?	iv. To compare the ABR acquisition time in infants via NB LS CE-Chirp and tone burst at frequency specific of 500, 1000, and 4000 Hz using two stopping criteria (visual detection and $F_{mp} \leq 3.1$ ) at 70 and 40 dBnHL.	iv. ABR to NB LS CE-Chirp using frequencies specific to 500, 1000, and 4000 Hz has lesser acquisition time in infants using $F_{mp} \leq 3.1$ compared with ABR to tone burst using visual detection.

## **CHAPTER FOUR**

### **EXPERIMENT ONE: THE EFFECTS OF STIMULUS TYPES ON ABR AMPLITUDE, LATENCY, AND HEARING THRESHOLD ESTIMATION**

#### **4.1 INTRODUCTION**

This chapter provides the materials and methodology used in this study. This chapter begins with study design, instrumentations, data collection procedure, data analysis, and discussion. This chapter will cover the first three objectives. The objective of the study has been highlighted in chapter three and as follows:

1. To compare the ABR amplitude (waves I, III, and V) in infants between NB LS CE-Chirp and tone burst of 500, 1000, and 4000 Hz at 70 and 40 dBnHL.
2. To compare the ABR latencies (waves I, III, and V) in infants between NB LS CE-Chirp and tone burst using frequency specific of 500, 1000, and 4000 Hz at 70 and 40 dBnHL.
3. To compare the ABR thresholds estimations between NB LS CE-Chirp and tone burst in infants using frequency specific of 500, 1000, and 4000 Hz.

#### **4.2 MATERIALS AND METHODOLOGY**

##### **4.2.1 Study Design and sampling**

A repeated measure study design was used in the current study. The current study identified the cause and effect of the independent variable (i.e., stimulus types) towards dependent variables (i.e., ABR amplitude, absolute latency, and hearing threshold estimation) (Thyer, 2012). In the current study, the convenience sampling technique was used to recruit a total of 50 ears of infants who passed the hearing screening. This sampling is used because the subject recruitment is based on the availability of the infants in the targeted location and

meets the inclusion criteria for participation in this study.

#### **4.2.2 Ethical Clearance**

This study was conducted after approval from the Kulliyyah Postgraduate and Research Committee (KPGRC) (see Appendix I), IIUM Research Ethics Committee [IREC 2023-065] (see Appendix J), Medical Research and Ethics (MREC), National Medical Research Registration [(NMRR) ID-23-01821-J12 (IIR)] (see Appendix K), and Sultan Ahmad Shah Medical Centre (SASMEC) approval from Department of Ear, Nose, and Throat (ENT) and Department of Obstetrics and Gynaecology (O & G) (see Appendix L). For data collection, parent or caretakers consent was obtained via phone calls and an appointment date was prearranged for the parents. Written consent form with the particulars of the study was obtained from the subjects' parents or caretakers before the assessments were conducted (see Appendix A until D). For data collection, the demographic data form, audiological report form, and consent form are in Appendix E to H.

#### **4.2.3 Study Location**

This study was conducted in a sound-treated room at IIUM Hearing and Speech Clinic, Jalan Hospital Campus, Kuantan, Pahang. Figure 4.1 illustrates the experimental setup of the study. The room that has been specifically designed for the evaluation of auditory electrophysiology (AEP) with electrical protection, follows the standards outlined by the American National Standards Institute (ANSI) (ANSI S3.1-1999 and ANSI S3.6-2004). The reference levels for 0 dBnHL for tone burst and narrow band chirp are shown in Table 4.1 based on the ISO 389-6 (2007) and recommended by (BSA, 2019).

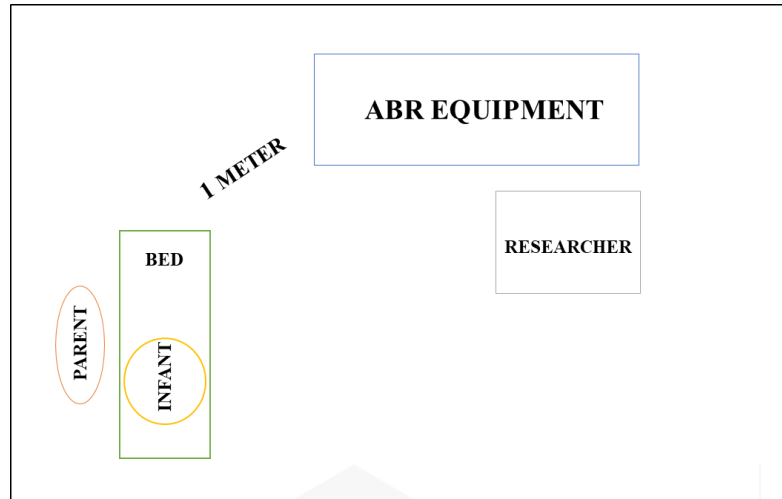


Figure 4.1 ABR clinical setting layout in IIUM Hearing and Speech Clinic.

Table 4.1 ABR Reference Levels for Stimulus Calibration (BSA, 2019)

ABR Reference Level for Stimulus Calibration						
AC RETSPL dBppeSPL for insert earphones	Tone Burst			Narrow Band Chirps		
	500	1000	4000	500	1000	4000
ER-3A/ IEC 60318-4 (IEC 60711) Occluded ear simulator	23.5	21.5	32.5	25.5	24.5	35.0
ER-3A/ IEC 60318-5 (IEC 60711) 2cc coupler, HA-2	19.5	16.0	23.0	22.5	18.5	25.0

#### 4.2.4 Study Population

A total of 50 normal hearing ears (27 females, 23 males) were recruited from the low-risk ward, Obstetrics & Gynecology (O & G) Department, SASMEC IIUM, Kuantan, Pahang. The ABR data collection was conducted over a period of nine months, from July 2023 to April 2024. The age range of the subjects is from birth to less than six months with a mean age of 2.55 months (SD = 0.83).

Fifty normal hearing ears who passed the DPOAE/ AABR hearing screening were done by SASMEC audiologists or nurses. The normal hearing sensitivity was defined as athreshold  $\leq 35$  dB HL from 500 to 4000 Hz. The ABR results from the left and right were

round to be not statistically significantly different. Therefore, the results of the right and left ear were pooled and averaged ( $p > 0.05$ ). The summary of the demographic data is shown in Table 4.1.

Table 4.2 Demographic data

Variables		n	Mean	SD
Age (months)		50	2.55	0.83
Gender	Male	27		
	Female	23		

#### ***4.2.4.1 Inclusion Criteria***

To be part of this study, the participants need to be:

1. Months of age and below; before the diagnosis age of 6 months old to follow a recommendation by JCIH (EHDI, 2007).
2. Clear external auditory canal and intact tympanic membrane (TM) via otoscopic examination.
3. Type A tympanogram suggesting normal middle ear function using high frequency tympanometry.
4. “PASS” hearing screening either using distortion products otoacoustic emissions (DPOAE) or automated auditory brainstem response (AABR) test at 35 dBnHL bilaterally.

#### ***4.2.4.2 Exclusion Criteria***

The study participants with the following criteria, were excluded from the study:

1. Subjects with otological or middle ear problems or upper respiratory tract

infection (URTI) symptoms two weeks prior appointment day.

2. Subjects with high risk factors of hearing loss, according to JCIH (2019), as per Appendix O.

#### **4.2.5 Instrumentation**

The instruments used in this study are as follows:

1. Welch Allyn Otoscope is a clinical procedure that visualizes the structures of the ear, including the external auditory canal and tympanic membrane. This otoscope consists of magnifying lenses and light to evaluate ear anatomical structures' visibility.
2. GSI 33 Tympanometry is an acoustic immittance test to evaluate the mobility of the tympanic membrane and the middle ear health status. This test runs by small probe tip insertion into the ear, the middle ear function is reflected back, and picked up by the equipment.
3. Interacoustics Titan Automated Auditory Brainstem Response (AABR) is a hearing screening tool that assesses the entire auditory pathway up to the brainstem. This test runs by small earphones inserted into the ear and it elicits acoustic stimulus which is CE- Chirp at 35 dBnHL. As a screening tool, AABR detects either “PASS” or “REFER” from the intact response of the auditory pathway up to brainstem response.
4. A laptop with Interacoustics Eclipse EP25 ABR analyzing software system is located in the AEP sound-treated room and the stimulus is given via ER-3A (Etymotic Research) insert earphones. This study used NB LS CE-Chirp stimulus and tone burst stimulus. The specific frequencies chosen are 500, 1000, and 4000 Hz as these frequencies represent low, middle and high frequencies regions. Multiple intensity levels of 70 and 40 dBnHL were used in this study.

#### ***4.2.5.1 Informed Consent***

On the scheduled appointment date, verbal and written consent from (see Appendix C and D) the subjects' parents or caretaker was obtained before the preliminary audiological routine assessment and the ABR assessment were conducted. The purpose of the study, procedures, risks and benefits, confidentiality, and anonymity were informed to the parents (see Appendix C and D). Parents were allowed to ask questions only before or after the session without interrupting the study session. The inclusion criteria of the subjects as described in Section 4.2.4.1. Participation in this study was on a voluntary basis and parents can withdraw from volunteering and be advised to inform the researcher at least three days before the scheduled appointment date, and any data and information gained will be permanently destroyed, see Appendix C and D.

#### ***4.2.5.2 Demographic Data Form***

The demographic data form consists of the infant demographic data, prenatal, and postnatal history, and preliminary audiological routine tests results. During the history taking session, the researcher filled out the form. The form is in Appendix E and F.

#### **4.2.6 Data Collection Procedure**

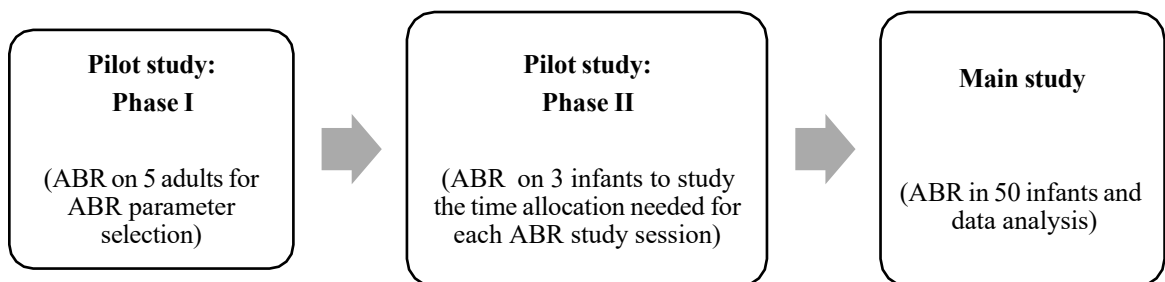


Figure 4.2 The study phases.

The study has three phases, as summarized in Figure 4.2. The first phase was a pilot study: phase I and II, and the main data collection and data analysis. The ethical clearance was obtained from IIUM and SASMEC for the data collection, see 4.2.2.

#### ***4.2.6.1 Pilot Study: Phase I***

The pilot study: phase I was conducted in order for the researcher manipulated a few ABR test parameters on five adults. The stimulus frequencies used during this stage were 500, 1000, 2000, and 4000 Hz. The initial three intensity levels used were 70, 50, and 30 dBnHL. To control the test time for infant testing, only 70 dBnHL, 40 dBnHL, and hearing threshold estimations were included. The stimulus rate used was set to 33.3 clicks per second (cps). The aim of this phase 1 is to finalize the ABR parameter to be used in the study. Based on these five case studies, the ABR recordings was obtained using the parameter in Table 4.2.

#### ***4.2.6.2 Pilot Study: Phase II***

The pilot study: phase II was conducted to study the ABR parameters selected from the pilot study: Phase I and to estimate the time allocation needed for each ABR study session. In this phase, there were three infants involved. Three frequencies of 500, 1000, and 4000 Hz with 70, 40 dBnHL and hearing threshold estimations were selected to control the test time. In addition, to avoid lethargy from the subjects in completing the ABR assessment for both ears, the time allocation for data collection of the main study was set not to exceed two hours for each ABR session. Based on these three subjects from the pilot study, the ABR obtained using the parameter in Table 4.2 is the best and able to produce reliable and consistent findings (NHSP, 2013; Rouillon et al., 2016). Thus, the ABR parameter used in the pilot study: phase II was feasible to be used in the main study data collection.

### ***4.2.6.3 Main Study***

The main study was divided into two parts: preliminary audiological routine testing and main data collection. First, the preliminary audiological routine testing was conducted prior to the main study to rule out any subjects that do not meet the inclusion criteria for this study. Second, the main data collection is the ABR research study.

#### ***4.2.6.3.1 Preliminary audiological routine testing***

- i. The preliminary audiological routine tests were conducted on the same ABR research study appointment date.
- ii. History taking was obtained using a pediatric patient history form.
- iii. An otoscopic examination was done to check the external auditory canal and tympanic membrane condition.
- iv. High frequency tympanometry test was used to measure middle ear function. A probe tip was inserted to get the best seal and consistent tympanometry result. This test took less than 1 minute to complete for each ear, and the result is shown in the tympanogram graph. The results showed ear canal volume, static compliance, and middle ear pressure values. In this study, the normative range for the paediatric population use is the ear canal volume is between 0.3 ml to 0.9 ml, static compliance is from 0.25 ml to 1.05 ml, and the middle ear pressure is from -100 daPa to +50 daPa. The values within the normative range were considered Type A suggesting normal middle ear function.
- v. DPOAE or AABR assessment was conducted to screen the normal hearing subjects as a part of the inclusion criteria mentioned in Section 4.2.4.1. For DPOAE, a probe tip of DPOAE was inserted into the ear. Meanwhile, for AABR, an integrated headphone that delivers acoustic stimulus to the ear of the infants which is a single-sided headphone that is put on the infant's ear, forehead, and mastoid, respectively. Both the DPOAE and AABR recording was recorded automatically.

#### 4.2.6.3.2 Main data collection of ABR research study

In this study, ABR measurements were conducted using the Interacoustics Eclipse EP25 system. ABR assessment was performed in a sound-treated room; the lights were dimmed. Subjects need to be in a relaxed state and, if possible, sleep on the bed or on the caretaker's lap during the recording session to reduce muscle or movement artifact. Subjects were under natural sleep without sedation. The parameter of the main study is described and outlined in section 4.2.6.3. Moreover, the total time to complete this main study for each subject was about 1.5 to 2 hours. The ABR parameters used in this study were based on the stimulus and acquisition factors. The details of the ABR parameters are described below, and the summary is in Table 4.2.

#### 4.2.6.3.3 Stimulus Factors

Stimulus factors included in the ABR parameters are types, frequency, intensity, and polarity. These stimulus factors of ABR were employed in the current study.

##### a. Stimulus Types

The stimulus used in this study were tone burst and NB LS CE-Chirp. The tone burst and NB LS CE-Chirp were used as a part of the study objectives one, two, and three based on the literature review, see subsections 2.3.2.3.

##### b. Stimulus Frequency

In this study, the ABR was obtained at 500, 1000, and 4000 Hz using NB LS CE-Chirp and tone burst. The stimulus frequencies were chosen as a part of the study objectives one, two, and three using the stimulus frequencies of 500, 1000, and 4000 Hz, represent low, middle, and high-frequency parts, respectively.

### c. Stimulus Polarity

In this study, the Eclipse 25 ABR system was used and it provides 3 types of polarity which are condensation, rarefaction, and alternating. However, in this study, alternating polarity was chosen because the system enables separate visualization of positive and negative polarity waveforms; further explanation of polarity was discussed in subsection 2.3.2.2.3.

### d. Stimulus intensity

The threshold seeking steps for each frequency were using Randomization software for randomization of step selection. First, NB LS CE-Chirp or tone burst stimulus was given on the right or left ear through insert earphones starting either at 500, 1000, or 4000 Hz with 70 and 40 dBnHL. The researcher will insert 6 combination possibilities of stimulus types and frequency based on three frequencies (500 Hz, 1000 Hz, and 4000 Hz) and two ABR stimuli (NB LS CE-Chirp and tone burst) in the software. The Randomisation software will automatically list the 6 combinations of stimulus types and frequencies; see Table 4.3. For instance, presentation level starting with 500 Hz NB LS CE-Chirp at 70 dB, 40 dB and threshold level, and secondly, proceed with 500 Hz tone burst at 70 dB, 40 dB and threshold level. Third, 1000 Hz tone burst at 70 dB, 40 dB and threshold level, and forth, using 1000 Hz NB LS CE-Chirp at at 70 dB, 40 dB and threshold level. Fifth step, 4000 Hz tone burst at 70 dB, 40 dB and threshold level, and then, 4000 Hz NB LS CE-Chirp at 70 dB, 40 dB and threshold level. The example of the lists are as in Table 4.3.

Next, for the threshold seeking step, stimulus presentation technique used were 10 dB down and 5 dB up method until reproducible waveforms were obtained to estimate the threshold of each subject. The test was conducted to obtain the ABR threshold where the test was done at 10 dB below the last ABR which was identified at the level at which wave V was not reproducible. After completing seeking one true threshold of NB LS CE-Chirp or tone burst at any frequency and in either ear, the threshold of other frequencies was employed. The same parameters were repeated with randomization steps to avoid any bias and fatigue to the ears. The summarization of the ABR parameters used in this study is

shown in Table 4.3.

Table 4.3 Example lists of randomization steps using Randomization

No.	List 1	List 2	List 3	List 4
1.	500 Hz NB LS CE-Chirp	1000 Hz tone burst	4000 Hz NB LS CE-Chirp	500 Hz tone burst
2.	500 Hz tone burst	500 Hz NB LS CE-Chirp	1000 Hz tone burst	4000 Hz tone burst
3.	1000 Hz tone burst	4000 Hz NB LS CE-Chirp	500 Hz NB LS CE-Chirp	500 Hz NB LS CE-Chirp
4.	1000 Hz NB LS CE-Chirp	500 Hz tone burst	1000 Hz NB LS CE-Chirp	4000 Hz NB LS CE-Chirp
5.	4000 Hz tone burst	1000 Hz NB LS CE-Chirp	4000 Hz tone burst	1000 Hz NB LS CE-Chirp
6.	4000 Hz NB LS CE-Chirp	4000 Hz tone burst	500 Hz tone burst	500 Hz tone burst

#### 4.2.6.3.4 Acquisition parameters

The acquisition factors were electrode montage, filter, analysis time, amplification, common mode rejection, and signal averaging. These acquisition factors of ABR were deployed in the current study.

##### a. Electrodes placement and montages

ABR was recorded using two channels function through four electrode locations. Before placing the electrode, the subject was prepared by scrubbing the respective places for electrode placement using NuPrep Skin Preparation electrode gel. Ipsilateral/contralateral electrode montage were used by placing Ambu Neuroline 720 disposable electrodes on high forehead marks as non-inverting (Cz) electrode, lower forehead marks as ground electrode (Fpz), inverting electrodes on left (M1) electrode, and right (M2) electrode on both mastoids, respectively (Dzulkarnain et al., 2018) as shown in Figure 4.2. The electrodes impedance was retained below 5 k $\Omega$  during all measurements, measured by the

ABR Interacoustics Eclipse EP25 impedance check function, and balance inter-electrode impedance will be maintained. These two-channel configurations were used to get information from two different locations of the inverting electrode that are prominent to capture all the ABR peaks (Dzulkarnain et al., 2021). The non-inverting electrode on the forehead risks a smaller ABR recording, for mastoid electrodes far from the ear, and the wave I amplitude recording is small. However, the placement was chosen for comfort of the subjects.

#### b. Filters

The recorded signal was filtered from 33 Hz (high pass) to 3000 Hz (low pass) with a 6-dB/octave slope (Sininger et al., 2000). The stimulus filters were selected based on the review of the literature and were discussed in subsection 2.4.2.

#### c. Stimulus rate

The stimulus rate that was used was 33.33 clicks per second (cps). This stimulus rate is recommended for use in infant subjects as this is an intermediate stimulus rate that allows the test to run rapidly before the subject awakes; further discussion is in subsection 2.3.2.2.2.

#### d. Analysis time

Analysis time, which is also known as “epoch” for ABR recordings following stimulus presentation is essential for auditory evoked response. The analysis time used was 0 to 14 ms which was used as a part of the study objectives one, two, and three because, based on the literature review, see subsection 2.4.3.

#### e. Transducer

The acoustic stimulus will be given via ER3A earphones for comfort purposes and better clinical findings (Muhler et al., 2013). TDH-39 headphones prompt an electromagnetic shield that results in stimulus artifacts at higher intensity levels. In contrast, earphones have

electromagnetic shielding to abolish electromagnetic artifacts (Coats et al., 1979). The ER-3A insert earphones decrease the stimulus crossover likelihood from the test ear to the non-test ear. Earphones offer several advantages in clinical ABR measurements, particularly for infants and young children. These advantages include improved transducer placement, enhanced control over the signal presentation, and the ability to optimize tone burst parameters.

#### f. Amplification

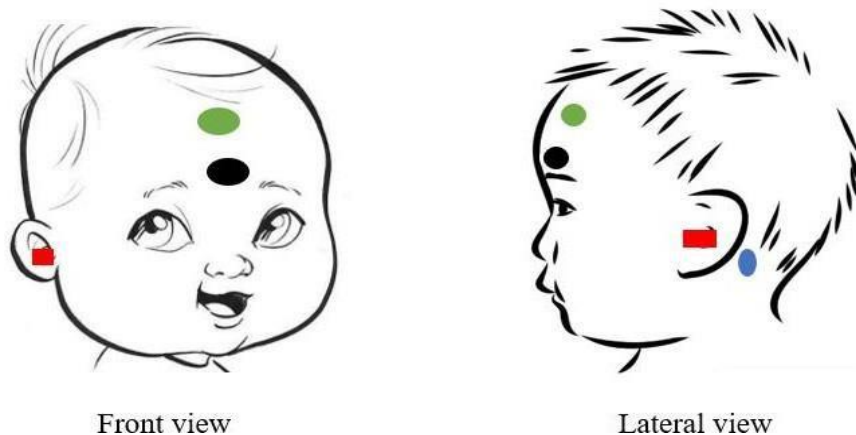
The amplifier gain is set at 100 000 amplifier gain level and EEG samples exceeding  $\pm 40\text{nV}$  will be rejected; further discussion in subsection 2.5.5.

#### g. Common mode rejection

Common mode rejection (CMR) has a function of differential amplification and is essential in ABR recording.

#### h. Signal averaging

The amount of signal averaging (i.e., maximum number of sweeps per run) was pre-set at 2000. The signal averaging was used as a part of study objectives one, two, and three because based on the literature found in subsection 2.4.4.



### Indicators

- Non-inverting (+ve)
- Ground
- Inverting (-ve)
- Insert earphone

Figure 4.3 Electrodes placement in ABR assessment on the infant.

Table 4.4 Recommended recording parameters for ABR to NB LS CE-Chirp and ABR to tone burst

Type	Narrowband level specific CE-Chirp	Tone burst
<b>Transducer</b>	Etymotic Research ER-3A earphones (Muhler et al., 2013) Infant insert ear tip 3.5 mm or 4.0 mm	
<b>Electrode montage</b>	2 Channels Ipsilateral/ Contralateral	
<b>EEG filters</b>	33 Hz (high pass) to 3000 Hz (low pass) band-pass filter (Sininger et al., 2000)	
<b>Intensities</b>	Intensity levels: 70 dBnHL and 40 dBnHL Steps: Down by 10 dB, up by 5 dB (Dau et al., 2000)	
<b>Rate</b>	33.3 clicks per second (cps) (Rasetshwane et al., 2013)	
<b>Polarity</b>	Alternating (Rodrigues et al., 2013)	
<b>Impedance</b>	< 5000 $\Omega$	
<b>Fmp</b>	$\geq 3.1$	
<b>Residual Noise (RNL)</b>	$\leq 40$ nV	

#### 4.2.7 Waveform Analysis

The variables of this study were the amplitudes and absolute latencies of waves of I, III, and V. The latency was measured from the time of the stimulus onset to the peak of wave I, III, and V, respectively. The amplitude of waves I, III, and V were determined from each peak to its subsequent trough in microvolts (V). The illustration of the methods of ABR waveform analysis is summarized in Figure 4.3. The ABR waveform was identified and interpreted by one single audiologist. Prior to the ABR waveform analysis, a session was conducted involved two audiologists to ensure a reliable and consistent interpretation can be made. This process involves two audiologists with 12 and 20 years of experience. In this process both audiologists, independently interpreting few sample of ABR waveforms by determining the presence or absence of the waveforms and peaks, and subsequently to determine the amplitudes and latencies. They discussed any discrepancies until an inter-rater agreement of at least 90% agreement of descriptive comparison was achieved. There is no statistical analysis was done to compare inter rater agreement as the number of samples of ABRs are small for a statistical analysis. Upon reaching the 90% agreement, the first audiologist (main researcher) then independently identified and interpreted the ABR waveforms.

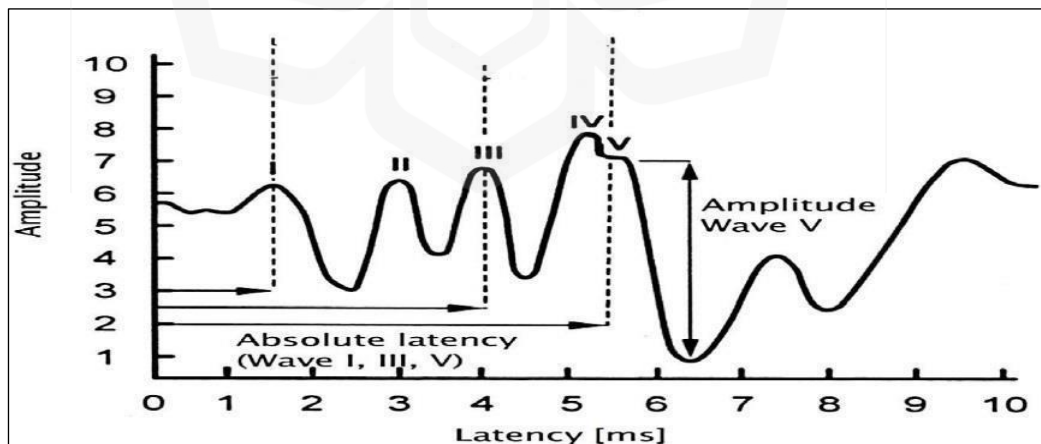


Figure 4.4 The illustration of ABR waveform analysis (Hall, 2013).

The estimation of hearing thresholds referred to the lowest intensity level identified at which wave V of ABR was detectable. Two repetitions of ABR recordings were conducted to determine these thresholds for both stimuli. The study assessed the replicability and consistency of the ABR waveform to confirm the accuracy of the hearing threshold estimation. In determining the presence of ABRs, the study required a clear waveform response at either 5 dB or 10 dB above the corresponding intensity level with a minimum signal-to-noise ratio (SNR) of 3.0. Conversely, ABRs were considered absent if the recording displayed a flat waveform at 5 dB or 10 dB below the respective intensity level and the Residual Noise Level (RNL) was  $\leq 40$  nV. This research adhered to the standard threshold procedure outlined by the British Society of Audiology (2018) which mandates meeting three criteria: i) a clear response indicating an ear-specific threshold, ii) a distinct response at 5 or 10 dB above the threshold, and iii) no response at 5 or 10 dB below the threshold. Additionally, responses at 5 dB or 10 dB above the threshold were expected to be more prominent and sander compared to the threshold findings.

#### **4.2.8 Variables of the study from the ABR elicited via NB LS CE-Chirp and tone burst**

The study divided two variables category which were independent and dependent. There were two independent variables used which were stimulus types and frequencies. In the current study, the stimulus types used were NB LS CE-Chirp and tone burst, whilst for stimulus frequencies were 500, 1000, and 4000 Hz. For the dependent variables, there were amplitude, latency, and hearing threshold estimation. The analysis of the data which assessed the stimulus types affected the amplitude, latency, and threshold estimation level of ABR, underwent statistical comparison as outlined in section 4.2.9. The summary of the independent and dependent variables of the study is illustrated in Figure 4.5.

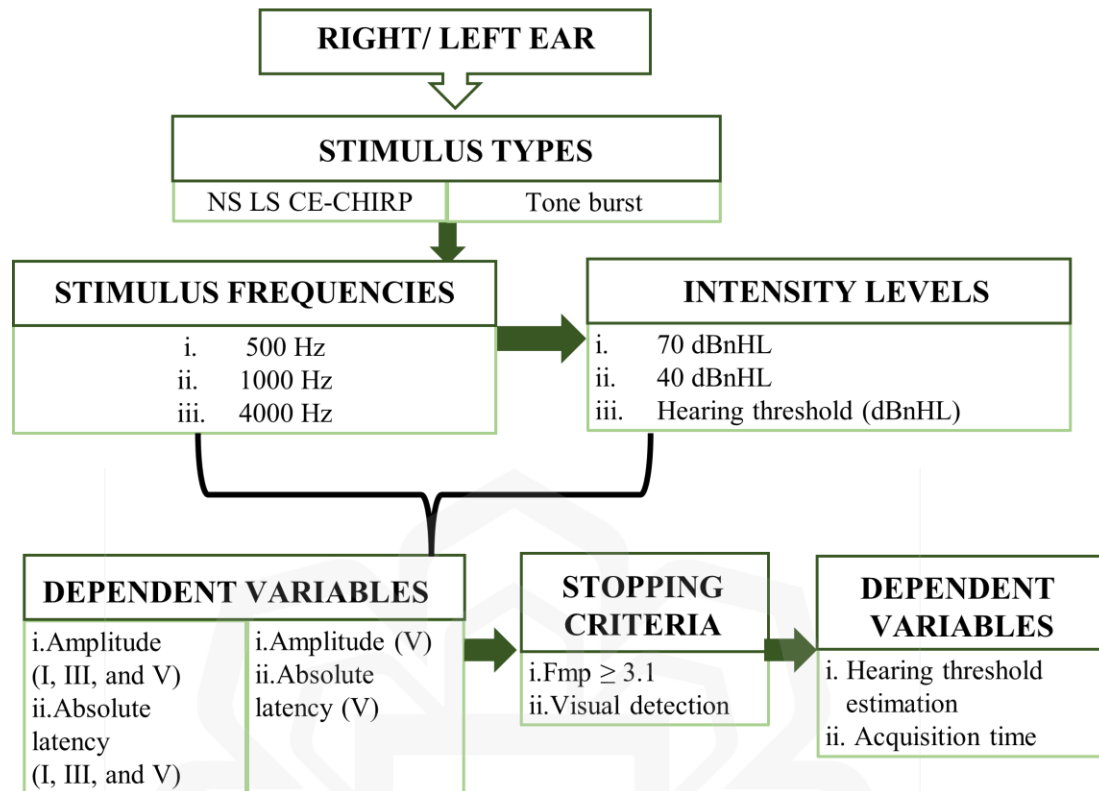


Figure 4.5 Summary of independent and dependent variables of the study.

#### 4.2.9 Statistical Analysis

Statistical analysis was measured using IBM SPSS Statistics for Windows, Version 27.0. (IBM Corp., Armonk, NY, USA). For quantitative data, differences in variable means and standard deviations (SD) were assessed. The normality of the data distribution was evaluated using the Kolmogorov-Smirnov test ( $p < 0.05$ ). Thus, the ABR recording data are non-normal distributed. Given that parametric assumptions were not met due to non-normality and heterogeneous variance, the Wilcoxon signed-rank test was employed with multiple comparisons adjustment to minimize Type I error (i.e., rejecting the null hypothesis the study objectives (i.e., each of the current study objectives is true).

Furthermore, controlling for between subject's variance separately enhanced the power of statistical analysis given the substantial within subject variability. The Wilcoxon signed-rank test was applied to assess statistical significance in amplitude and latency

measurements at 70 dBnHL, 40 dBnHL, the hearing threshold estimation level. The effect size of Wilcoxon signed-rank test value formula was computed by measuring the ratio of the statistic (Z score) divided by the square root of the number of the sample (N) ( $r = Z / \sqrt{N}$ ) (Pallant, 2011). The  $p < 0.01$  was chosen for the current study because of stricter standard for rejecting null hypothesis and reduce Type I error risk (e.g., false positive especially in medical research). Table 4.5 shows the interpretation of the r, Wilcoxon's signed-rank test effect size. The effect size helps to quantify the strength of the difference between the paired samples from the Wilcoxon signed rank test. A different was identified based on effect size. It provides sufficient insights for interpretation, comparison, power analysis, and clinical relevance.

Table 4.5 The Interpretation of the r, Wilcoxon's signed-rank test effect size

Interpretation	Wilcoxon's signed-rank test effect size, r
No effect	0 to < 0.10
Small effect	0.1 to < 0.3
Medium effect	0.3 to < 0.5
Large effect	$\geq 0.5$

Table 4.6 The summary of statistical analysis for each research objective

Specific objective	Independent variables	Dependent variable	Statistical analysis
i. To compare the ABR amplitude (waves I, III, and V) in infants between *NB LS CE-Chirp and tone burst using frequency specific of **500, 1000, and 4000 Hz at ***70 and 40 dBnHL.	<ol style="list-style-type: none"> <li>1. Stimuli; NB LS CE-Chirp and tone burst.</li> <li>2. Stimulus frequencies; 500, 1000, and 4000 Hz.</li> <li>3. Intensity levels; 70 and 40 dBnHL.</li> </ol>	Amplitude	
ii. To compare the ABR absolute latency (waves I, III, and V) in infants between *NB LS CE-Chirp and tone burst using frequency specific of **500, 1000, and 4000 Hz at ***70 and 40 dBnHL.	<ol style="list-style-type: none"> <li>1. Stimuli; NB LS CE-Chirp and tone burst.</li> <li>2. Stimulus frequencies; 500, 1000, and 4000 Hz.</li> <li>3. Intensity levels; 70 and 40 dBnHL.</li> </ol>	Latency	Wilcoxon signed-rank
iii. To compare ABR thresholds between *NB LS CE-Chirp and tone burst in infants using frequency specific of **500, 1000, and 4000 Hz.	<ol style="list-style-type: none"> <li>1. Stimuli; NB LS CE-Chirp and tone burst.</li> <li>2. Stimulus frequencies; 500, 1000, and 4000 Hz.</li> </ol>	Hearing threshold estimation level	
iv. To compare the ABR acquisition time in infants via *NB LS CE-Chirp and tone burst at frequency specific of **500, 1000, and 4000 Hz using ***two stopping criteria at ***70 and 40 dBnHL.	<ol style="list-style-type: none"> <li>1. Stimuli; NB LS CE-Chirp and tone burst.</li> <li>2. Stimulus frequencies: 500, 1000, and 4000 Hz.</li> <li>3. Intensity levels: 70 and 40 dBnHL.</li> <li>4. Stopping criteria; Fmp <math>\geq</math> 3.1 and visual observation.</li> </ol>	Acquisition time	Wilcoxon signed-rank and Friedman test

### 4.3 RESULTS

Fifty ABRs of normal hearing infants using NB LS CE-Chirp and tone burst were collected in this study. The summary of the ABR identification (presence versus absent) across different stimulus types (NB LS CE-Chirp and tone burst) and frequencies (500, 1000, and 4000 Hz) at two intensity levels (70 and 40 dBnHL) are shown in Table 4.7. The ABR waves I and III at 70 dBnHL were not 100% present for all frequencies tested; however, there was a 100 % presence of ABR wave V at 70 and 40 dBnHL for all frequencies tested. The example of the ABR waveform from one study participant of normal hearing infants at three frequencies and different intensity levels is shown in Figures 4.6, 4.7, and 4.8, respectively.

In this study, not all participants have ABRs waves I and III at all frequencies tested. The number and percentages of ABR peak identification according to the stimulus types and stimulus frequencies are shown in Table 4.7. The median and interquartile range (IQR) of ABR amplitudes and latencies at 500, 1000, and 4000 Hz for each presentation level at 70 and 40 dBnHL, including hearing threshold estimations using both stimuli are shown in Table 4.8.

Table 4.7 Number of infants with present ABR waveform in each stimulus type and stimulus frequencies

<b>STIMULUS TYPE</b>				
<b>Frequency (Hz)</b>	<b>INTENSITY LEVEL (dBnHL)</b>	<b>WAVE</b>	<b>NB LS CE- CHIRP</b>	<b>TONE BURST</b>
<b>500</b>	<b>70</b>	<b>I</b>	19 (38 %)	2 (4 %)
		<b>III</b>	25 (50 %)	7 (14 %)
		<b>V</b>	50 (100 %)	50 (100 %)
<b>1000</b>	<b>40</b>	<b>V</b>	50 (100 %)	50 (100 %)
	<b>70</b>	<b>I</b>	32 (64 %)	21 (42 %)
		<b>III</b>	35 (70 %)	23 (46 %)
		<b>V</b>	50 (100 %)	50 (100 %)
<b>4000</b>	<b>40</b>	<b>V</b>	50 (100 %)	50 (100 %)
	<b>70</b>	<b>I</b>	45 (90 %)	44 (88 %)
		<b>III</b>	48 (96 %)	40 (80 %)
		<b>V</b>	50 (100 %)	50 (100 %)
	<b>40</b>	<b>V</b>	50 (100 %)	50 (100 %)

500 Hz

NB LS CE-Chirp

Tone burst

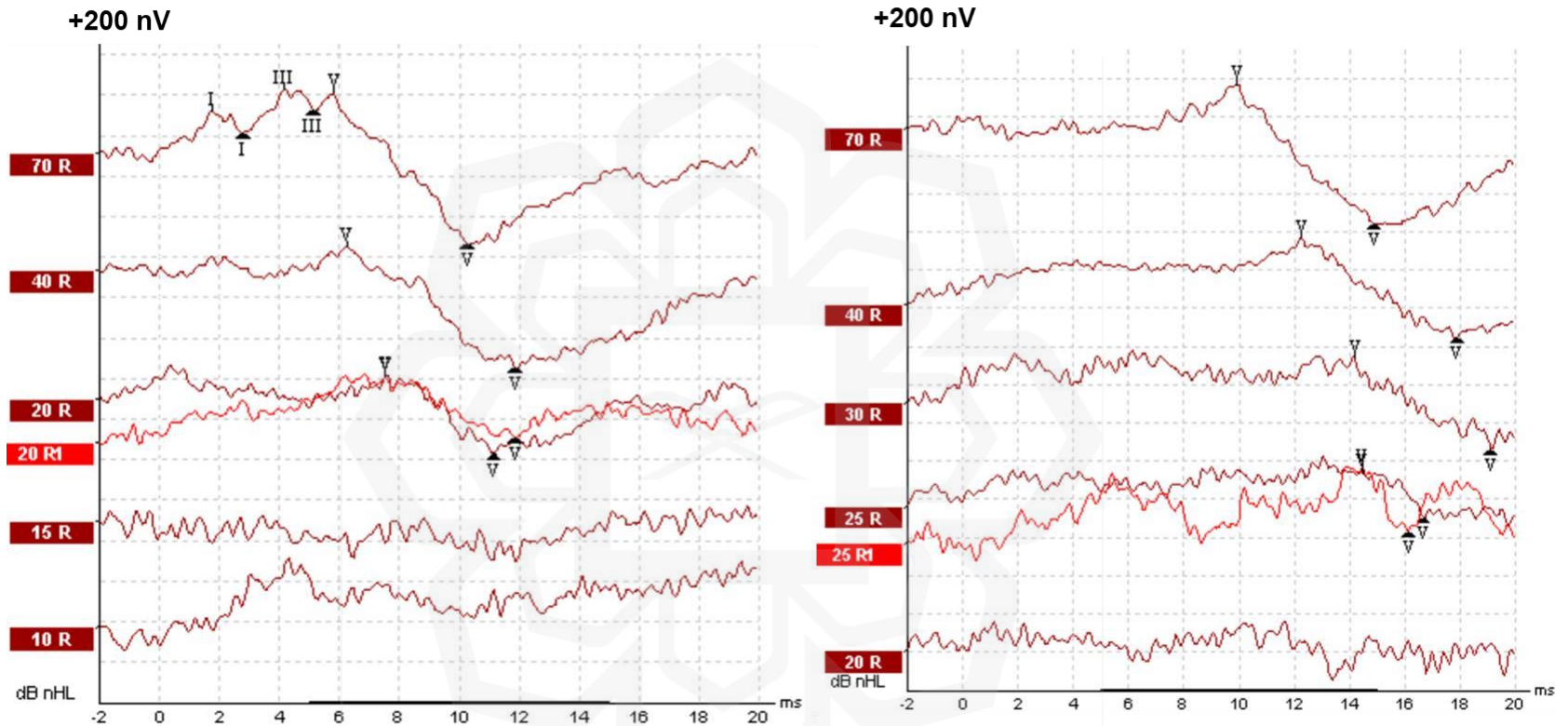


Figure 4.6 ABR waveforms obtained using NB LS CE-Chirp (left side) and tone burst (right side) stimuli at 500 Hz were found in the right ear (red waveform) in one of the normal hearing infants.

500 Hz

NB LS CE-Chirp

Tone burst

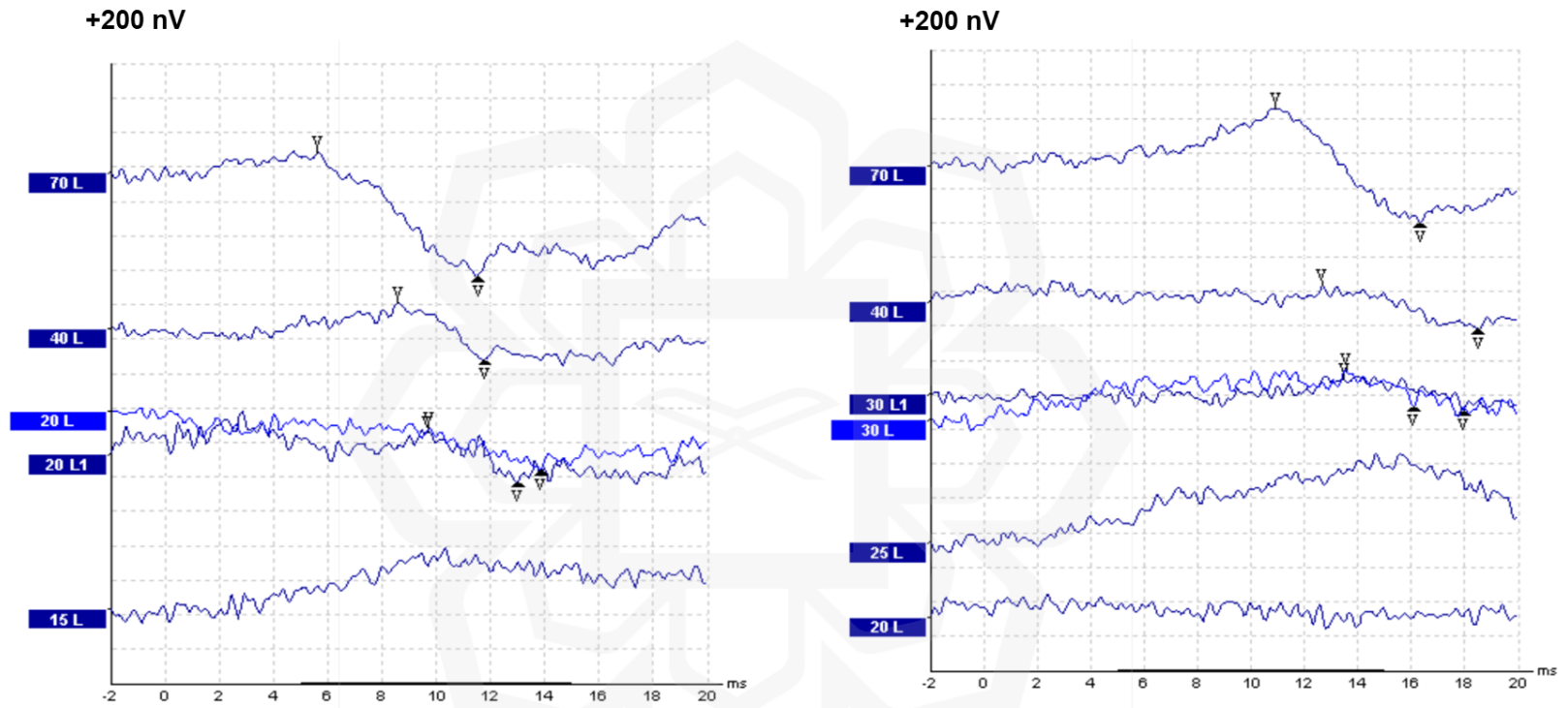
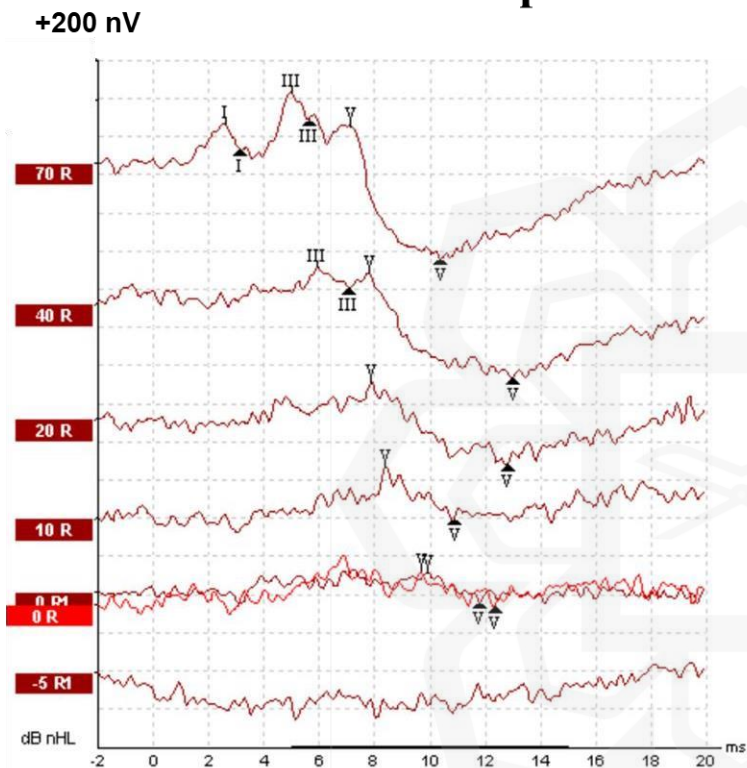


Figure 4.7 ABR waveforms obtained using NB LS CE-Chirp (left side) and tone burst (right side) stimuli at 500 Hz were found in the left ear (blue waveform) in one of the normal hearing infants.

1000 Hz

NB LS CE-Chirp



Tone burst

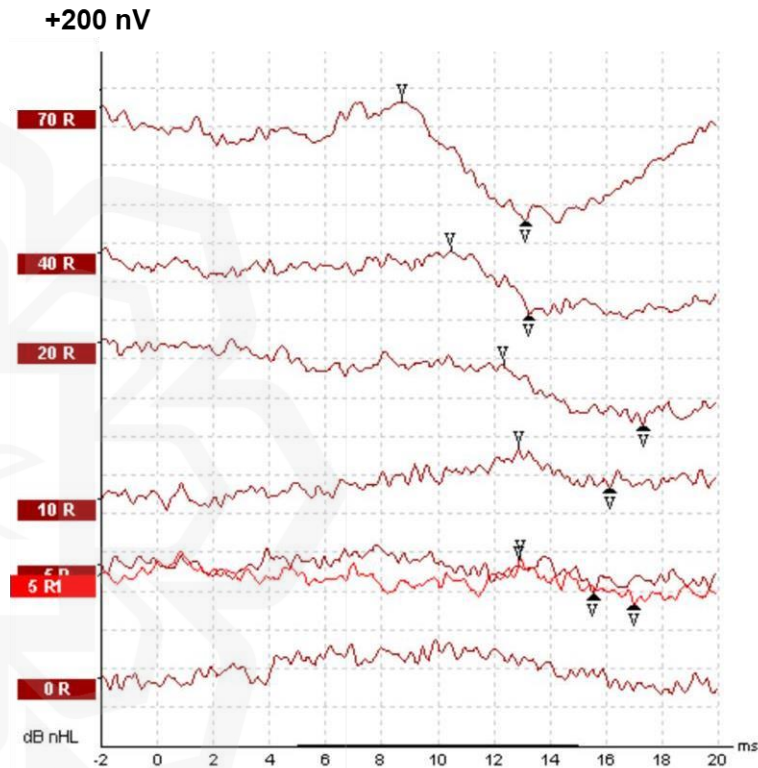


Figure 4.8 ABR waveforms obtained using NB LS CE-Chirp (left side) and tone burst (right side) stimuli at 1000 Hz were found in the right ear (red waveform) in one of the normal hearing infants.

1000 Hz

NB LS CE-Chirp

Tone burst

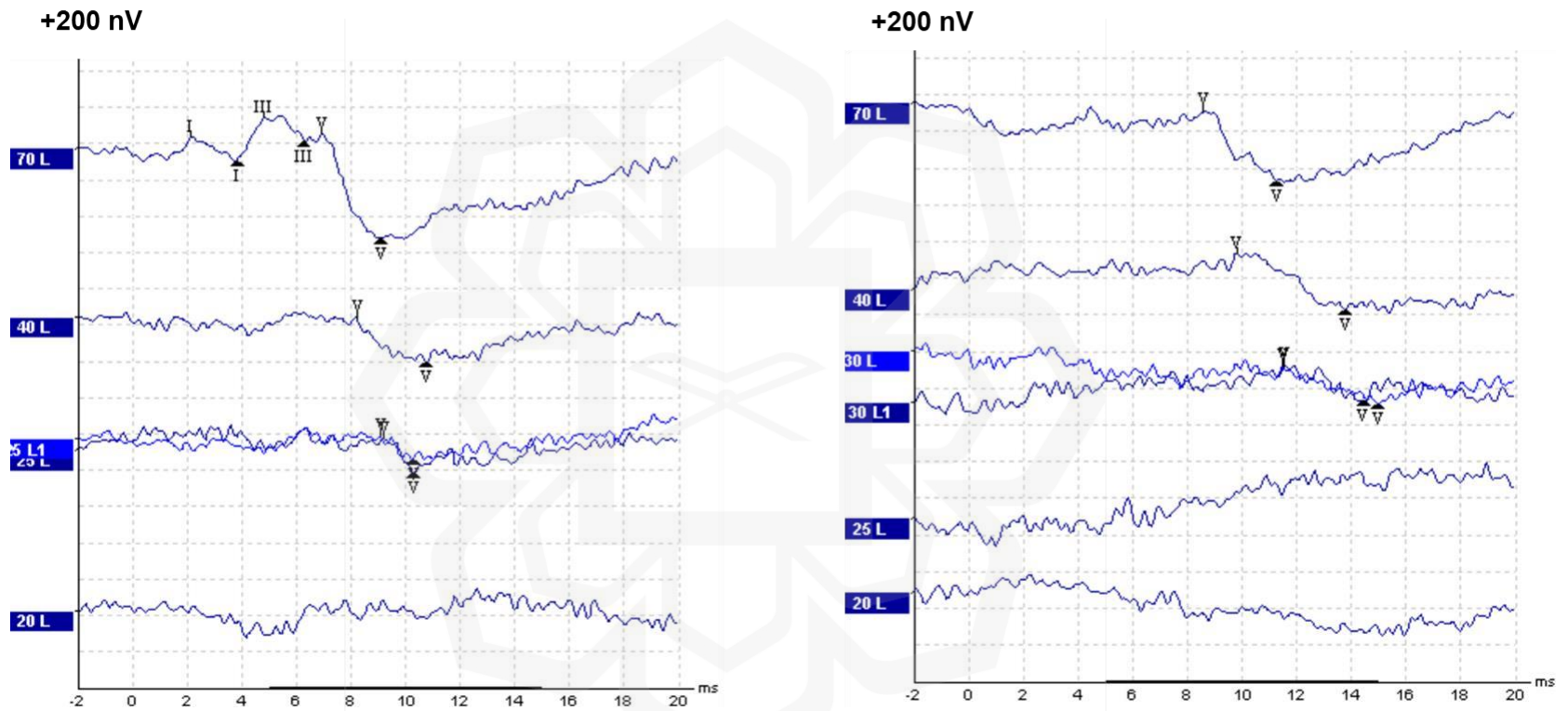


Figure 4.9 ABR waveforms obtained using NB LS CE-Chirp (left side) and tone burst (right side) stimuli at 1000 Hz were found in the left ear (blue waveform) in one of the normal hearing infants.

4000 Hz

NB LS CE-Chirp

Tone burst

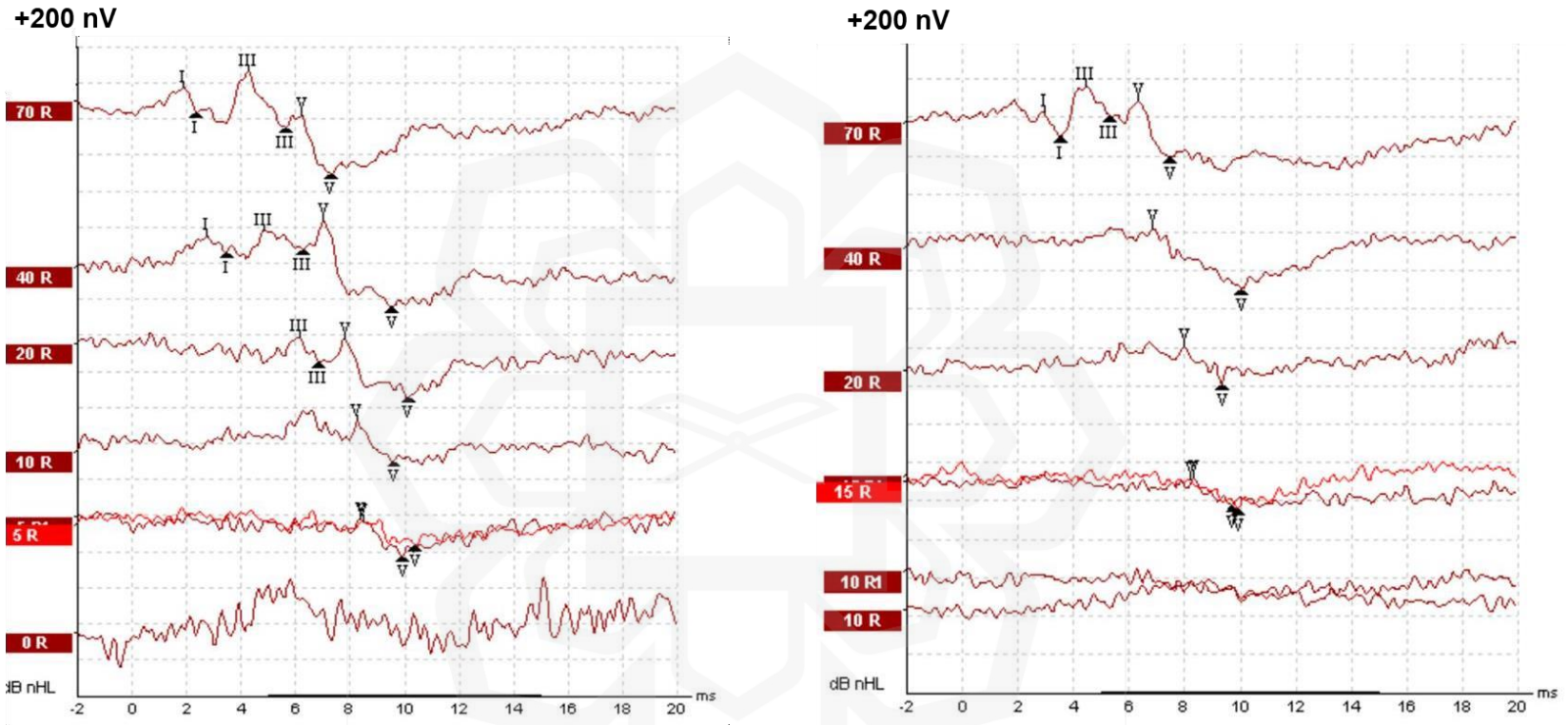


Figure 4.10 ABR waveforms obtained using NB LS CE-Chirp (left side) and tone burst (right side) stimuli at 4000 Hz were found in the right ear (red waveform) in one of the normal hearing infants.

4000 Hz

NB LS CE-Chirp

Tone burst

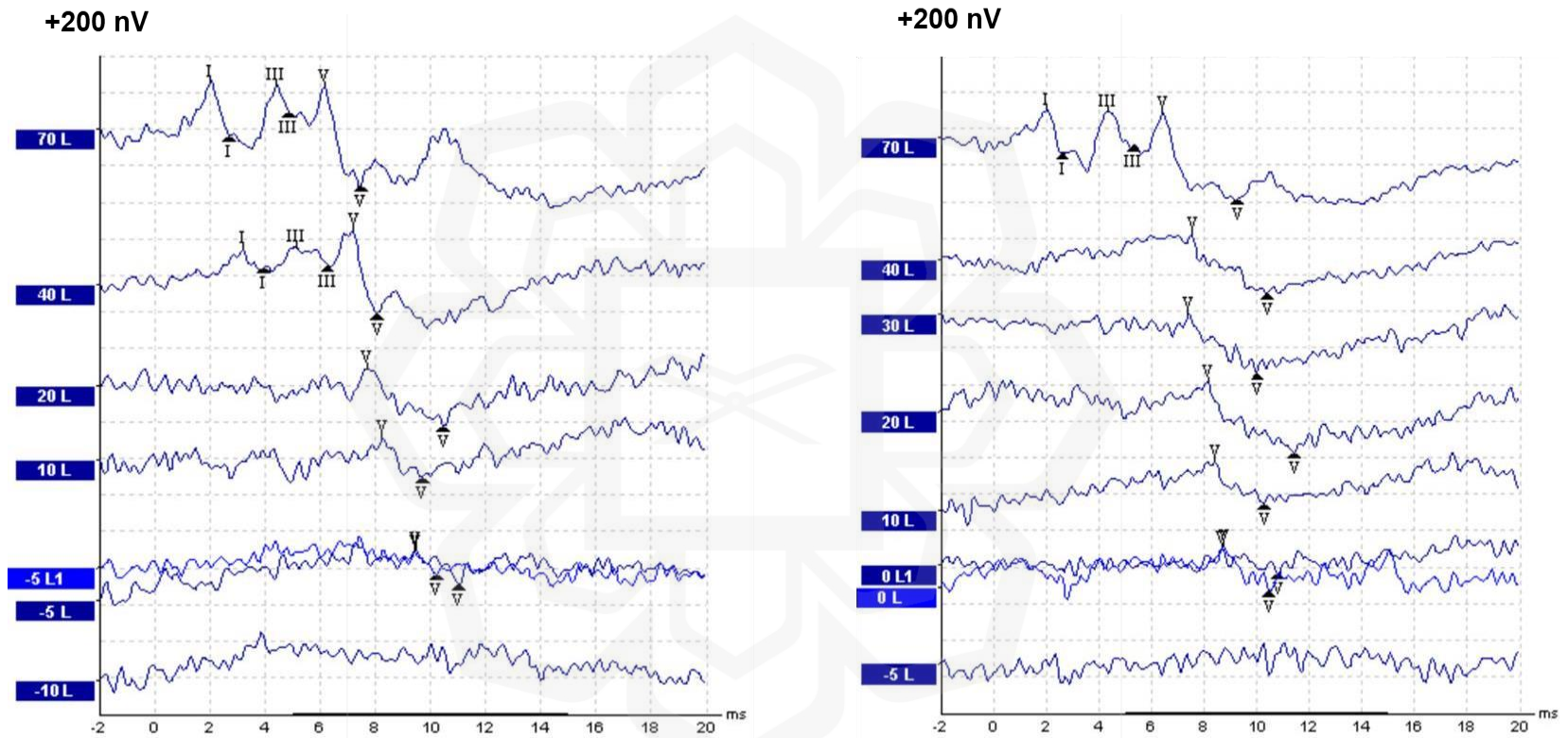


Figure 4.11 ABR waveforms obtained using NB LS CE-Chirp (left side) and tone burst (right side) stimuli at 4000 Hz were found in the left ear (blue waveform) in one of the normal hearing infants.

### **4.3.1 Analysis of amplitudes of waves I, III, and V with NB LS CE-Chirp versus tone burst stimuli at frequencies (500, 1000, and 4000 Hz) and intensities (70 and 40 dBnHL)**

#### ***4.3.1.1 Stimulus types (NB LS CE-Chirp vs tone burst stimulus)***

##### *4.3.1.1.1 70 dBnHL*

The median and interquartile range (IQR) for the amplitude of waves I, III, and V in the ABR elicited by NB LS CE-Chirp and tone burst stimuli at different frequencies (500 Hz, 1000 Hz, and 4000 Hz) in infants were shown in Table 4.8. According to Wilcoxon signed-rank test and/or the effect size values in Table 4.9, the NB LS CE-Chirp is considered to have significantly larger ABR amplitude of waves I, III, and V than tone burst stimulus at all combinations of frequencies and intensities ( $p < 0.01$ ) with medium to large effect size ( $r = 0.30$  to  $0.62$ ) except for wave V at 500 Hz and 4000 Hz ( $p > 0.01$ ) with small effect size ( $r = 0.06$  to  $0.16$ ). The increment of ABR waves V amplitude from tone burst to NB LS CE-Chirp was  $-2.04\%$ ,  $34.78\%$ , and  $16.22\%$  at 500, 1000, and 4000 Hz, respectively.

##### *4.3.1.1.1 70 dBnHL*

The summary of median and IQR for ABR amplitudes of wave V elicited using both stimuli types of three different specific frequencies (500, 1000, and 4000 Hz) are shown in Table 4.8. From Table 4.9, the analysis of Wilcoxon signed-rank test showed that wave V amplitude of NB LS CE-Chirp was larger than tone burst ( $p < 0.01$ ) for all the frequencies tested with medium effect size ( $r = 0.33$  to  $0.54$ ). The particulars of Z-distribution, p-value, and effect size for amplitude values are shown in Table 4.9. The increment of ABR waves V amplitude from tone burst to NB LS CE-Chirp was  $19.23\%$ ,  $20\%$ , and  $25\%$  at 500, 1000, and 4000 Hz, respectively.

Table 4.8 The median and interquartile range (IQR) for amplitude, absolute latency of waves (I, III, and V), and hearing threshold estimation level using ABR to NB LS CE-Chirp and ABR to tone burst at multiple frequencies in normal hearing infants.

		NB LS CE-Chirp			Tone burst		
Intensity (dBnHL)	Wave			Frequencies (Hz)			
		500	1000	4000	500	1000	4000
<b>Amplitude (<math>\mu</math>V)</b>							
<b>70</b>	<b>I</b>	0.15 (0.01)	0.17 (0.07)	0.25 (0.16)	0.10 (0.16)	0.17 (0.10)	0.20 (0.17)
	<b>III</b>	0.10 (0.03)	0.17 (0.09)	0.19 (0.11)	0.11 (0.01)	0.13 (0.09)	0.16 (0.08)
	<b>V</b>	0.48 (0.20)	0.62 (0.27)	0.43 (0.15)	0.49 (0.26)	0.46 (0.26)	0.37 (0.19)
<b>40</b>	<b>V</b>	0.31 (0.16)	0.36 (0.12)	0.35 (0.17)	0.26 (0.16)	0.30 (0.15)	0.28 (0.11)
<b>Latency (ms)</b>							
<b>70</b>	<b>I</b>	2.22 (0.89)	2.53 (0.65)	2.00 (0.14)	4.93 (1.75)	4.03 (0.98)	2.13 (0.20)
	<b>III</b>	4.67 (0.50)	4.90 (0.34)	4.60 (0.33)	7.80 (1.40)	6.60 (2.14)	4.73 (0.40)
	<b>V</b>	6.67 (1.15)	6.93 (0.70)	6.60 (0.37)	10.60 (0.82)	8.80 (0.76)	6.93 (0.62)
<b>40</b>	<b>V</b>	8.20 (1.03)	7.90 (0.92)	7.67 (0.42)	12.80 (1.87)	10.50 (1.42)	7.80 (0.48)
<b>Threshold (dBnHL)</b>							
		25 (10)	20 (10)	10 (10)	35 (5)	30 (15)	15 (10)

Table 4.9 Z distribution values, p-values of Wilcoxon signed-rank test and effect size (r) for amplitude of waves I, III, and V at multiple stimulus frequencies and intensities in normal hearing infants

Intensity (dBnHL)	Stimulus	Wave	Frequency (Hz)	Z value			p-value			Effect size		
				Tone burst			Tone burst			Tone burst		
				500	1000	4000	500	1000	4000	500	1000	4000
70	NB LS CE- Chirp	I	500	-1.069			0.285			*0.617		
			1000		-1.193			0.233			*0.308	
			4000			-2.088			0.037			*0.322
	NB LS CE- Chirp	III	500	-0.674			0.500			*0.301		
			1000		-1.650			0.099			*0.379	
			4000			-4.089			*<0.001			*0.655
	NB LS CE- Chirp	V	500	-0.405			0.685			0.057		
			1000		-4.976			*<0.001			*0.704	
			4000			-1.120			0.263			0.158
40	NB LS CE- Chirp	V	500	-2.313			0.021			*0.327		
			1000		-2.805			*0.005			*0.340	
			4000			-3.818			*<0.001			*0.540

\* Indicator: Significant p-value, ( $p < 0.01$ ) or effect size ( $r \geq 0.3$ )

Table 4.10 Z distribution values, *p*-values of Wilcoxon signed-rank test and effect size (*r*) for absolute latency of waves I, III, and V at multiple stimulus frequencies and intensities in normal hearing infants

Intensity (dBnHL)	Stimulus	Wave	Frequency (Hz)	Z value			p-value			Effect size		
				Tone burst			Tone burst			Tone burst		
				500	1000	4000	500	1000	4000	500	1000	4000
70	NBLS CE- Chirp	I	500	-1.604			0.109			*0.926		
			1000		-3.410			*<0.001			*0.880	
			4000			-4.202			*<0.001			*0.648
	NBLS CE- Chirp	III	500	-2.023			0.043			*0.905		
			1000		-3.665			*<0.001			*0.841	
			4000			-4.132			*<0.001			*0.662
	NBLS CE- Chirp	V	500	-6.155			*<0.001			*0.870		
			1000		-6.155			*<0.001			*0.870	
			4000			-4.228			*<0.001			*0.598
40	NBLS CE- Chirp	V	500	-6.155			*<0.001			*0.870		
			1000		-6.145			*<0.001			*0.869	
			4000			-2.540			0.011			*0.359

\*Indicator: Significant *p*-value, ( $p < 0.01$ ) or effect size ( $r \geq 0.3$ )

Table 4.11 Z distribution values, *p*-values of Wilcoxon signed-rank test and effect size (*r*) for hearing threshold estimation in normal hearing infants

Stimulus	Frequency (Hz)	Tone burst								
		Z value			p-value			Effect size		
		500	1000	4000	500	1000	4000	500	1000	4000
NB LS CE-Chirp	500	-5.175			*<0.001			*0.732		
	1000		-4.452			*<0.001			*0.630	
	4000			-4.431			*<0.001			*0.627

\* Indicator: Significant *p*-value, ( $p < 0.01$ ) or effect size ( $r \geq 0.3$ )

## **4.3.2 Analysis of latency of waves I, III, and V with NB LS CE-Chirp versus tone burst stimuli at various frequencies and intensities (70 and 40 dBnHL)**

### ***4.3.2.1 Stimulus types (NB LS CE-Chirp versus tone burst)***

#### *4.3.2.1.1 70 dBnHL*

The summary of the median and inter-quartile range (IQR) for absolute latencies of waves I, III, and V produced by ABR to NB LS CE-Chirp and ABR to tone burst of three different frequencies specific (500, 1000, and 4000 Hz) are shown in Table 4.8. From Table 4.10, the Wilcoxon signed-rank test analysed that this modified NB LS CE-Chirp stimulus has shorter ABR latency ( $p < 0.01$ ) for all waves compared to tone burst with large effect size for wave I, III, and V ( $r = 0.66$  to  $0.88$ ). The exception was for wave I and III at 500 Hz large effect size ( $r = 0.91$  to  $0.93$ ), and wave V of 4000 Hz with large effect size ( $r = 0.60$ ). The particulars of Z distribution, p-value, and effect size for absolute latency are as in Table 4.10.

#### *4.3.2.1.2 40 dBnHL*

Table 4.8 shows a summary of the median and IQR of ABR latencies of waves I, III, and V elicited via NB LS CE-Chirp and tone burst stimuli at frequency specifics of 500, 1000, and 4000 Hz. From Wilcoxon signed-rank analysis, the study found a significantly shorter ABR modified latency of NB LS CE-Chirp than tone burst in all wave V ( $p < 0.01$ ) with medium to large effect size ( $r = 0.36$  to  $0.87$ ). The details of Z distribution, p-value, and effect size for absolute latency are as in Table 4.10.

### **4.3.3 ABR hearing threshold estimation using both stimulus types**

#### ***4.3.3.1 Stimulus types (NB LS CE-Chirp versus tone burst)***

The summary of median and IQR for ABR hearing threshold estimation evoked by NB LS CE-Chirp and tone burst stimuli at multiple frequencies tested in normal hearing infants are shown in Table 4.8. From the Wilcoxon signed-rank analysis in Table 4.11, ABR to NB LS CE-Chirp has significantly lower ABR threshold estimations compared to ABR to tone burst across all frequencies tested ( $p < 0.01$ ) with large effect size ( $r = 0.63$  to  $0.73$ ). The hearing threshold estimation differences between NB LS CE-Chirp and tone burst were 10, for 500 and 1000 Hz, and 5 dBnHL for 4000 Hz. The particulars of Z-distribution, p-value, and effect size of the hearing threshold estimation are shown in Table 4.11.

## **4.4 DISCUSSION**

This section discusses the results of ABR data in relation to the first three research objectives. Specifically, this chapter addresses the effect of stimulus types on the ABR i) amplitude, ii) absolute latency, and iii) hearing threshold estimation.

### **4.4.1 The Effect of Stimulus Types and Frequency Specifics on ABR Amplitude**

#### ***4.4.1.1 General effect of NB LS CE-Chirp versus tone burst on ABR amplitudes***

The current study revealed that the larger ABR amplitude of wave I, III, and V from NB LS CE-Chirp than ABR elicited from tone burst across frequencies and two intensities tested. The ABR findings from NB LS CE-Chirp were expected to be consistent with the previous findings that showed larger amplitudes of wave V elicited from NB LS CE-Chirp than tone burst; however, the previous study was conducted in adult subjects (Bal et al., 2022; Dzulkarnain et al., 2018). In addition, previous literature revealed that larger ABR amplitudes from the narrow band (NB) CE-Chirp than tone burst in infants (Cobb and

Stuart, 2016); in children (Talaat et al., 2020); and in adult subjects (Ceylan et al., 2020).

The larger amplitude from ABR to NB LS CE-Chirp is expected because it is frequencies specific and elicits higher neural synchronization. The NB LS CE-Chirp delivers each frequency component to the cochlea with a precise adjournment designed to offset the cochlear delay at the position linked to its frequency characteristic. It is hypothesized that the observed rate of amplitude growth for chirp stimulus will not persist at higher intensities. Given that the stimulus intensities level in this study did not surpass 50 dBnHL for any frequencies, the observed steeper amplitude growth rate in the newborn may be attributed to the unique characteristics of the chirp stimulus. Once the optimal intensity is surpassed, the amplitude responses to chirp stimuli are anticipated to converge with those elicited by tone bursts, diminishing the potential advantage of using chirps. Overstimulation of the cochlear can lead to desynchronization. At higher frequencies (HF), tone burst elicited the same ABR amplitude due to the earlier HF parts at the basilar membrane of the cochlear (Rodrigues et al., 2013). Hence, there was no difference at 500 and 4000 Hz at 70 dBnHL.

#### ***4.4.1.2 Influence of stimulus intensity on ABR amplitudes elicited by NB LS CE-Chirp***

The ABR amplitude of waves I, III, and V from NB LS CE-Chirp stimulus was larger than tone burst except for wave V of 500 and 4000 Hz at 70 dBnHL. The amplitude enhancement of NB LS CE-Chirp to only certain frequencies indicate that optimum neural synchronization provided by NB LS CE-Chirp could be only limited to fast component but not for slow component with subjected to frequency spectral (Bal et al., 2022; Suleman, 2021). There were only few studies on the use of ABR to NB LS CE-Chirp especially among infants' population. Previous literature also reported similar ABR amplitude values between NB CE-Chirp and tone burst stimuli across various frequencies and at higher intensity levels (Rodrigues et al., 2013; Megha et al., 2019), except at 4000 Hz (Ceylan et al., 2020), and except at 1000 and 4000 Hz (Ferm et al., 2013). The similar ABR amplitudes elicited from NB CE-Chirp and tone burst stimuli is anticipated because of the rate of

amplitude growth will not continue at higher levels (Ferm et al., 2013; Ferm et al., 2015). This condition was observed at higher intensity levels, that NB LS CE-Chirp stimulus has a possibility of neural desynchronization changes as a consequence of overstimulation on the basilar membrane of the cochlea and caused the decrement of the wave V amplitude (Elberling & Don, 2008; Dau et al., 2000). However, those findings are not from NB LS CE-Chirp studies.

As discussed before, this is consistent with the expected response from the NB LS CE-Chirp stimulus at higher stimulation levels, the components activate restricted cochlear regions and the excitation spreads more broadly potentially leading to a decrease in amplitude response, subsequently reducing peak V amplitude. In the current study, the similar ABR amplitude of wave V of NB LS CE-Chirp and tone burst at 500 and 4000 Hz.

The previous study used NB CE-Chirp stimulus across all the octave bands and the levels never exceeded 50 dBnHL suggesting that the design of this stimulus was observed to elicit larger amplitude growth in the ABR recordings of infants. Once the optimal level is surpassed, the amplitudes of NB CE-Chirp are expected to be better than tone burst (Elberling & Don, 2010). One of the closest studies was by Elberling & Don (2010) on NB CE-Chirp stimulus elicited optimal responses at lower intensities, approximately 40 dBnHL for 1000 Hz and 45 dBnHL for 4000 Hz (Elberling & Don, 2010). At lower stimulation levels, the frequencies specifically occupy a narrow region on the basilar membrane enabling components to synchronize in phase (Megha et al., 2019; Muhler et al., 2012). The efficacy of the chirp at 50 to 60 dBnHL were prominent in influencing the upward spread of excitation on octave frequency components (Elberling, 2008).

Next, larger ABR amplitude of wave V for all frequencies tested from NB LS CE-Chirp than tone burst at 40 dBnHL. In the current study, the ABR findings elicited larger amplitude of wave V from NB LS CE-Chirp than tone burst at lower intensity level are similar to previous studies but in adult subjects (Bal et al., 2022; Dzulkarnain et al., 2018) and between NB CE-Chirp and tone burst in infants (Talaat et al., 2020; Ceylan et al., 2020; Rodrigues et al., 2013; Ferm et al., 2013; Cobb et al., 2016). The findings of this study

indicated that the amplitudes of ABR elicited from NB LS CE-Chirp were significantly larger than those elicited from tone burst for all three frequencies tested and at lower intensity levels which was 40 dBnHL. This suggested that NB LS CE-Chirp stimulus may be more effective in eliciting robust neural responses in the auditory brainstem at lower intensity levels which was less than 60 dBnHL (Dau et al., 2000).

In addition, chirp has an upward spread of excitation to alleviate temporal dispersion in the cochlea travelling wave delay (Dau et al., 2000; Kristensen & Elberling, 2012). These findings align with the observations from previous studies investigating NB CE-Chirp elicited more robust ABR waveform and larger ABR amplitude compared to the tone burst in adult (Elberling & Don, 2010). Hence, this study suggested that NB LS CE-Chirp stimulus may be advantageous for eliciting larger ABR wave V amplitudes and robust waveforms in infant compared to tone bursts particularly at lower presentation levels. This is because the NB LS CE-Chirp elicited a non-monotonous level-dependent characteristic that may trigger the upward spread of excitation as the intensity level increases (Dau et al., 2000). The characteristics of NB LS CE-Chirp stimulus facilitate increased synchronization of neural firing across a broader area of the basilar membrane, producing a more pronounced ABR waveform (Ferm et al., 2013; Ferm et al., 2015).

#### ***4.4.1.3 Different effect on NB LS CE-Chirp on the ABR amplitudes between infant and adult population***

The ABR findings in infants and adult were expected to be different because of the maturation of the brain structure. The maturational from peripheral to the central auditory system lead to variation in ABR amplitude, latency, and waveform morphology (Eggermont & Salamy, 1988; Salamy, 1984). As age increases, the axonal myelination density in the cochlear nerve and brainstem pathways is increasing (Spitzer et al., 2015; Johnson et al., 2008). The brain maturational development in infants continue to grow between 18 months and 12 years old (Hall III, 2015; Sleifer et al., 2007; Ponton et al., 1996). Previous studies showed that ABR in infants of wave I is more robust than wave V and resulting the amplitude ratio of wave V/I is about one-half of the adult or about one-

third in infants than the adult; while, wave III and V decreased with age. (Stuart et al., 1996; Hecox & Burkard, 1980). In specific, there were significant differences ABR findings between children aged >36 months and <37 months. (Wang et al., 2023). However, unlike the cochlea, the brainstem pathways are not mature at term. This can be most clearly seen in ABR latency. ABR wave I latencies are adult-like soon after birth in full-term infants (Eggermont & Salamy, 1988) but absolute wave V and wave I–V interpeak latencies decrease over the first 2 to 3 years of life (Salamy, \1984). Myelination of auditory axons is present throughout the pathway by 29 weeks gestation; however, the density of myelin sheath remains to increase throughout the first year of life (Moore et al., 1995).

From the current study, there was a huge missing of waves I and III especially at lower frequencies of tone burst findings. Despite the enhancement of wave V through compensating for temporal delays across frequency and within channel phase dispersion tends to diminish the amplitudes of earlier ABR waves. The absence of ABR waves I and III elicited from tone burst was expected. In addition, this current study found that waves I and III were not observed from ABR to tone burst at 70 dBnHL, which is consistent with previous findings. Ribeiro & Carvalho (2008) similarly did not detect waves I and III in term and preterm newborns even at high intensities. ABR waves I and II are generated via auditory nerve fibres that exhibit 'phase-locking' which accurately reflects basilar membrane (BM) motion through the action potentials period. In contrast, frequency spectrum analysis of the ABR wave V characterized of a low frequency has a longer integration window which differs with waves I and II which are integrated at a shorter window (Kevanishvili & Aphonchenko, 1979). The higher susceptibility of wave I to phase dispersion compared to wave V can also be attributed to differences in the mechanisms. Specifically, it was expected that neural elements contribution to wave V are dendritic making them slower and monophasic, whereas those from wave I is axonal and resulting in faster and diphasic responses (Kevanishvili & Aphonchenko, 1979). However, in the current study, the waves I and III from NB LS CE-Chirp were observed.

In addition, the insignificant difference in ABR amplitude of wave V at 500 and 4000 Hz from both stimuli may be due to the immaturation of the brain structures. Previous

studies found that the ABR to NB LS CE-Chirp is more sensitive to stimulus changes at lower intensity levels than at higher intensity levels. This is because at lower intensity levels, CE-Chirp with an upward spread of excitation characteristic made the stimulus less distorted. Previous literature showed that there is a lack of earlier waveforms in the grand averages waveform, displayed greater variability in wave V latency, lower fast Fourier transform (FFT) magnitudes at higher component frequencies, and higher phase variance at these frequencies of ABR to click (Petoe et al., 2010). FFT functions are to convert a signal into specific spectral components and provides frequency data about the signal (Petoe et al., 2010).

#### **4.4.2 Shorter modified ABR latencies from NB LS CE-Chirp than tone burst**

NB LS CE-Chirp with 500, 1000, 2000, and 4000 Hz as a subset is anticipated that the latencies of NB LS CE-Chirp stimulus will be shorter than those of tone burst, particularly at lower frequencies, (e.g. Figure 4.10). This result was expected because the modified structures of NB LS CE-Chirp are shorter than the tone burst stimulus. A thorough evaluation should incorporate frequency specific ABR, as it offers enhanced clarity regarding the pattern and severity of hearing loss. In contrast, tone burst is a brief signal stimulus containing a single tone, commonly employed in testing, measurement, and calibration contexts. It is characterized by its narrow spectral. The current study demonstrated that ABR latencies were shorter when elicited via NB LS CE-Chirp stimulus compared to tone burst stimulus in infants. This accelerated neural response is attributed to several stimulus related factors. The optimized frequency and temporal characteristics of NB LS CE-Chirp stimulus align more closely with the physiological properties of the auditory system, potentially enhancing neural synchronization, and expediting auditory information transmission along the neural pathway (Elberling & Don, 2008; Cobb & Stuart, 2016).

Activation of the cochlea regions occurs simultaneously in both low and high frequencies, ensuring that every part of the basilar membrane reaches peak depolarization and produces a synchronized neural response (Rodrigues et al., 2013). Previous studies

have reported that latencies are prolonged at 500 Hz compared to higher frequencies, suggesting that the low frequency response originates from the apex of the cochlea region (Yamada et al., 1983; Sininger et al., 1997; Ribeiro & Carvallo, 2008; Almeida et al., 2014). The shorter latency is mainly due to the temporal alignment of frequency components in the NB LS CE-Chirp stimulus which compensates for cochlear traveling wave delay. This design effectively synchronizes neural responses and resulting in earlier ABR wave latencies. Additionally, since NB CE-Chirp maximally stimulates the cochlea, any delay in the cochlear travelling wave is compensated by achieving varying timings across different frequencies (Rodrigues & Lewis, 2012; Dau et al., 2000). Specifically, regions centred at 500 Hz and 1000 Hz receive the stimulus earlier, resulting in shorter peak latency. This data suggests that NB LS CE-Chirp stimulus might be advantageous over the traditional tone bursts for eliciting shorter absolute latencies in ABR recordings of infants. The use of NB CE-Chirp stimulus resultant in shorter ABR latencies compared to tone burst stimulus, particularly evident at lower frequencies. This characteristic of NB LS CE-Chirp is particularly valuable in ABR clinical practice for assessing auditory function in young children and optimizing early intervention strategies for those with hearing loss or auditory processing disorders.

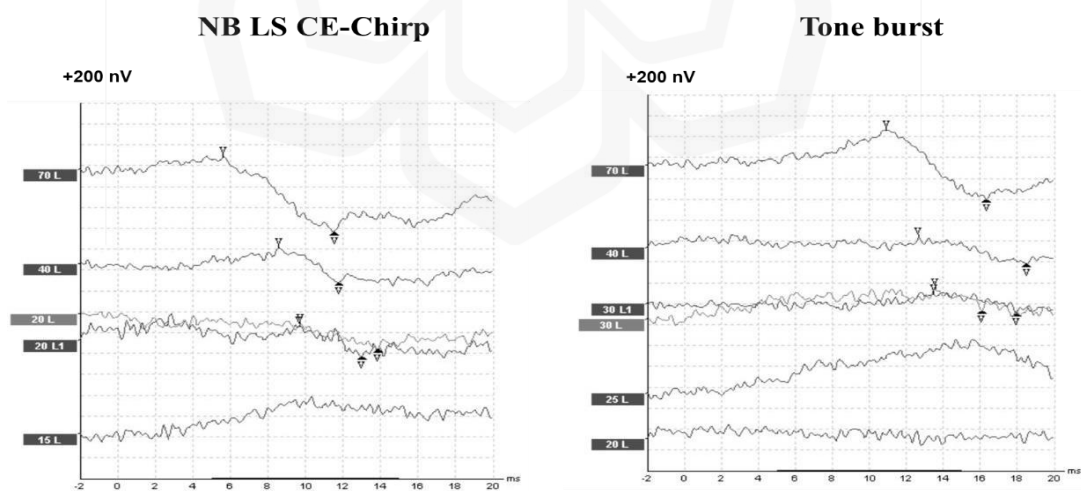


Figure 4.12 The ABR waveform morphology elicited via NB LS CE-Chirp versus tone burst.

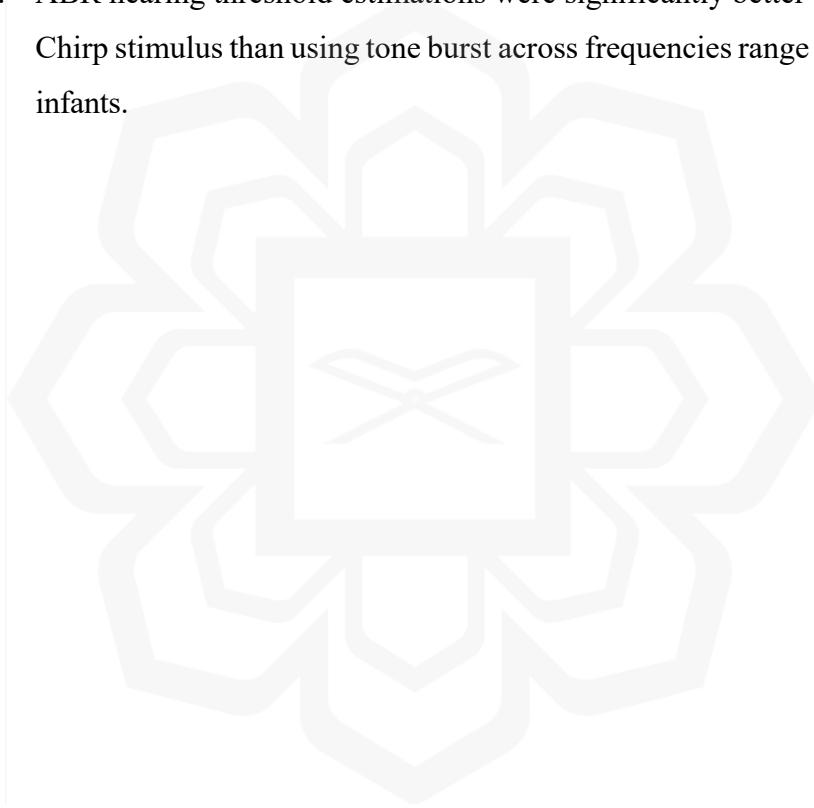
#### **4.4.3 Better ABR threshold in NB LS CE-chirp at lower frequencies**

ABR findings showed lower hearing threshold estimation evoked by NB LS CE-Chirp stimulus compared to tone burst stimulus. This is because of the adjusted latency, improved amplitude, and clearer waveform made the ABR threshold can be found in the lower intensity levels in chirp. Therefore, better ABR threshold estimations elicited via NB LS CE-Chirp than tone burst. Previous literature found that ABR hearing threshold estimation elicited from NB CE-Chirp is more highly correlated with behavioural thresholds than with tone burst stimulus (Talaat et al., 2020). This increases the possibility of the thresholds to estimate the audiogram better and closer to the behavioral audiogram and suggests that NB LS CE-Chirp stimulus is indeed more sensitive in detecting hearing loss in infants. However, the ABR findings may be attributed to the attenuation from low frequency as it propagates towards the apex of the basilar membrane. Variations in the vibration pattern of the basilar membrane near the apex of the basilar membrane can impact neuronal synchrony, potentially resulting in elevated ABR thresholds for low frequencies, irrespective of the stimulus modality (Almeida et al., 2014).

#### **4.5 SUMMARY**

This chapter discussed experiment one, which justifies the three earlier research objectives. The research objectives include an analysis of the differences in ABR amplitude, latency, and hearing threshold estimations using two different types of stimuli. In conclusion, based on the results and discussions described in the earlier sections of this chapter, the summary is as follows: The Joint Committee on Infant Hearing (JCIH) recommends the tone burst auditory brainstem response (ABR) as the standard test for determining the audiogram in infants between 1 and 3 months old. Numerous clinicians currently hesitate to adopt tone burst stimuli for ABR assessment as suggested by JCIH. A commonly cited issue is the challenge of identifying wave V, especially with low frequency stimuli (Ferm et al., 2015). Thus, the frequency specific ABR elicited via NB LS CE-Chirp and tone burst were compared, and the findings are as follow:

- i. ABR to NB LS CE-Chirp has a slightly larger amplitude of waves I, III, and V at higher intensity levels (70 dBnHL) except at waves V 500 and 4000 Hz in normal hearing infants.
- ii. ABR to NB LS CE-Chirp elicited a larger amplitude of wave V than in ABR to tone burst for all frequencies tested at 40 dBnHL in normal hearing infants.
- iii. Latencies of ABR to NB LS CE-Chirp were significantly shorter compared to ABR using tone burst for all frequencies tested at both stimulus intensity levels in normal hearing infants.
- iv. ABR hearing threshold estimations were significantly better using NB LS CE-Chirp stimulus than using tone burst across frequencies range in normal hearing infants.



## **CHAPTER FIVE**

### **EXPERIMENT TWO: THE EFFECTS OF STIMULUS TYPES AND STOPPING CRITERIA ON THE ABR ACQUISITION TIME**

#### **5.1 INTRODUCTION**

Part two of the experiment in this thesis will be discussed in this chapter. The second experiment will highlight the fourth objective, which is to compare the ABR acquisition time in infants using NB LS CE-Chirp and tone burst with various grouping of stimulus frequencies and stopping criteria at 70 and 40 dBnHL. This chapter will describe the study design, instrumentations, data collection procedure, and data analysis. At the end of this chapter, the results, discussion, and conclusion will be discussed.

#### **5.2 MATERIALS AND METHODOLOGY**

##### **5.2.1 Study Design**

This study employed a repeated measures study design to investigate the causal relationship between independent variables (i.e., stimulus types and stopping criteria) and dependent variables (i.e., ABR acquisition time) (Thyer, 2012). A convenience sampling technique was utilized to recruit a total of 50 infant ears that had passed a hearing screening. This experiment used the same study design as in experiment one, see Section 4.2.1.

##### **5.2.2 Ethical Clearance**

This experiment was done simultaneously with experiment one. The same written and verbal consent was obtained from the subjects before assessments were conducted in parallel with the first experiment. IIUM Research Ethics Committee (IREC), National Medical Research Registration (NMRR), and Medical Research Ethics Committee

(MREC) were approved for this study (see Section 4.2.2). For data collection, the demographic data form, report form, and consent form are in Appendixes A, B, and C.

### **5.2.3 Study Population and Location**

A total of 50 normal hearing ears from the low-risk ward, Obstetrics & Gynecology Department, SASMEC IIUM, Kuantan, Pahang were recruited in this study. The subjects inclusion criteria are as in Section 4.2.4. This study was conducted at IIUM Hearing and Speech Clinic, Jalan Hospital Campus, IIUM, Kuantan, Pahang. The setting of the study is shown in Figure 4.1; see Section 4.2.3.

#### ***5.2.3.1 Inclusion Criteria***

This experiment was done with the same subjects as in experiment one (refer to subsection 4.2.4.1). Hence, the inclusion criteria were infants aged less than 6 months pass hearing screening with normal outer and middle ear conditions, as described in subsection 4.2.4.1.

#### ***5.2.3.2 Exclusion Criteria***

The exclusion criteria were any criteria that did not meet the inclusion criteria. For details on the exclusion criteria of experiment two, see subsection 4.2.4.2.

### **5.2.4 Instrumentation**

The same instruments were used as in experiment one which were Welch Allyn 3.5V 97150-BIM Diagnostic Professional otoscope (Welch Allyn, Inc. Skaneateles Falls, New York), Grason Stadler Interacoustic (GSI) Tymptar Pro Middle Ear Analyser (Grason Stadler, Eden Prairie, MN, USA), Two-channel Eclipse ABR Equipment and 170 EP15

module (Interacoustic A/S. Middelfart, Denmark), and two screening tool forms were used in this experiment. The particulars were described in subsection 4.2.5.

#### ***5.2.4.1 Informed Consent***

The same verbal and written consent forms (see subsection 4.2.5.1, Appendix C and D) were obtained before the assessment. Any data and information gained were permanently destroyed; see Appendix A and B.

#### ***5.2.4.2 Demographic Data Form***

The demographic data form consists of the infant demographic data, prenatal and postnatal history, and preliminary audiological routine test results. The information gained is the same as in experiment one; see subsection 4.2.5.2 and Appendix E and F.

### **5.3 DATA COLLECTION PROCEDURE**

The data collection procedures were similar to those in experiment one, including the subject recruitment, pilot study, and preliminary audiological routine test to investigate the ABR acquisition time (see Section 4.2.6). The data collection procedure for experiment two will be explained further in the next Section.

#### **5.3.1 Auditory Brainstem Response Assessment**

- i. The results from ABR assessment obtained from the three earlier research objectives in chapter four using NB LS CE-Chirp and tone burst stimuli at three frequencies (i.e., 500 Hz, 1000 Hz, and 4000 Hz) with intensity levels of 70 and 40 dBnHL were used in this experiment.

- ii. The ABR was recorded using an ipsilateral/contralateral electrode configuration with a non-inverting electrode on the high forehead (Fz), the ground electrode on the low forehead (Fpz), and an inverting electrode on both mastoids. The artifact rejection level was set  $\pm 40$  nV, and the filter setting was set to 33 to 3000 Hz. The same parameter was used in the first experiment; see Section 4.2.4.1.
- iii. In this experiment, to obtain the ABR acquisition time, the ABR recording was reviewed using two types of stopping criteria, Fmp and visual detection, until the signal averaging stops at 2500 sweeps.
- iv. To quantify the ABR acquisition time, the researcher initiated the ABR assessment based on N=2500 sweeps (as described in the steps mentioned as follows:
  - a. In this experiment, the researcher “pauses” the signal averaging immediately as the Fmp hits 3.1 ( $Fmp \geq 3.1$ ). The ABR peaks from the waveforms were plotted and the number of sweeps was noted (equivalent to the test time). Two audiologists confirmed the presence or absence of ABR wave V with those identified by  $Fmp \geq 3.1$  by looking into the waveform morphology and the development of the ABRs as the signal averaging continued until 2500 sweeps to ensure the correct wave V was identified. The Fmp is the statistical F-value for multiple points and provides a better confidence level and detection rate of ABR in shorter time. This methodology is to verify whether the detection of Fmp is equivalent to the gold standard of human visual detection. Thus, the detection of ABR waves via Fmp and visual detection will be analyzed using sweeps, and the time taken to get a true ABR wave will be calculated with time.
  - b. In terms of visual detection technique, the research “paused” the averaging as soon as the ABR waveform occurred and visually identified by the audiologist. The wave V was plotted, and the number of sweeps at the point was recorded.
- v. The ABR acquisition time with various combinations of stimulus types, frequencies, and stopping criteria were documented and analyzed.
- vi. The ABR sessions were recorded via Bandicam screen recorder software to record the details of the ABR waveform data for every pause until the signal averaging stops to obtain the ABR acquisition time based on Fmp and visual detection.

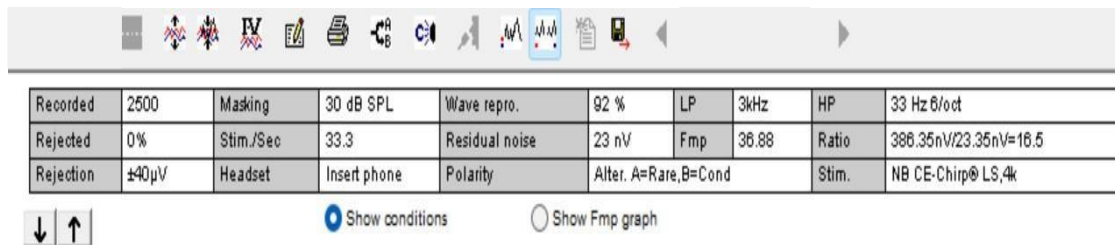


Figure 5.1 The Eclipse ABR equipment system carried out the signal averaging evoked potential for every hundred stimulus presentations.

## 5.4 DATA ANALYSIS

In this study, the two independent variables involved were the stimulus types (NB LS CE-Chirp and tone burst) and stopping criteria ( $Fmp \geq 3.1$  and visual detection). The dependent variable was the ABR acquisition time. Statistical analysis was used to compare the acquisition time among the stimulus types and stopping criteria. The analysis was to determine the accuracy of  $Fmp \leq 3.1$  detection with visual detection.

### 5.4.1 Main Variable

The main variable for this experiment is the test time. ABR test time refers to the time elapsed during ABR acquisition. This study examined the ABR test time required to obtain a recordable ABR waveform under two conditions which were (1) until the Fmp value reached or exceeded 3.1, indicating a 99% confidence level in ABR presence (Don et al., 1984), and (2) until visual identification of Wave V.

ABR recordings were stopped upon satisfaction of either criterion. It is important to note that the Eclipse ABR equipment employed signal averaging in increments of 100 stimulus presentations (Figure 5.1). Consequently, the number of averages required to attain an Fmp of 3.1 might have been rounded up to the nearest hundred, potentially overestimating the actual average count. The ABR test time is calculated based on the

number of sweeps needed to achieve  $F_{mp} \geq 3.1$ . The exact acquisition time is determined by dividing the total number of sweeps used by the stimulus repetition rate, for example, how many stimuli are presented in seconds.

Test time (seconds):

$$\frac{\text{Number of sweeps per averaging}}{\text{Stimulus repetition rate}} \quad (\text{Equation 5.1})$$

#### 5.4.2 Statistical Analysis

The present study was analyzed using SPSS software version 27.0. The non-parametric tests used in this research were Friedman test and post-hoc Wilcoxon signed-rank test when the hypothesis does not assume a normal distribution. In this experiment, the Wilcoxon signed-rank test was used to compare the acquisition time in two related samples between NB LS CE-Chirp and tone burst. The Friedman test is a non-parametric test to assess two factors (i.e. stimulus types and stopping criteria) individually affect a dependent variable (i.e. acquisition time) and to investigate whether there is an interaction effect between these two factors. The rationale of choosing Friedman test, as this test is designed for situations where the same individuals or matched subjects are measured under three or more different conditions, treatments, or time points. This "within-subjects" design is crucial.

### 5.5 RESULTS

Table 5.1 showed the number of ABR wave V identification by Eclipse system  $F_{mp} \geq 3.1$  versus the number of wave V interpreted by audiologists with frequency specifics (70 and 40 dBnHL) in normal hearing infants. The highest number of wave V identified by  $F_{mp} \geq 3.1$  was found from ABR to NB LS CE-Chirp and ABR to tone burst at frequency specifics (1000 and 4000 Hz) of 70 and 40 dBnHL in all 50 ABR recordings. There was zero (0 %) discrepancies of ABR wave V identification between  $F_{mp} \geq 3.1$  and visual detection as confirmed by audiologist at 1000 Hz from NB LS CE-Chirp and tone burst stimuli at 70

dBnHL.

Table 5.1 Number of ABR wave V identification using Fmp 3.1 versus number of wave V confirmed by an audiologist at frequency specifics and intensities in normal hearing infants.

Stimulus types	Stimulus frequency (Hz)	Intensity (dBnHL)	No. of wave V identified by Fmp $\geq$ 3.1	No. of wave V confirmed by Audiologist	Percentages of discrepancies (%)
NB LS CE-Chirp	500	70	49	48	2.04
Tone burst			49	47	4.08
NB LS CE-Chirp	500	40	48	46	4.17
Tone burst			47	46	2.13
NB LS CE-Chirp	1000	70	50	50	0
Tone burst			50	50	0
NB LS CE-Chirp	1000	40	50	47	4.00
Tone burst			50	45	10.00
NB LS CE-Chirp	4000	70	50	47	6.00
Tone burst			50	47	6.00
NB LS CE-Chirp	4000	40	50	45	10.00
Tone burst			50	46	4.00

### 5.5.1 Analyzing acquisition time variations based on combinations of stimulus types and stopping criteria at 70 and 40 dBnHL

#### 5.5.1.1 Stimulus types (NB LS CE-Chirp versus tone burst)

##### 5.6.1.1.1 70 dBnHL

##### i. 500 Hz

The median and interquartile range (IQR) of the ABR acquisition time from NB LS CE-Chirp and tone burst at multiple frequencies specific using two types of stopping criteria (Fmp  $\geq$  3.1 and visual detection) at 70 dBnHL is shown in Table 5.2. The Friedman test identified a significant difference in ABR acquisition time among the different stimulus types combination ( $\chi^2$  (3) = 37.22,  $p < 0.001$ ) for 500 Hz at 70 dBnHL. According to post hoc analysis using the Wilcoxon signed-rank test shown in Table 5.3, 5.4, and 5.5 for ABR elicited via NB LS CE-Chirp has significantly faster acquisition time ( $p < 0.001$ ) than tone

burst with large effect size ( $r = 0.54$  to  $0.79$ ) at 500 Hz in both types of ABR detection methods. The Z distribution, p-value, and effect size particulars were described in Table 5.3, 5.4 and 5.5, respectively. The ABR acquisition time saving from tone burst to NB LS CE-Chirp was between 9.01 s to 10.51 s at 500 Hz.

ii. 1000 Hz

The median and interquartile range (IQR) of the ABR acquisition time from NB LS CE-Chirp and tone burst at multiple frequencies specific using two types of stopping criteria ( $F_{mp} \geq 3.1$  and visual detection) at 70 dBnHL was shown in Table 5.2. The Friedman test identified a significant difference in ABR acquisition time among the different stimulus types combination ( $\chi^2(3) = 54.23$ ,  $p < 0.001$ ) for 1000 Hz at 70 dBnHL. Based on post hoc analysis using the Wilcoxon signed-rank test in Tables 5.3, 5.4, and 5.5, the ABR acquired from NB LS CE-Chirp has significantly faster acquisition time ( $p < 0.001$ ) than in tone burst with medium to large effect size ( $r = 0.41$  to  $0.74$ ) at 1000 Hz in both types of ABR detection methods. The Z distribution, p-value, and effect size particulars were described in Table 5.3, 5.4, and 5.5, respectively. The ABR acquisition time saving from tone burst to NB LS CE-Chirp was between 4.51 s to 9.01 s at 1000 Hz.

iii. 4000 Hz

The median and interquartile range (IQR) of the ABR acquisition time from NB LS CE-Chirp and tone burst at multiple frequencies specific using two types of stopping criteria ( $F_{mp} \geq 3.1$  and visual detection) at 70 dBnHL was shown in Table 5.2. The Friedman test identified a significant difference in ABR acquisition time among the different stimulus types combination ( $\chi^2(3) = 11.59$ ,  $p = 0.009$ ) for 4000 Hz at 70 dBnHL. For 4000 Hz, post hoc analysis Wilcoxon signed-rank test showed similar ABR acquisition time from both stimuli using  $F_{mp}$  of 3.1 method ( $p = 0.46$ ) with small effect size ( $r = 0.15$ ), whilst ABR from NB LS CE-Chirp has significantly faster acquisition time ( $p < 0.001$ ) than tone burst using visual detection with large effect size ( $r = 0.79$ ). The Z distribution, p-value, and

effect size particulars were described in Table 5.3, 5.4, and 5.5, respectively. The ABR acquisition time saving from NB LS CE-Chirp to tone burst was between 2.95 s to 12.01 s at 4000 Hz.

#### 5.6.1.1.2 40 dBnHL

##### i. 500 Hz

The median and interquartile range (IQR) of the ABR acquisition time from NB LS CE-Chirp and tone burst at multiple frequencies specific using two types of stopping criteria ( $F_{mp} \geq 3.1$  and visual detection) at 40 dBnHL was shown in Table 5.2. Analysis using the Friedman test demonstrated a significant difference in ABR acquisition time at 40 dBnHL of 500 Hz ( $\chi^2(3) = 14.16, p = 0.003$ ). According to the post hoc analysis Wilcoxon signed-rank test, NB LS CE-Chirp has a faster ABR acquisition time ( $p < 0.01$ ) than tone burst with medium to large effect size ( $r = 0.41$  to  $0.77$ ) at 500 Hz in both types of ABR detection methods. The Z distribution, p-value, and effect size particulars were described in Table 5.6, 5.7, and 5.8, respectively. The ABR acquisition time saving from tone burst to NB LS CE-Chirp was between 12.02 s to 16.51 s at 500 Hz.

##### ii. 1000 Hz

The median and interquartile range (IQR) of the ABR acquisition time from NB LS CE-Chirp and tone burst at multiple frequencies specific using two types of stopping criteria ( $F_{mp} \geq 3.1$  and visual detection) at 40 dBnHL was shown in Table 5.2. Analysis using the Friedman test demonstrated a significant ABR acquisition on ABR findings at 40 dBnHL of 1000 Hz ( $\chi^2(3) = 42.81, p < 0.001$ ) at 40 dBnHL. For 1000 Hz, ABR to NB LS CE-Chirp has significantly faster acquisition time than tone burst ( $p < 0.01$ ) with medium effect size ( $r = 0.38$  to  $0.41$ ) in both types of ABR detection methods. The Z distribution, p-value, and effect size particulars were described in Table 5.6, 5.7, and 5.8, respectively. The ABR acquisition time saving from tone burst to NB LS CE-Chirp was 15.02 s to 18.02 s at 1000

Hz.

iii. 4000 Hz

The median and interquartile range (IQR) of the ABR acquisition time from NB LS CE-Chirp and tone burst at multiple frequencies specific using two types of stopping criteria ( $F_{mp} \geq 3.1$  and visual detection) at 40 dBnHL is shown in Table 5.2. Analysis using the Friedman test demonstrated a significant difference in ABR acquisition time at 40 dBnHL of 4000 Hz ( $\chi^2(3) = 21.67, p < 0.001$ ). For 4000 Hz, post hoc analysis Wilcoxon signed-rank test showed similar ABR acquisition time using  $F_{mp}$  of 3.1 from both stimuli using ( $p = 0.062$ ) with small effect size ( $r = 0.13$ ), whilst ABR from NB LS CE-Chirp has significantly faster acquisition time ( $p < 0.001$ ) than tone burst using visual detection method with large effect size ( $r = 0.87$ ). The Z distribution, p-value, and effect size particulars were described in Table 5.6, 5.7, and 5.8, respectively. The ABR acquisition time saving from tone burst to NB LS CE-Chirp was between 3.00 s to 13.51 s at 4000 Hz.

Table 5.2 The median and inter-quartile range (IQR) for ABR acquisition time produced via NB LS CE-Chirp and tone burst stimuli at multiple frequencies and intensities using both stopping criteria in normal hearing infants.

Acquisition time (s)	Intensity (dBnHL)	Fmp						Visual	
		Frequency (Hz)							
Stimuli		500	1000	4000	500	1000	4000		
NB LS CE-Chirp	70	6.01 (9.01)	4.50 (9.01)	9.01 (12.76)	12.01 (9.01)	12.01 (9.01)	9.01 (9.01)		
		Tone burst	16.52 (25.33)	9.01 (12.76)	6.06 (9.76)	21.02 (18.77)	21.02 (12.01)	21.02 (6.76)	
NB LS CE-Chirp	40	16.52 (27.03)	12.01 (24.77)	12.01 (21.77)	15.01 (6.76)	15.01 (6.77)	10.51 (9.01)		
		Tone burst	33.03 (40.54)	30.03 (45.80)	15.01 (27.03)	27.03 (15.77)	30.03 (21.02)	24.02 (12.01)	

Table 5.3 Z distribution value from post hoc analysis signed-rank test for acquisition time at multiple stimulus frequencies and intensities in normal hearing infants

Intensity (dBnHL)	Stopping criteria	Stimulus	Frequency (Hz)	Z-distribution													
				Fmp						Visual							
				NB LS CE- Chirp			Tone burst			NB LS CE- Chirp			Tone burst				
			500	1000	4000	500	1000	4000	500	1000	4000	500	1000	4000			
70	Fmp	NB LS CE- Chirp	500				-3.843			-1.055							
			1000					-2.932			-2.912						
			4000									-0.956					
		Tone burst	500											-0.217			
			1000												-2.158		
			4000													-4.708	
	Visual	NB LS CE- Chirp	500											-3.543			
			1000												-5.569		
			4000													-0.226	
		Tone burst	500														-3.970
			1000														-4.987
			4000														-4.646

\*Significant p-value  $p < 0.01$ , effect size ( $r \geq 0.3$ )

Table 5.4 The p-values of the post hoc analysis Wilcoxon signed-rank test for acquisition time at multiple stimulus frequencies and intensities in normal hearing infants

Intensity (dBnHL)	Stopping criteria	Stimulus	Frequency (Hz)	p-value												
				Fmp						Visual						
				NB LS CE- Chirp			Tone burst			NB LS CE- Chirp			Tone burst			
				500	1000	4000	500	1000	4000	500	1000	4000	500	1000	4000	
70	Fmp	NB LS CE- Chirp	500				*<0.001				0.048					
			1000				*<0.001				*<0.001					
			4000						0.046			*0.001				
		Tone burst	500										0.138			
			1000											*0.005		
			4000												*<0.001	
	Visual	NB LS CE- Chirp	500				*<0.001							*<0.001		
			1000					0.088						*<0.001		
			4000							0.137					*<0.001	
		Tone burst	500				*<0.001									
			1000					*<0.001								
			4000						*<0.001							

\*Significant p-value  $p < 0.01$ , effect size ( $r \geq 0.3$ )

Table 5.5 Effect size (r) for testing time at multiple stimulus frequencies and intensities in normal hearing infant

Intensity (dBnHL)	Stopping criteria	Stimulus	Frequency (Hz)	r, effect size													
				Fmp						Visual							
				NB LS CE- Chirp			Tone burst			NB LS CE- Chirp			Tone burst				
				500	1000	4000	500	1000	4000	500	1000	4000	500	1000	4000		
70	Fmp	NB LS CE- Chirp	500				*0.54				0.15						
			1000					*0.41				*0.41					
			4000							0.15			0.27				
		Tone burst	500												0.03		
			1000													*0.31	
			4000														*0.67
	Visual	NB LS CE- Chirp	500				*0.50								*0.79		
			1000					0.09								*0.74	
			4000							0.03							*0.79
		Tone burst	500	*0.56													
			1000		*0.71												
			4000			*0.66											

\*Significant p-value  $p < 0.01$ , effect size ( $r \geq 0.3$ )



Table 5.7 The p-values of the post hoc analysis Wilcoxon signed-rank test for acquisition time at multiple stimulus frequencies at 40 dBnHL in normal hearing infants

Intensity (dBnHL)	Stopping criteria	Stimulus	Frequency (Hz)	p-value												
				Fmp						Visual						
				NB LS CE- Chirp			Tone burst			NB LS CE- Chirp			Tone burst			
				500	1000	4000	500	1000	4000	500	1000	4000	500	1000	4000	
40	Fmp	NB LS CE- Chirp	500				*0.001				*<0.001					
			1000					*0.001				0.021				
			4000						0.062				*<0.001			
		Tone burst	500										0.028			
			1000											0.094		
			4000												*<0.001	
	Visual	NB LS CE- Chirp	500				*<0.001							*<0.001		
			1000					*<0.001						*<0.001		
			4000						*<0.001						*<0.001	
		Tone burst	500	0.030												
			1000		*<0.001											
			4000			*0.006										

\*Significant p-value  $p < 0.01$ , effect size ( $r \geq 0.3$ )

Table 5.8 Effect size (r) for testing time at multiple stimulus frequencies at 40 dBnHL in normal hearing infant

Intensity (dBnHL)	Stopping criteria	Stimulus	Frequency (Hz)	r, effect size													
				Fmp						Visual							
				NB LS CE- Chirp			Tone burst			NB LS CE- Chirp			Tone burst				
				500	1000	4000	500	1000	4000	500	1000	4000	500	1000	4000		
40	Fmp	NB LS CE- Chirp	500				*0.41				*0.45						
			1000					*0.41				0.02					
			4000							0.13							
		Tone burst	500														
			1000														
			4000														
	Visual	NB LS CE- Chirp	500					*0.71									
			1000						*0.65								
			4000								*0.56						
		Tone burst	500	*0.71													
			1000		*0.44												
			4000			*0.30											

\*Significant p-value  $p < 0.01$ , effect size ( $r \geq 0.3$ )

### ***5.5.1.2 Stopping criteria (Fmp 3.1 and visual detection)***

#### ***5.6.1.2.1 70 dBnHL***

##### ***i. 500 Hz***

The median and interquartile range (IQR) of the ABR acquisition time from NB LS CE-Chirp and tone burst at multiple frequencies specific using two types of stopping criteria (Fmp  $\geq$  3.1 and visual detection) at 70 dBnHL are shown in Table 5.2. The Friedman test revealed a significant difference in ABR acquisition time among the different stimulus and stopping criteria combination ( $\chi^2$  (3) = 37.22,  $p < 0.001$ ) for 500 Hz at 70 dBnHL. According to the post hoc Wilcoxon signed-rank test in Table 5.3, 5.4 and 5.5, the acquisition time was similar between Fmp of 3.1 and visual detection method for both stimuli ( $p = 0.048$  and  $p = 0.138$ ) with no/ small effect size ( $r = 0.03$  to  $0.15$ ) at 500 Hz. The Z distribution, p-value, and effect size particulars were described in Table 5.3, 5.4 and 5.5, respectively.

##### ***ii. 1000 Hz***

The median and interquartile range (IQR) of the ABR acquisition time from NB LS CE-Chirp and tone burst at multiple frequencies specific using two types of stopping criteria (Fmp  $\geq$  3.1 and visual detection) at 70 dBnHL was shown in Table 5.2. The Friedman test revealed a significant difference in ABR acquisition time among the different stimulus and stopping criteria combination ( $\chi^2$  (3) = 54.23,  $p < 0.001$ ) for 1000 Hz at 70 dBnHL. According to the post hoc Wilcoxon signed-rank test in Tables 5.3, 5.4, and 5.5, the detection time using Fmp of 3.1 was a significantly faster acquisition time ( $p < 0.01$ ) than visual detection with medium effect size ( $r = 0.31$  to  $0.41$ ) at 1000 Hz from both NB LS CE-Chirp and tone burst stimuli. The Z distribution, p-value, and effect size particulars were described in Table 5.3, 5.4 and 5.5, respectively. The ABR acquisition time saving from visual detection to Fmp  $\geq$  3.1 was between 7.51 s to 12.01 s using at 1000 Hz.

iii. 4000 Hz

The median and interquartile range (IQR) of the ABR acquisition time from NB LS CE-Chirp and tone burst at multiple frequencies specific using two types of stopping criteria ( $F_{mp} \geq 3.1$  and visual detection) at 70 dBnHL are shown in Table 5.2. The Friedman test revealed a significantly faster ABR acquisition time among the different stimulus types and detection technique combinations ( $\chi^2(3) = 11.59, p = 0.009$ ) for 4000 Hz at 70 dBnHL. The ABR to NB LS CE-Chirp detected using  $F_{mp}$  of 3.1 was significantly faster than the visual detection method ( $p < 0.01$ ) with small effect size ( $r = 0.27$ ). Meanwhile, the ABR detection using  $F_{mp}$  of 3.1 was significantly faster than visual detection method ( $p < 0.01$ ) with large effect size ( $r = 0.67$ ). The Z distribution, p-value, and effect size particulars were described in Table 5.3, 5.4 and 5.5, respectively. The ABR acquisition time saving from visual detection to  $F_{mp} \geq 3.1$  was between 0 s to 14.96 s at 4000 Hz.

5.6.1.2.2 40 dBnHL

i. 500 Hz

The median and interquartile range (IQR) of the ABR acquisition time from NB LS CE-Chirp and tone burst at multiple frequencies specific using two types of stopping criteria. ( $F_{mp} \geq 3.1$  and visual detection) at 40 dBnHL was shown in Table 5.2. Analysis using the Friedman test demonstrated a significant difference in ABR acquisition time o at 40 dBnHL of 500 Hz ( $\chi^2(3) = 14.16, p = 0.003$ ) at 40 dBnHL. According to the post hoc Wilcoxon signed-rank test, ABR to NB LS CE-Chirp using  $F_{mp}$  has faster acquisition time than using visual detection as stopping criteria ( $p < 0.001$ ) with medium effect ( $r = 0.45$ ), whilst ABR to tone burst has similar acquisition time using both stopping criteria ( $p = 0.028$ ) but a different was identified based on the ( $r = 0.20$ ). The Z distribution, p-value, and effect size particulars were described in Table 5.6, 5.7, and 5.8, respectively. The ABR acquisition time saving from  $F_{mp} \geq 3.1$  to visual detection was between 1.51 s and 6.00 s at 500 Hz.

ii. 1000 Hz

The median and interquartile range (IQR) of the ABR acquisition time from NB LS CE-Chirp and tone burst at multiple frequencies specific using two types of stopping criteria ( $F_{mp} \geq 3.1$  and visual detection) at 40 dBnHL are shown in Table 5.2. Analysis using the Friedman test demonstrated a significant difference in the ABR acquisition time at 40 dBnHL of 4000 Hz ( $\chi^2(3) = 42.81, p < 0.001$ ) at 40 dBnHL. From the post hoc Wilcoxon signed-rank test, the ABR acquisition time from both stopping criteria using both stimuli, however, was not significantly different based on post hoc analysis ( $p > 0.01$ ) with no effect size ( $r = 0.02$  to  $0.08$ ). The Z distribution, p-value, and effect size particulars were described in Table 5.6, 5.7, and 5.8, respectively. The ABR acquisition time saving from visual detection to  $F_{mp} \geq 3.1$  was between 0 s to 3.00 s at 1000 Hz.

iii. 4000 Hz

The median and interquartile range (IQR) of the ABR acquisition time from NB LS CE-Chirp and tone burst at multiple frequencies specific using two types of stopping criteria ( $F_{mp} \geq 3.1$  and visual detection) at 40 dBnHL are shown in Table 5.2. Analysis using the Friedman test demonstrated a significant difference in the ABR acquisition time at 40 dBnHL of 4000 Hz ( $\chi^2(3) = 21.67, p < 0.001$ ) at 40 dBnHL. ABR waveforms using  $F_{mp}$  of 3.1 has a significantly faster test time ( $p < 0.001$ ) than visual detection with medium effect size ( $r = 0.44$ ) using NB LS CE-Chirp and ( $r = 0.35$ ) using tone burst at 4000 Hz. The Z distribution, p-value, and effect size particulars were described in Table 5.6, 5.7, and 5.8, respectively. The ABR acquisition time saving from visual detection to  $F_{mp} \geq 3.1$  was between 1.50 s to 9.01 s at 4000 Hz.

### ***5.5.1.3 Combinations of stimulus types and stopping criteria***

#### ***5.6.1.3.1 70 dBnHL***

i. 500 Hz

The median and interquartile range (IQR) of the ABR acquisition time from NB LS CE-Chirp and tone burst at different frequencies using two types of stopping criteria (Fmp  $\geq$  3.1 and visual detection) at 70 dBnHL are shown in Table 5.2. The Friedman test revealed a significant difference in ABR acquisition time among the different stimulus types and stopping criteria combination ( $\chi^2$  (3) = 37.22,  $p < 0.001$ ) for 500 Hz at 70 dBnHL. According to the post hoc Wilcoxon signed-rank test in Table 5.3, 5.4, and 5.5, the ABR to NB LS CE-Chirp stimulus detected using Fmp of 3.1 method has the fastest acquisition time ( $p < 0.001$ ) with large effect size ( $r = 0.56$ ) than the other combinations. The second fastest ABR acquisition time is from NB LS CE-Chirp using visual detection ( $p < 0.001$ ) with large effect size ( $r = 0.50$ ) than tone burst using Fmp. ABR to NB LS CE-Chirp using Fmp has the shortest time, 6.01 s. ABR to NB LS CE-Chirp using visual detection has the second shortest time, 12.01 s. The longest time is ABR to tone burst using visual detection, which is about 21.10 s.

ii. 1000 Hz

The median and interquartile range (IQR) of the ABR acquisition time from NB LS CE-Chirp and tone burst at different frequencies using two types of stopping criteria (Fmp  $\geq$  3.1 and visual detection) at 70 dBnHL are shown in Table 5.2. The Friedman test revealed a significant difference in ABR acquisition time among the different stimulus types and stopping criteria combinations ( $\chi^2$  (3) = 54.23,  $p < 0.001$ ) for 1000 Hz at 70 dBnHL. According to the post hoc Wilcoxon signed-rank test in Table 5.3, 5.4, and 5.5, ABR to NB LS CE-Chirp stimulus using Fmp of 3.1 method has the fastest acquisition time ( $p < 0.001$ ) than ABR to tone burst using visual detection with large effect size ( $r = 0.71$ ). ABR acquisition time was similar between NB LS CE-Chirp using visual detection and tone

burst using Fmp ( $p = 0.088$ ) with no effect size ( $r = 0.09$ ). The ABR acquisition timesaving from NB LS CE-Chirp using Fmp  $\geq 3.1$  to tone burst using visual detection was between 0 s to 16.52 s at 1000 Hz. The ABR acquisition time saving from NB LS CE-Chirp using visual detection to tone burst using Fmp  $\geq 3.1$  was between 0 s to 3.00 s at 1000 Hz. ABR to NB LS CE-Chirp using Fmp has the shortest time, 4.50 s. ABR to NB LS CE-Chirp using visual detection has the second shortest time, 12.01 s. The slowest time combination was ABR to tone burst using visual detection 21.02 s.

iii. 4000 Hz

The median and interquartile range (IQR) of the ABR acquisition time from NB LS CE-Chirp and tone burst at multiple frequencies specific using two types of stopping criteria (Fmp  $\geq 3.1$  and visual detection) at 70 dBnHL was shown in Table 5.2. The Friedman test revealed a significantly faster ABR acquisition time among the different stimulus types and detection technique combinations ( $\chi^2(3) = 11.59$ ,  $p = 0.009$ ) for 4000 Hz at 70 dBnHL. According to the post hoc Wilcoxon signed-rank test in Table 5.3, 5.4, and 5.5, ABR to NB LS CE-Chirp stimulus using Fmp of 3.1 has a significantly faster acquisition time ( $p < 0.01$ ) than ABR to tone burst using visual detection with large effect size ( $r = 0.66$ ). However, ABR acquisition time was similar between NB LS CE-Chirp using visual detection and tone burst using Fmp ( $p = 0.137$ ) with no effect size ( $r = 0.03$ ). The Z distribution, p-value, and effect size particulars were described in Table 5.3, 5.4, and 5.5, respectively.

5.6.1.3.2 40 dBnHL

i. 500 Hz

The median and interquartile range (IQR) of the ABR acquisition time from NB LS CE-Chirp and tone burst at multiple frequencies specific using two types of stopping criteria (Fmp  $\geq 3.1$  and visual detection) at 40 dBnHL are shown in Table 5.2. The Friedman test revealed a significant difference in ABR acquisition time among the different stimulus

types combination ( $\chi^2 (3) = 14.16, p = 0.003$ ) for 500 Hz at 40 dBnHL. According to the posthoc Wilcoxon signed-rank test in Table 5.3, 5.4, and 5.5, ABR to NB LS CE-Chirp stimulus using Fmp of 3.1 method has significant faster acquisition time ( $p = 0.03$ ) than ABR to tone burst using visual detection with large effect size ( $r = 0.71$ ). Whilst, ABR to NB LS CE-Chirp stimulus using visual detection has a faster acquisition time ( $p < 0.001$ ) than ABR to tone burst using Fmp  $\geq 3.1$  with a large effect size ( $r = 0.71$ ). The ABR acquisition time saving from NB LS CE-Chirp using Fmp  $\geq 3.1$  to tone burst using visual detection was between 0 s to 10.51 s at 500 Hz. The ABR acquisition time saving from NB LS CE-Chirp using visual detection to tone burst using Fmp  $\geq 3.1$  was between 0 s to 18.02 s at 500 Hz. ABR to NB LS CE-Chirp using visual detection has the shortest time, 15.01 s. ABR to tone burst using Fmp has the longest time, 33.03 s.

ii. 1000 Hz

The median and interquartile range (IQR) of the ABR acquisition time from NB LS CE-Chirp and tone burst at multiple frequencies specific using two types of stopping criteria (Fmp  $\geq 3.1$  and visual detection) at 40 dBnHL was shown in Table 5.2. The Friedman test revealed a significant difference in ABR acquisition time among the different stimulus types combination ( $\chi^2 (3) = 42.81, p < 0.001$ ) for a frequency of 1000 Hz at 40 dBnHL. According to the post hoc Wilcoxon signed-rank test in Table 5.3, 5.4, and 5.5, ABR to NB LS CE-Chirp stimulus using Fmp of 3.1 method has a significant faster acquisition time ( $p < 0.001$ ) than ABR to tone burst using visual detection with medium effect size ( $r = 0.44$ ). ABR to NB LS CE-Chirp stimulus using visual detection has a shorter acquisition time ( $p < 0.001$ ) than ABR to tone burst using Fmp  $\geq 3.1$  with a large effect size ( $r = 0.65$ ). NB LS CE-Chirp using visual detection, NB LS CE-Chirp using Fmp of 3.1, and tone burst using Fmp of 3.1. The ABR acquisition time saving from NB LS CE-Chirp using Fmp  $\geq 3.1$  to tone burst using visual detection was between 0 s to 18.02 s at 1000 Hz. The ABR acquisition time saving from NB LS CE-Chirp using visual detection to tone burst using Fmp  $\geq 3.1$  was between 0 s to 15.02 s at 1000 Hz. ABR to NB LS CE-Chirp using Fmp has the shortest time, 12.01 s. ABR to NB LS CE-Chirp using visual detection has the longest

time, 15.01 s. The slowest time is a combination of ABR to tone burst using Fmp and visual detection; both were 30.03 s.

iii. 4000 Hz

The median and interquartile range (IQR) of the ABR acquisition time from NB LS CE-Chirp and tone burst at multiple frequencies specific using two types of stopping criteria (Fmp  $\geq$  3.1 and visual detection) at 40 dBnHL was shown in Table 5.2. The Friedman test revealed a significantly faster ABR acquisition time among the different stimulus types and detection technique combinations ( $\chi^2(3) = 21.67$ ,  $p < 0.001$ ) for 4000 Hz at 40 dBnHL. NB LS CE-Chirp uses visual detection, NB LS CE-Chirp uses Fmp of 3.1, and tone burst uses visual detection. The Z distribution, p-value, and effect size particulars were described in Tables 5.3, 5.4, and 5.5, respectively. According to the post hoc Wilcoxon signed-rank test, ABR to NB LS CE-Chirp stimulus using Fmp of 3.1 method has a significantly faster acquisition time ( $p < 0.001$ ) than ABR to tone burst using visual detection with medium effect size ( $r = 0.30$ ). ABR to NB LS CE-Chirp stimulus using visual detection has a shorter acquisition time than ABR to tone burst using Fmp  $\geq$  3.1 ( $p = 0.006$ ) with large effect size ( $r = 0.56$ ). The ABR acquisition time saving from NB LS CE-Chirp using Fmp  $\geq$  3.1 to tone burst using visual detection was between 0 s to 12.01 s at 4000 Hz. The ABR acquisition time saving from NB LS CE-Chirp using visual detection to tone burst using Fmp  $\geq$  3.1 was between 0 s to 4.50 s at 4000 Hz. ABR to NB LS CE-Chirp using visual detection has the shortest time, 10.51 s. ABR to NB LS CE-Chirp using Fmp has the second shortest time 12.01s. The slowest time combination using ABR to tone burst visual detection was 24.02 s.

## 5.6 DISCUSSION

This section discusses the results of the fourth objective based on the comparison of stimulus types (NB LS CE-Chirp and tone burst) and stopping criteria (Fmp  $\geq$  3.1 and visual detection) at two intensity levels (70 and 40 dBnHL) in normal hearing infants.

## **5.6.1 The impact of stimulus types and stopping criteria on ABR acquisition time**

### ***5.6.1.1 NB LS CE-Chirp has a shorter ABR acquisition time than tone burst***

The present study found that the ABR acquisition time was faster using NB LS CE-Chirp than tone burst at both 70 and 40 dBnHL either  $F_{mp} \geq 3.1$  or visual detection as a stopping criterion except at 4000 Hz at 70 and 40 dBnHL infants. NB CE-Chirp is a subset of CE-chirp and was expected to elicit larger wave V amplitudes. This likely results from the simultaneous depolarization of specific cochlear regions, a characteristic of NB CE-Chirp stimulus (Ferm et al., 2013; Ferm et al., 2015; Wegner & Dau, 2002; Elberling et al., 2010). This condition elicited greater ABR waves amplitude and improved signal-to-noise ratio (SNR); thus, this leads to shorter ABR test times. (Ferm et al., 2013; Ferm et al., 2015; Wegner & Dau, 2002; Elberling et al., 2010). However, even NB LS CE-Chirp is a non-monotonic level-dependent stimulus and it is likelihood that ABR amplitude reduced due to broadening neural excitation with increasing stimulus intensity level (Dau et al., 2000). This broadening neural excitation leads to neural desynchronization in which reduces the peak V amplitude of the ABR recordings (Cebulla et al., 2010). Therefore, even when estimated hearing thresholds are normal, prolonged ABR latencies are observed using NB CE-Chirp stimulus at higher intensities (Rodrigues et al., 2012; Dau et al., 2000). This was consistent with the current findings, no significant difference in peak V amplitude was observed between tone burst and NB CE-Chirp stimulus at 70 dBnHL.

The NB CE-Chirp stimulus elicited significantly larger wave V amplitudes than the conventional click stimulus across all frequencies and intensity levels with the exception of 80 and 60 dBnHL at 500 Hz, where no significant difference was observed (Cebulla et al., 2010; Rodrigues et al., 2012). This may be due to the upward spread of excitation, a phenomenon where the cochlear excitation broadens at higher intensities, leading to a reduced amplitude response (Fobel & Dau, 2004; Elberling & Don, 2010). In contrast, Wegner and Dau (2002) compared low frequency chirps and 250 Hz tone burst with similar duration and spectral content elicited larger ABR amplitudes at low and medium intensity levels. In the current study, at intensity levels of 40 dBnHL, the amplitude of wave V for the NB CE-Chirp stimulus was greater than the tone burst stimulus. Figure 4.10 illustrates

the ABR findings from both stimuli showed wave V was clearly visible in all stimulus conditions and was consistently larger in amplitude for the CE - Chirp compared to the tone burst, aligning with previous research (Dau et al., 2000; Fobel & Dau, 2004; Elberling et al., 2007).

From previous literature, there was no significant difference in the amplitude of wave V between tone burst and NB CE - Chirp stimuli of 80 dBnHL at higher frequencies of 1000, 2000, and 4000 Hz (Megha et al., 2019). Whilst, at lower intensity levels of 60, 40, and 20 dBnHL, the amplitude of wave V for NB CE - Chirp stimulus was greater than the tone burst stimulus (Megha et al., 2019). Previous literature revealed that hearing thresholds from ABR to NB CE-Chirp and behavioural assessment at 4000 Hz were similar (Talaat et al., 2020). ABR findings from NB LS CE-Chirp and tone burst elicited larger ABR amplitude which can improve SNR performance and elicited robust ABR waveforms at very high intensity levels (Hall III, 2015). Thus, the faster ABR waveform identification led to reduce ABR testing time. The similarities in ABR acquisition times were expected to be seen in ABR assessment from both stimuli (NB LS CE-Chirp and tone burst) at higher frequencies (e.g., 4000 Hz). Therefore, the shorter ABR acquisition time elicited via NB LS CE-Chirp translates to potential benefits for both testers (i. e., increased efficiency and confidence level) and infants (i. e., reduced testing duration and potentially improved comfort). Integration of Fmp enhances ABR testing effectiveness and demonstrably reduces the total duration of individual testing sessions (NHSP, 2013; BSA, 2018). This improvement holds significant value in clinical settings, where infant tolerance for prolonged testing procedures may be limited.

The enhanced efficiency observed from NB LS CE-Chirp stimulus may be attributed to improved SNR and stemming from increased neural synchrony. ABR assessment utilizing NB CE-Chirp stimulus demonstrated reduced acquisition times compared to tone burst stimulus. This finding aligns with Dau et al. (2000), who proposed that chirp stimuli shorten testing time by synchronizing the arrival of each frequency component with its corresponding activation site along the basilar membrane. This compensation mechanism enhances stimulus efficiency by promoting improved temporal synchronization

of evoked potential across various neural parts involved in generating not only the auditory compound action potential but also the ABR and auditory steady state response (ASSR).

Furthermore, this tone burst stimulus has neural synchrony reduction at a lower intensity level due to the temporal dispersion. Hence, an extended test time is needed to complete a consistent ABR waveform from tone burst. Although NB LS CE-Chirp produces a larger amplitude which improves overall SNR, the result was similar as the tone burst can evoke clearer ABR waveform at high intensity levels (Hall III, 2015). The current study suggested that using NB LS CE-Chirp stimulus in ABR assessments can significantly improve clinical efficiency by reducing acquisition time.

#### ***5.6.1.2 Rapid ABR identification using $Fmp \geq 3.1$***

The ABR acquisition time was faster using objective algorithm  $Fmp \geq 3.1$  than the usage of visual detection as stopping criteria across stimulus types and intensities range. However, at higher intensity levels of 70 dBnHL, ABR to NB LS CE-Chirp acquisition time was similar using both detection methods at 500 Hz. At 40 dBnHL, ABR to NB LS CE-Chirp showed a similar acquisition time at 1000 Hz. For tone burst, ABR showed a similar acquisition time using both  $Fmp$  and visual detection methods at 500 Hz across the intensities range and 1000 Hz at 40 dBnHL. Previous studies found that ABR to tone burst and behavioural assessment have similar hearing thresholds at higher frequencies, which was 4000 Hz (McCreery et al., 2015; Talaat et al., 2020; Gengel & Watson, 1971). Whilst, Talaat et al. (2020) study revealed that hearing thresholds from ABR to NB CE-Chirp and behavioural assessment at 4000 Hz were similar too. Thus, at 4000 Hz, the similarities in hearing thresholds were observed from ABR to NB LS CE-Chirp, ABR to tone burst, and behavioral assessment. ABR provides thresholds estimation; whilst, behavioral assessment provides behavioral hearing thresholds. Therefore, similar acquisition times were expected to be seen in ABR to NB LS CE-Chirp and ABR to tone burst at higher frequencies.

The present study found similar acquisition time between NB LS CE Chirp and tone

burst ABRs at 500 Hz. This indicates that there is no clear advantage of NB LS CE Chirp over tone burst to improve the test time at the frequency of 500 Hz. Given the acquisition time is determined either by SNR via Fmp or visual detection, it can be safely to conclude that the NB LS CE chirp ABR does not provide advantage of SNR that can resulted to time savings or faster detection by audiologist.

Utilizing Fmp as a stopping criterion effectively improves the ABR test time by terminating the test once adequate data is acquired, thereby minimizing superfluous auditory stimulation (Dzulkarnain et al., 2018). This larger amplitude of ABR recordings may assist the visual detection, specifically at low intensity levels. This feature is particularly advantageous in infant populations, where minimal testing durations is important. The objective algorithm Fmp enhances ABR testing efficiency and demonstrably reducing the total duration of individual testing sessions (NHSP, 2013; BSA, 2018). This improvement holds significant value in clinical settings where infant tolerance for prolonged testing procedures may be limited. Furthermore, as the Fmp indices rely solely on SNR, reduced sensitivity is expected. It is crucial to note that comparing methods solely based on detection rates can be misleading, as those with higher false positive rates may appear more sensitive than more conservative approaches with lower false positive rates (McKearney et al., 2010).

Infants are particularly vulnerable to sensory overload and extended exposure to auditory stimulus can induce fatigue or discomfort (Graven & Browne, 2008). This approach ensures that ABR waveforms are captured during periods of optimal responsiveness of auditory system in infants enhancing the reliability and accuracy of the test results. Accurate ABR testing is crucial for early identification of hearing impairments, enabling timely intervention and improved long term outcomes (JCIH, 2009). While the Fmp offers significant advantages, successful clinical implementation necessitates vigilant consideration of infant characteristics.

The ABR findings based on visual detection are relied on the tester's experience and knowledge. Visual detection is the detection based on manual observation in the ABR

waveform identification. The visual detection is also influenced by the number of ABR sweeps compared to  $F_{mp} \geq 3.1$ . The ABR waveform was seen to be stable with the larger sweep numbers which made the visual detection tranquil especially ABR recordings from tone bursts. Determining the ABR thresholds via visual observation can be challenging due to inherent variability. Additionally, previous study on the confidence level can reduce inter-audiologist ABR waveform agreement by less than 85% and intra-audiologist ABR waveform agreement by less than 79% from the visual detection as a stopping criterion (Dzulkarnain et al., 2014). However, objective algorithms for wave V detection can mitigate this challenge to a significant extent. To address this issue, researchers have explored the use of NB CE-Chirps for ABR assessments, as employed in the current study (Venail et al., 2014). The reason for a higher frequency of tone bursts that showed significantly faster time in  $F_{mp}$  than visual detection is that a smaller number of sweeps and SNR improvement are required for clear and robust ABR detection. ABR results using  $F_{mp}$  need a smaller number of sweeps compared to visual detection because the averaging to reach  $F_{mp}$  of 3.1 suggests high statistical confidence (99%) of the response is present; thus, ABR assessment can be stopped immediately (NHS, 2013; BSA, 2018). Moreover, the larger ABR amplitude from NB LS CE-Chirp has led to shorter acquisition time to reach  $F_{mp} \geq 3.1$  because of SNR improvement. Thus, the ABR assessment can be ended promptly.

Lower frequency (e.g., 500 Hz) has lower external auditory canal resonance and requires higher sound pressure levels to activate the apical region of the cochlea. It has been suggested that the maximum synchronization for 500 Hz occurs at 30 dBnHL (Dau et al., 2000). Thus, exceeding this level diminishes the amplitude advantage of chirp stimulus compared to other frequencies. Additionally, since the spectral overlap between tone burst and chirp stimuli is more pronounced at 500 Hz, the number of activated neural fibers becomes similar. Consequently, the amplitude advantage of chirp stimulus is less significant at this frequency (Cobb et al., 2016; Bal et al., 2022). The observed performance variability including the clinicians unfamiliarity with the simulation software (Vidler & Parker, 2004). This factor contributed to the variability in ABR interpretation. Hence, better SNR allows the tester to determine the faster ABR presence elicited from both stopping

criteria, Fmp and visual detection which results in faster ABR acquisition time. Despite this, inter-rater reliability among experienced clinicians is notably inconsistent (Cohen et al., 1978; Vidler & Parker, 2004). As Cohen et al. (1978) emphasized human visual observation surpasses pattern recognition in inherent subjectivity often results in discrepancies in visual scoring. Therefore, ABR testing using Fmp 3.1 as a stopping criterion has a faster testing time than using the visual detection method.

#### ***5.6.1.3 The accuracy differences between $Fmp \geq 3.1$ and visual detection***

The current study described the Fmp accuracy analysis. The results revealed that the percentage of discrepancies between wave V identification via  $Fmp \geq 3.1$  by ABR Eclipse system and wave V confirmed by the audiologist was from the lowest to highest within the range of 0 % to 10 % in infants. ABR to NB LS Cein add-Chirp and ABR to tone burst at 70 dBnHL have 100 % accuracy (i.e. 0 % discrepancies) of wave V identification using  $Fmp \geq 3.1$  compared to visual detection. The current study findings indicate a limitation in the exclusive reliance on the  $Fmp \geq 3.1$  as a stopping criterion for ABR recordings in the clinical setting. The Fmp is a statistical measure of SNR recording and provides a confidence level for ABR waves reproducibility. The higher Fmp value indicates a better ABR waveform quality and greater confidence of ABR waves presence or absence in which facilitate in shorter testing time and better objectivity of the ABR results.

The cut-off Fmp value of 3.1 indicates a 99% confidence that the true deterministic ABR signals are distinguished from indeterministic noise. At lower intensity levels, less conservative confidence levels of 95% or 68% (corresponding to Fmp values of 2.25 and 1.85, respectively) may be used. This approach allows Fmp-based detection to converge with visual detection rates at lower intensity levels. The efficacy for ABR threshold seeking based on SNR as stopping criterion is empirically validated by the reduction in test duration demonstrated herein. These time efficiencies serve as a compelling argument for the integration of NB LS CE-Chirps into audiology clinics, complementing other advantages documented in the existing literature. The current study findings indicate a limitation in the

exclusive reliance on the  $F_{mp} \geq 3.1$  as a stopping criterion for ABR recordings in the clinical setting especially at lower intensity levels (e.g. 40 dBnHL), where discrepancies were observed. Furthermore, a manual evaluation of the SNR from the recorded ABR waveforms is advised prior to accepting the results or terminating the recording. In the current study, the limitation was intensity dependent. Therefore, it is recommended that clinicians use independent judgment.

#### ***5.6.1.4 Combinations of NB LS CE-Chirp as a stimulus type and $F_{mp} \geq 3.1$ as a stopping criteria***

The current study findings of ABR acquisition time have been discussed comprehensively in previous sections. The primary aim is to identify the optimal combination of ABR parameters that minimizes ABR acquisition time while maintaining diagnostic accuracy. The optimal combination is defined as the selected combination of independent and dependent variables within this study that demonstrates greater performance compared to other combinations. The best combination of stimulus types and detection method is ABR to NB LS CE-Chirp and  $F_{mp}$ . The current study showed that NB LS CE-Chirp stimulus using  $F_{mp}$  has a shorter testing time than tone burst due to greater ABR waveform resolution and larger amplitude that influenced the decision of the tester to confirm the presence of the ABR waveform. A study by Talaat et al. (2020) studied on ABR test time; however, did not emphasize on stopping criteria methods. Moreover, Dzulkarnain et al. (2018) compared NB LS CE-Chirp and tone burst using  $F_{mp}$  and residual noise level (RNL) in normal hearing adults.

The specific temporal organization of NB LS CE-Chirp stimulus has the ability to synchronize neural firing across a wide range of auditory nerve fibers that elicit faster and more synchronized neural responses. This synchronization enhances the clarity and timing of ABR waveforms resulting in improved SNR that makes it easier to distinguish, detect, and interpret the ABR in a faster testing time. In addition, the usage of  $F_{mp} \geq 3.1$  accurateness and inaccuracy as a standalone ABR waveform identification may combine with visual observation. There were discrepancies between  $F_{mp}$  and confirmation

by an audiologist. Employing SNR as the stopping criterion allows for the termination of the test upon achieving the optimal SNR. This is because further averaging would not necessarily be completed to achieve a minimal residual noise level (e.g., 40 nV) or a predefined number of averages (e.g., 2000 sweeps). The current study findings suggested that using  $F_{mp} \geq 3.1$  may activate the auditory pathway more efficiently and lead to faster identification of the ABR waveform.

As a result, ABR results provide a shorter acquisition time to reach  $F_{mp} \geq 3.1$  in ABR recordings than visual detection in infants, especially in the high frequency range. This can be explained by the increased sensitivity of cochlear travelling wave delay relative to frequency specific at higher frequency (Elberling et al., 2010).  $F_{mp} \geq 3.1$  is a superior stopping criterion to visual detection. Thus, this increases the confidence level of the tester, as 99% of the confidence level using  $F_{mp}$  of 3.1 is present in the ABR (Elberling & Don, 1987). The shortest ABR acquisition time was observed from ABR to NB LS CE-Chirp using  $F_{mp} \geq 3.1$ . The longest testing time was observed from ABR to tone burst using visual detection.

## **5.7 SUMMARY**

This chapter discussed experiment two, which justifies the research objective four. The research objectives include the evaluation of the ABR acquisition time using different types of stimuli and stopping criteria. In conclusion, based on the results and discussions described in the earlier sections of this chapter, the summary is as follows:

1. The best combination of stimulus type and stopping criterion is ABR to NB LS CE-Chirp with  $F_{mp}$ .
2. The least combination of stimulus type and stopping criterion is ABR to tone burst with visual detection.

# **CHAPTER SIX**

## **SUMMARY, CLINICAL IMPLICATIONS, AND FUTURE RECOMMENDATIONS**

### **6.1 INTRODUCTION**

The outcomes of experiments one and two were explained in-depth in chapter 4 and 5. Consequently, the current chapter offers a concise overview of each thesis chapter, highlighting the clinical implications derived from this current study. Additionally, it addresses the limitations of the study and proposes future recommendations.

### **6.2 THESIS SUMMARY**

In conclusion, the three earlier chapters in this study described in detail the background of the study, literature review, problem statements, and the gap of the study. Numerous studies stated that ABR assessment is the gold standard for hearing threshold estimations, specifically in the infant population. Therefore, the ABR assessment was commonly employed and was consistent with the JCIH 1-2-3 benchmark recommendation from the EHDI (2019) program. The suggested FS ABR using conventional stimulus is the tone burst which usually takes a longer time to produce ABR recordings. This is because of the natural characteristics of tone burst (see Section 2.3.2.3.2) and the ABR as a far-field recording that entails a thousand stimuli in order to mend signal averaging using SNR to acquire the ABR. Therefore, several studies were done to improve ABR findings including the newly engineered ABR stimulus which is NB LS CE-Chirp. This NB LS CE-Chirp improved ABR findings in terms of greater neural synchronization and upward spread of excitation which elicited larger ABR amplitude, improved SNR, and clearer waveform resolution. These conditions enable the ABR acquisition time to be lessened. Generally, the research gap, problem statements, and literature reviews lead to the current study. The main objective of the present study is to examine the efficacy of ABR to NB LS CE-Chirp in normal hearing infants. The ABR parameter using NB LS CE-Chirp and wave V detection

using the Fmp objection algorithm was applied to decrease the ABR acquisition time.

In Chapter 4, experiment one demonstrated that NB LS CE-Chirp stimulus elicited larger ABR amplitudes for all waves I, III, and V compared to tone burst stimulus except for wave V at 500 and 4000 Hz at 70 dBnHL. However, NB LS CE-Chirp showed larger amplitude for wave V across the frequency range at 40 dBnHL. NB LS CE-Chirp also showed shorter ABR absolute latencies for all waves I, III, and V across all stimulus intensities and frequency ranges. Moreover, hearing threshold estimations via ABR to NB LS CE-Chirp were significantly lower than ABR to tone burst across frequencies in normal hearing infants.

In Chapter 5, experiment two revealed that ABR acquisition was influenced by stimulus types (i.e., NB LS CE-Chirp and tone burst) and stopping criteria ( $Fmp \geq 3.1$  and visual detection) in normal hearing infants. ABR to NB LS CE-Chirp with  $Fmp \geq 3.1$  and significantly reduced ABR acquisition times in terms of robust waveform that easily detects amplitude, latency, and hearing threshold estimation in infants.

### **6.3 CLINICAL IMPLICATION**

The outcomes of this study may suggest that NB LS CE-Chirp serve as a feasible substitute for tone burst in diagnostic assessments of infants. The amplitudes and resulting SNR of ABR to NB LS CE-Chirps are comparable to those elicited by tone burst. Combinations of stimulus types of NB LS CE-Chirp and stopping criteria  $Fmp \geq 3.1$  led to fewer variables and high assurance of ABR interpretations. As this ABR to NB LS CE-Chirp became rapid and in estimates of the lower hearing threshold of infants, minimal duration was needed for ABR testing time and increased ABR appointment sessions per day. This NB LS CE-Chirp may be needless for anesthetics and sedation medicines. As in previous studies revealed that a high correlation between NB LS CE-Chirp and behavioural audiogram thresholds mostly in adult population. In the future, with this latest stimulus of NB LS CE-Chirp, hopefully, ABR assessment will facilitate in reducing test time, early diagnosis of hearing

threshold estimations as early as 2 months of age, and early intervention can be received for those with hearing impairment as recommended by JCIH (2019). This is because early diagnosis can lead to an early intervention of hearing amplification (e.g., hearing aids or cochlear implants) and aural rehabilitation. An early intervention may have a huge impact on speech, language, academic, and psychosocial development. Hence, in terms of rapid testing time, the waiting list and time could be shortened for audiological services. All of these conditions mentioned above would lead to a decrement in national expenditure in all aspects.

These experiments collectively highlight the effectiveness of NB LS CE-Chirp stimulus and specific parameter modifications in optimizing ABR testing efficiency in infant populations. The current study has several clinical implications and contributes significantly to the field of ABR which are testing time efficacy, recommendations for clinical practice, practical advantages, and greater implications. In terms of time efficacy in ABR assessment, the current study demonstrates that using NB LS CE-Chirp combined with Fmp as a stopping criterion significantly reduces ABR test durations in normal hearing infants. For instance, NB LS CE-Chirp achieved 10.01 seconds per average, faster than tone burst stimuli with visual detection at 70 dBnHL. Meanwhile, NB LS CE-Chirp achieved 11.52 seconds per average, faster than tone burst stimuli with visual detection at 40 dBnHL.

In terms of clinical practice recommendation, based on the ABR findings, shorter ABR acquisition time and larger ABR amplitudes with NB LS CE-Chirp stimulus. The current study suggested adopting NB LS CE-Chirp by utilising Fmp as a stopping criterion in clinical settings. This approach allows ABR tests to be conducted more efficiently, enabling audiologists to complete tests quickly and reducing the need for follow-up sessions. In addition, implementing ABR to NB LS CE-Chirp with optimized parameters enhances the feasibility of ABR recordings from relaxed infants during clinical sessions. This improvement increases the likelihood of testing more infants per session, thereby optimizing clinical resources and improving overall diagnostic efficacy. By improving the effectiveness of ABR testing in infants, particularly those with hearing impairments, the

study contributes valuable insights to the field of pediatric audiology. These insights can lead to enhanced diagnostic accuracy, reduce testing burdens on both infants and caregivers, and ultimately improve outcomes in early hearing detection and intervention programs.

National expenditure saving was the impact of time-saving for hearing assessment, and this will decrease the time and cost for sedation or anesthetics, and hearing follow-up appointments. Based on the medical cost per patient calculator (see Appendix 1a and 1b), the time for ABR to NB LS CE-Chirp bilateral ears to be completed is approximately 60 minutes. Meanwhile, for ABR to tone burst, both ears were expected to be completed in approximately 180 minutes. It was observed it was 3 times longer period to complete the ABR assessment. In terms of cost, ABR to NB LS CE-Chirp costs about RM 93.30, while ABR to tone burst costs RM 197.70 for each patient. The cost mentioned was the cost per patient. The average number of infants who needed to do advanced hearing assessment was approximately 50 patients per month. Therefore, approximately 600 infants were tested using ABR to NB LS CE-Chirp per year in a hospital, which will cost about RM 55,980. For ABR to tone burst, the cost is about RM 118 620. This will save the cost of around RM 62,640 per year in a hospital. Generally, the recommendation to adopt the NB LS CE-Chirp stimulus will save annual costs of approximately RM 2 881 440 in 48 government hospitals in Malaysia with audiological ABR services.

Moreover, Table 4.5 provides comprehensive descriptive data on ABR waveform presence across different stimulus types and frequencies. These findings contribute to the evidence base for optimizing ABR testing protocols in clinical settings, emphasizing the need for standardized approaches for the infant population that consider both stimulus characteristics and frequencies ABR specific responses. The findings contribute valuable knowledge to the field, guiding future research and clinical practices aimed at optimizing early detection and intervention for auditory disorders in infants.

In conclusion, understanding the variability in ABR responses across different stimuli and frequencies for better decision-making in clinical settings. Clinicians may

prioritize NB LS CE-Chirp stimulus, especially when testing infants at lower intensity levels, to ensure consistent and reliable ABR recordings. This personalized approach is crucial for optimizing patient care and outcomes in pediatric audiology. The summarization of the thesis in terms of clinical application is shown in Figure 6.1.



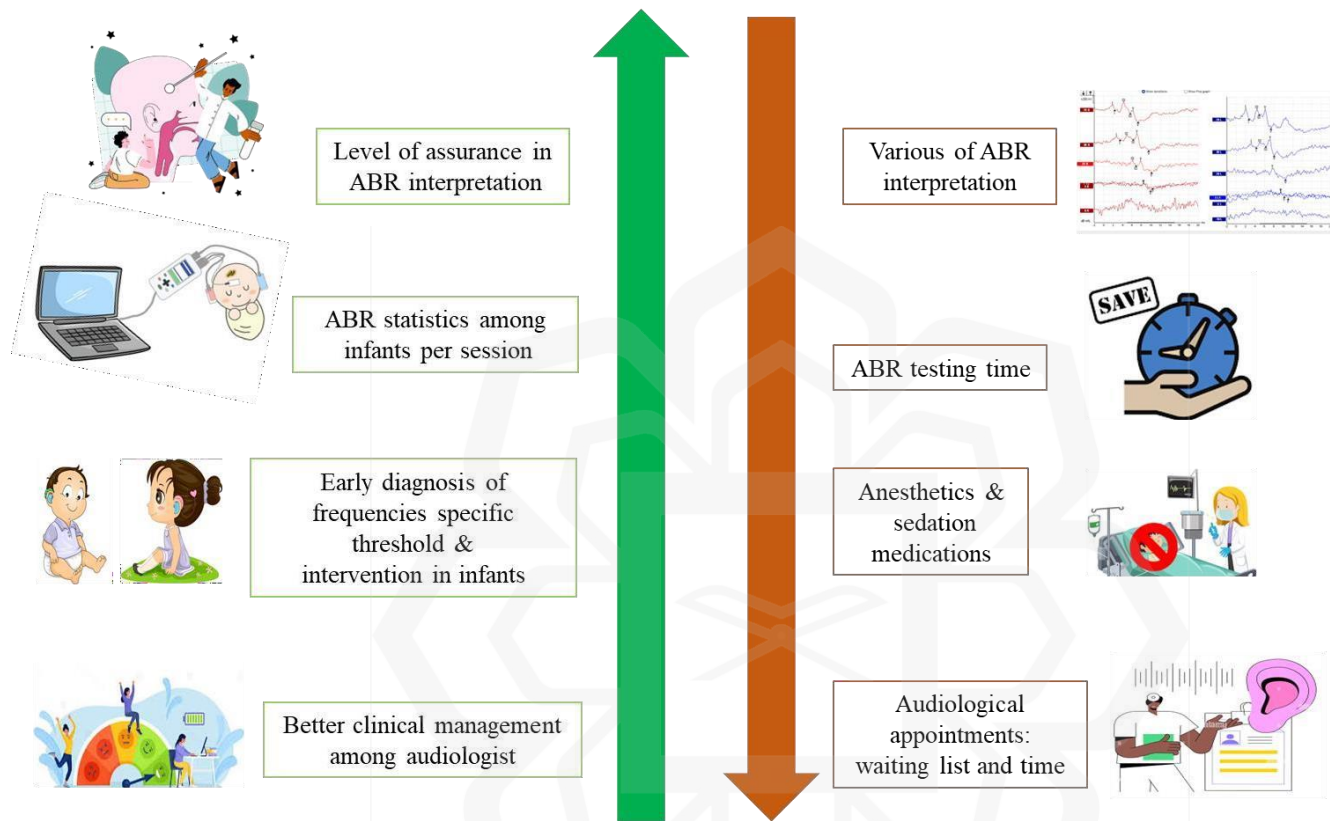


Figure 6.1 Summary of the thesis in terms of clinical implication.

## **6.4 LIMITATIONS OF THE STUDY**

The limitations of the current study are sample and data limitation. Firstly, in term of the sample data limitation as this study only involve normal hearing infants. Thus, it limits the knowledge of ABR parameters and findings for hearing impaired infants such as conductive hearing loss (CHL), mixed hearing loss (MHL), and sensorineural hearing loss (SNHL) with variable degree of hearing loss. Secondly, the current study was only done in infants less than 6 months of age; thus, this limits the generalizability of the ABR findings from NB LS CE-Chirp and tone burst in older infants and children.

## **6.5 FUTURE RECOMMENDATION**

Future research should aim to validate these findings across broader populations, encompassing various types and severities of hearing loss. Additionally, longitudinal studies are recommended to confirm the accuracy of ABR thresholds using NB LS CE-Chirp in comparison with behavioural audiograms. This study can be enhanced for the hearing impaired population to discover the outcome of conductive and sensorineural hearing loss from NB LS CE-Chirp. As this study only used air conduction as the transducer, it is advisable to investigate bone conduction using NB LS CE-Chirp in the hearing impaired population. In addition, the ABR stimulus intensity is suggested at every intensity levels (e.g., 60, 40, and 20 dBnHL). This will expand the usage of NB LS CE-Chirp. With that, hopefully, NB LS CE-Chirp may facilitate the hearing assessment in infants for better time-saving, cost-saving, and quality of life. Furthermore, the study suggests exploring alternative parameters like maximum length sequence (MLS), stimulus rates, and other objective detection methods such as cross-correlation which were not employed in this research but could potentially elicit improved outcomes. Moreover, the current study can suggest that in the future, compiled assessments aligned with a behavioural hearing assessment to compare the correlation between objective and subjective hearing threshold levels.

## REFERENCES

- Adelman, C., Levi, H., Linder, N., and Sohmer, H. (1990). Neonatal auditory brain-stem response threshold and latency: 1 hour to 5 months. *Electroencephalography and Clinical Neurophysiology/Evoked Potentials Section*, 77(1), 77–80. [https://doi.org/10.1016/0168-5597\(90\)90019-A](https://doi.org/10.1016/0168-5597(90)90019-A)
- Alberti, P. W., Hyde, M. L., Corbin, H., Riko, K., and Abramovich, S. (1983). An Evaluation of BERA For Hearing Screening in High-Risk Neonates. *Laryngoscope*, 93, 1115– 1121.
- Allison, T., Wood, C. C., and Goff, W. R. (1983). Clinical Section Brain Stem Auditory, Pattern-Reversal Visual, And Short-Latency Somatosensory Evoked Potentials: Latencies in Relation to Age, Sex, and Brain and Body Size. *Electroencephalography and Clinical Neurophysiology*, 55(6), 619-636. [https://doi.org/10.1016/0013-4694\(83\)90272-9](https://doi.org/10.1016/0013-4694(83)90272-9)
- Akin, A., Esmoğlu, A., Tosun, Z., Gulcu, N., Aydoğan, H., and Boyacı, A. (2005). Comparison of Propofol with Propofol-Ketamine Combination in Pediatric Patients Undergoing Auditory Brainstem Response Testing. *International Journal Pediatric Otorhinolaryngology*, 69, 1541–1545.
- Akinpelu, O. V., Peleva, E., Funnell, W. R. J., and Daniel, S. J. (2014). Otoacoustic emissions in newborn hearing screening: A systematic review of the effects of different protocols on test outcomes. *International Journal of Pediatric Otorhinolaryngology*, 78(5), 711–717. <https://doi.org/10.1016/j.ijporl.2014.01.021>
- Almeida, M. G., Rodrigues, G. R. I., and Lewis, D. R. (2014). Frequency-Specific Auditory Brainstem Response in Infants with Normal Hearing, *Rev. CEFAC* 13(3), 489–495.
- American Speech-Language-Hearing Association. (2004). Guidelines for the Audiologic Assessment of Children from Birth to 5 Years of Age [Guidelines]. Available from [www.asha.org/policy](http://www.asha.org/policy)
- Aoyagi, M., Yokoya, M., Nakamura, T., Tojima, H., Kim, Y., Suzuki, Y., Koike, Y., and

- Nakai, O. (1990). Preservation and Improvement of Auditory Brainstem Response Findings after Acoustic Neuroma Surgery. *Acta Oto-Laryngologica*, 114, 40-46. <https://doi.org/10.3109/00016489409128299>
- April, J., and Al, Y. (2007). Habituation of auditory evoked potentials: The dynamics of waveform morphology. *Australian and New Zealand Journal of Audiology*, 29(2), 77– 88. <https://doi.org/10.1375/audi.29.2.77>
- Arnold, S. A. (1985). Objective versus Visual Detection of the Auditory Brain Stem Response. *Ear and Hearing* 6(3), 144-150.
- Ayas, M., and Yaseen, H. (2021). Emerging Data from a Newborn Hearing Screening Program in Sharjah, United Arab Emirates. *International Journal of Pediatrics*. <https://doi.org/10.1155/2021/2616890>
- Bal, N., Toker, O. G., Husam, H., Ozdemir, S., and Lien, B. D. (2022). Optimizing Auditory Brainstem Response Test with Narrow Band Level-Specific CE-Chirps. *Ann OtolNeurotol*, 5, 50–54. <https://doi.org/10.1055/s-0043-1764180>
- Ballachanda, B. B., Moushegian, G., and Stillman, R.D. (1992). Adaptation of the auditory brainstem response: effects of click intensity, polarity, and position. *Journal of American Academy Audiology*, 3, 275-282.
- Bargen, G. A. (2015). Chirp-evoked auditory brainstem response in children: A review. *American Journal of Audiology*, 24(4), 573-583. [https://doi.org/10.1044/2015\\_aja-15-0016](https://doi.org/10.1044/2015_aja-15-0016)
- Barnet, A. B., Friedman, S. L., Weiss, I. P., Ohlrich, E. S., Shanks, B., and Lodge, A. (1980). VEP development in infancy and early childhood. A longitudinal study. *Electroencephalography and Clinical Neurophysiology*, 49(5–6), 476-489. [https://doi.org/10.1016/0013-4694\(80\)90390-9](https://doi.org/10.1016/0013-4694(80)90390-9)
- Beagley, H. A. and Sheldrake, J. B. (1978). Differences in Brainstem Response Latency with Age and Sex. *British Journal of Audiology*, 12, 69-77. <https://doi.org/10.3109/03005367809078858>
- Benita, M., and Conde, H. (1972). Effects of local cooling upon conduction and synaptic

transmission. *Brain Research*, 36(1), 133-151. [https://doi.org/10.1016/0006-8993\(72\)90771-8](https://doi.org/10.1016/0006-8993(72)90771-8)

Bershad, N. J. and Rockmore, A. J. (1974). On estimating signal-to-noise ratio using the sample correlation coefficient. *IEEE Trans. Inf. Theor*, 20, 112-113. <https://doi.org/10.1109/TIT.1974.1055159>

Bonino, A. Y. and Leibold, L. J. (2017). Behavioral Assessment of Hearing in 2 to 4 Year-old Children: A Two-interval, Observer-based Procedure Using Conditioned Play-based Responses. *Journal of Visualized Experiments*, 119, 21-7. <https://doi.org/10.3791/54788>

Bramhall, N., Konrad-Martin, D., McMillan, G., and Griest, S. (2017). Auditory brainstem response altered in humans with noise exposure despite normal outer hair cell function. *Ear and Hearing*, 38(1),1-12. <https://doi.org/10.1097/aud.0000000000000370>

British society of audiology, NHSP Clinical Group, Guidance for auditory brainstem response testing in babies, Version 2.1, March 2013.

British Society of Audiology. (2018). *Recommended Procedure Auditory Brainstem Response (ABR) Testing in Babies* (Issue February). [www.thebsa.org.uk](http://www.thebsa.org.uk)

British Society of Audiology (2019). Recommended Procedure Auditory Brainstem Response (ABR) Testing in Babies. Available from: <https://www.thebsa.org.uk/wp-content/uploads/2019/06/OD104-81-Recommended-Procedure-forABR-Testing-in-Babies.pdf>.

Britt, R. and Rossi, G. (1980). Neural generators of brain stem auditory evoked responses. Part I. Lesion studies. *Neuroscience Abstracts*, 6, 594.

Bruhn, E., and Ferraro, J. (2018). Effects of Subject Activity on the Auditory Brainstem Response Measured with Two Different Recording Instruments.

Brown, M. C., Smith, D. I., and Nuttal, A. L. (1983). The temperature dependency of neural and hair cell responses evoked by high frequencies. *Journal of Acoustical Society Am*, 73(5), 1662-1670.

- Canale, A., Dagna, F., Lacilla, M., Piumetto, E., and Albera, R. (2012). Relationship between pure tone audiometry and tone burst auditory brainstem response at low frequencies gated with Blackman window. *European Archives of Oto-Rhino-Laryngology*, 269(3), 781–785. <https://doi.org/10.1007/s00405-011-1723-7>
- Cargnelutti, M., Cóser, P.L., and Biaggio, E.P.V. (2017). LS CE-Chirp® vs. click in the neuroaudiological diagnosis by ABR. *Brazilian Journal Otorhinolaryngology*, 83(3), 313-317. <https://doi.org/10.1016/j.bjorl.2016.04.018>
- Caruso, S., Maiolino, L., Rugolo, S., Intelisano, G., Farina, M., Salvatore Cocuzza, S., and Serra, A. (2003). Auditory brainstem response in premenopausal women taking oral contraceptives, *Human Reproduction*, 18, 1, 85–89, <https://doi.org/10.1093/humrep/deg003>
- Cebulla, M. and Elberling, C., (2010). Auditory brain stem responses evoked by different chirps based on different delay models. *J Am Academy Audiology*. 21, 452-460.
- Cebulla, M., Lurz, H. and Shehata-Dieler, W. (2014). Evaluation of waveform, latency and amplitude values of chirp ABR in newborns. *International Journal of Pediatric Otorhinolaryngology*, 78(4), 631–636.
- Cebulla, M., Stürzebecher, E., Don, M., and Müller-Mazzotta, J. (2012). Auditory brainstem response recording to multiple interleaved broadband chirps. *Ear And Hearing*, 33(4), 466–479. <https://doi.org/10.1097/aud.0b013e318241e85a>
- Cebulla, M. and Stürzebecher, E. (2013). Detectability of newborn chirp-evoked ABR in the frequency domain at different stimulus rates. *International Journal of Audiology*, 52: 698–705. <https://10.3109/14992027.2013.804634>
- Ceylan, S. and Yılmazözkul, Y. Y. (2020). Advantages of narrow band CE-Chirp ABR compared to tone burst ABR in adults with normal hearing. <https://doi.org/10.22541/au.160279749.95978498/v1>
- Cheng, T.Y., Tsai, C.F., and Luan, C.W. (2021). The correlation between click-evoked auditory brainstem responses and future behavioral thresholds determined using universal newborn hearing screening. *The Journal of Health Care Organization*,

- Provision, and Financing*, (58), 1–13. <https://doi.org/10.1177/00469580211049010>
- Ching, T. Y. C., Dillon, H., Button, L., Seeto, M., Buynder, P. Van, Marnane, V., Cupples, L., and Leigh, G. (2017). Age at intervention for permanent hearing loss and 5-year language outcomes. *Pediatrics*, 140(3). <https://doi.org/10.1542/peds.2016-4274>
- Coats et al (1979) Coats, A. C. (1978). Human Auditory Nerve Action Potentials and Brain Stem Evoked Responses: Latency-Intensity Functions in Detection of Cochlear and Retrocochlear Abnormality. *Archives of Otolaryngology - Head and Neck Surgery*, 104(12), 709– 717. <https://doi.org/10.1001/archotol.1978.00790120035006>
- Cobb, K. M. and Stuart, A. (2016). Neonate Auditory Brainstem Responses to CE-Chirp and CE-Chirp Octave Band Stimuli I: Versus Click and Tone Burst Stimuli versus click and tone burst stimuli. *EarHear* 37(6) <https://doi.org/10.1097/aud.0000000000000343>
- Coenraad, S., Van Immerzeel, T., Hoeve, L. J., & Goedegebure, A. (2010). Fitting model of ABR age dependency in a clinical population of normal hearing children. *European Archives of Oto-Rhino-Laryngology*, 267(10), 1531–1537. <https://doi.org/10.1007/s00405-010-1291-2>
- Cohen, M. M. and Rapin, I. (1978). Evoked potential audiometry in neurologically impaired children. In R. F. Naunton & C. Fernandez (Eds.), *Evoked electrical activity in the auditory nervous system*. New York: Academic Press.
- Cone, B. & Norrix, L. (2015). Measuring the Advantage of Kalman-Weighted Averaging for Auditory Brainstem Response Hearing Evaluation in Infants. *American Journal of Audiology*, 24, 153-168. [https://doi.org/10.1044/2015\\_AJA-14-0021](https://doi.org/10.1044/2015_AJA-14-0021).
- Crumley, W. (2011). Good practices in auditory brainstem response, part 1. <https://www.audiologyonline.com/articles/good-practices-in-auditory-brainstem-827>
- Dagna, F., Canale, A., Lacilla, M., and Albera, R. (2014). Tone burst stimulus for auditory brainstem responses: Prediction of hearing threshold at 1kHz. *Auris Nasus Larynx*, 41(1), 27–30. <https://doi.org/10.1016/j.anl.2013.07.004>

- Dau, T., Wegner, O., Mellert, V., and Kollmeier, B. (2000). Auditory brainstem responses with optimized chirp signals compensating basilar-membrane dispersion. *The Journal of the Acoustical Society of America*, 107, 1530-1541. <https://doi.org/10.1121/1.428438>
- Dawson, G. (1951). A summation technique for detecting small signals in a large irregular background. *The Journal of Physiology*, 115(2).
- de Boer, E. (1980). Auditory physics. Physical principles in hearing theory. I. *Physics Reports*, 62(2), 87–174. [https://doi.org/10.1016/0370-1573\(80\)90100-3](https://doi.org/10.1016/0370-1573(80)90100-3)
- De Lima et al (2018) De Lima, J. P., Alvarenga, K. D. F., Foelkel, T. P., Monteiro, C. Z., & Agostinho, R. S. (2008). Polarity stimulation effects on brainstem auditory evoked potentials. *Brazilian Journal of Otorhinolaryngology*, 74(5), 725–730. [https://doi.org/10.1016/S1808-8694\(15\)31383-5](https://doi.org/10.1016/S1808-8694(15)31383-5)
- Dehan, C. P. and Jerger, J. (1990). Analysis of Gender Differences in the Auditory Brainstem Response. *Laryngoscope* 100, 18-24.
- Diao, T., Duan, M. and Ma, X. (2022). The impairment of speech perception in noise following pure tone hearing recovery in patients with sudden sensorineural hearing loss. *Sci Rep* 12, 866. <https://doi.org/10.1038/s41598-021-03847-y>
- Dillon, H. (2001). Hearing Aids: Hearing Aid Earmolds, Earshells, and Coupling Systems. Boomerang Press, Sydney.
- Di Scipio, E. and Mastronardi, L. (2015). CE-Chirp® ABR in cerebellopontine angle surgery neuromonitoring: technical assessment in four cases. *Neurosurgical Review* 38, 381–384. <https://doi.org/10.1007/s10143-015-0609-3>
- Don, Manuel, Allen, A. R., and Starr, A. (1977). Effect of click rate on the latency of auditory brainstem response in humans. *Annals of Otolaryngology, Rhinology & Laryngology*, 86, 186–195.
- Don, M., Ponton, C. W., and Eggermont, J. J. (1998). The effects of sensorineural hearing loss on cochlear filter times estimated from ABR latencies. *Journal Acoustical Society America*, 104, 2280–2289.

- Don, Manuel, Kwong, B., and Tanaka, C. (2005). A diagnostic test for Ménière's disease and cochlear hydrops: Impaired high-pass noise masking of auditory brainstem responses. *Otology and Neurotology*, 26(4), 711–722. <https://doi.org/10.1097/01.mao.0000169042.25734.97>
- Don, M., and Elberling, C. (1996). Use of quantitative measures of auditory brain-stem response peak amplitude and residual background noise in the decision to stop averaging. *Journal of Acoustical Society of America* 99, 491–499.
- Downs, M. P., and Sterritt, G. M. (1964). Identification audiometry for neonates: A preliminary report. *Journal of Auditory Research*, 42(2), 69–80.
- Durieux-Smith, A., and Jacobson, J. T. (1985). Comparison of auditory brainstem response and behavioral screening in neonates. *Journal of Otolaryngology*, 14, 47–53.
- Durrant, J. D. (1977). Study of a combined noninvasive-ECochG and BSER recording technique. *The Journal of the Acoustical Society of America*, 62(S1), S87–S87. <https://doi.org/10.1121/1.2016427>
- Dyk, Z. (2019). Diagnostic accuracy of CE Chirp. [Master dissertation, Pretoria University]. Pretoria University Research Repository. [https://repository.up.ac.za/bitstream/handle/2263/72463/VanDyk\\_Diagnostic\\_2019.pdf?sequence=1&isAllowed=y](https://repository.up.ac.za/bitstream/handle/2263/72463/VanDyk_Diagnostic_2019.pdf?sequence=1&isAllowed=y)
- Dzulkarnain, A. A. A., Hadi, U. S. A., & Zakaria, N. A. (2013). The effects of stimulus rate and electrode montage on the auditory brainstem response in infants. *Speech, Language and Hearing* 16(4), 221–226. <https://doi.org/10.1179/2050572813Y.0000000017>
- Dzulkarnain, A. A. A., Buyong, A. S., & Sulaiman, N. H. (2014). Intra-subject variability in the auditory brainstem response using a vertical montage recording. *Speech, Language and Hearing*, 17(3), 160–167. <https://doi.org/10.1179/2050572814Y.0000000035>
- Dzulkarnain, A. A. A., Noor Ibrahim, S. H. M., Anuar, N. F. A., Abdullah, S. A., Tengku Zam Zam, T. Z. H., Rahmat, S., & Mohd Ruzai, M. A. (2017). Influence of two-

electrode montages on the level-specific (LS) CE-Chirp auditory brainstem response (ABR) at multiple intensity levels. *International Journal of Audiology*, 56(10), 723–732. <https://doi.org/10.1080/14992027.2017.1313462>

Dzulkarnain, A. A. A., Abdullah, S. A., Ruzai, M. A. M., Ibrahim, S. H. M. N., Anuar, N.F. A., and Rahim, A. E. A. (2018). Effects of different electrode configurations on the narrow band level-specific CE-chirp and tone-burst auditory brainstem response at multiple intensity levels and frequencies in subjects with normal hearing. *American Journal of Audiology*, 27(3), 294–305. [https://doi.org/10.1044/2018\\_aja-17-0087](https://doi.org/10.1044/2018_aja-17-0087)

Dzulkarnain, A. A. A., Salamat, S., Shahrudin, F. A., Jamal, F. N., and Zakaria, M. N. (2021). Influence of Stimulus Polarity on the Auditory Brainstem Response from Level-Specific Chirp. *Journal Audiology Otology*, 25(2), 199-208. <https://doi.org/10.7874/jao.2021.00248>

Dzulkarnain, A. A. A., Marzuki, M. N., Shahrudin, F. A., Jamal, F. N., Chahed, N., and Zakaria, M. N. (2023). Optimization Of Auditory Brainstem Response (ABR) Test Time Using Level Specific (LS) CE-Chirp®. *International Journal of Allied Health Sciences*, 7,(1), 2820–2826. <https://doi.org/10.31436/ijahs.v7i1.731>

Eggermont, J., & Salamy, A. (1988). Maturation time course for the ABR in preterm and full term infants. *Hearing Research*, 33(1), 35–47. [https://doi.org/10.1016/0378-5955\(88\)90019-6](https://doi.org/10.1016/0378-5955(88)90019-6)

Eggermont, J. J. (1979). Narrow-band AP latencies in normal and recruiting human ears, *Journal Acoustical Society Am.* 65, 463–470. <https://doi.org/10.1121/1.382345>

Elberling, C., Callo, J., & Don, M. (2010). Evaluating auditory brainstem responses to different chirp stimuli at three levels of stimulation. *The Journal of the Acoustical Society of America*, 128(1), 215–223. <https://doi.org/10.1121/1.3397640>

Elberling, C., and Don, M. (2008). Auditory brainstem responses to a chirp stimulus designed from derived-band latencies in normal-hearing subjects. *The Journal of the Acoustical Society of America*, 124(5), 3022–3037. <https://doi.org/10.1121/1.2990709>

- Elberling, C., Don, M., Cebulla, M., Stürzebecher, E. (2007). Auditory steady-state responses to chirp stimuli based on cochlear traveling wave delay. *The Journal Acoustical Society America*, 122(5), 2772-2785.  
<https://doi.org/10.1121/1.2783985>
- Elberling, C., and Wahlgreen, O. (1985). Estimation of Auditory Brainstem Response, ABR, by Means of Bayesian Inference. *Scandinavian Audiology*, 14(2), 89–96.  
<https://doi.org/10.3109/01050398509045928>
- El-Mously, M., Omara, A., and Mohamed, N. (2020). Auditory brainstem response to a chirp stimulus in infants with normal hearing. *The Scientific Journal of Al-Azhar Medical Faculty, Girls*, 4(2), 131. [https://doi.org/10.4103/sjamf.sjamf\\_10\\_20](https://doi.org/10.4103/sjamf.sjamf_10_20)
- Elsayed, A. M., Hunter, L.L., Keefe, D.H., Feeney, M. P., Brown D. K., Meinzen-Derr, J. K., Baroch, K., Sullivan-Mahoney, M., Francis, K., and Schaid, L.G. (2015). Air and Bone Conduction Click and Tone-Burst Auditory Brainstem Thresholds Using Kalman Adaptive Processing in Nonsedated Normal-Hearing Infants. *Ear Hear.* 36(4), 471-481. <https://doi: 10.1097/AUD.0000000000000155>
- Eysholdt, U., and Schreiner, C. (1982). Maximum length sequences - a fast method for measuring brain-stem-evoked responses. *Audiology*, 21(3), 242–250.  
<https://doi.org/10.3109/00206098209072742>
- Felix, R. A., Gourévitch, B., and Portfors, C. V. (2018). Subcortical pathways: Towards a better understanding of auditory disorders. *Hearing Research*, 362, 48–60.  
<https://doi.org/10.1016/j.heares.2018.01.008>
- Ferm, I., and Lightfoot, G. (2015). Further comparisons of ABR response amplitudes, test time, and estimation of hearing threshold using frequency-specific chirp and tone pip stimuli in newborns: Findings at 0.5 and 2 kHz. *International Journal of Audiology*, 54(10), 745–750. <https://doi.org/10.3109/14992027.2015.1058978>
- Ferreira, L., Gardin, L., Barbieri, R. B., Cargnelutti, M., Quinto, S. M. S., Michele Vargas Garcia, M. V., and Biaggio, E. P. V. (2019). The influence of gender on brainstem auditory evoked potentials' responses to different stimuli in newborns. *Audiology Communication Research*, 25, 1-6. <https://doi.org/10.1590/2317-6431-2019-2152>

- Ferm, I., Lightfoot, G., and Stevens, J. (2013). Comparison of ABR response amplitude, test time, and estimation of hearing threshold using frequency specific chirp and tone pip stimuli in newborns. *International Journal of Audiology*, 52(6), 419–423. <https://doi.org/10.3109/14992027.2013.769280>
- Ferraro, J., Murphy, G., and Ruth, R. (1986). A Comparative Study of Primary Electrodes Used in Extratympanic Electrocochleography. *Seminars in Hearing*, 7(03), 279–286. <https://doi.org/10.1055/s-0028-1091464>
- Fria, T. J., and Doyle, W. J. (1984). Maturation of the Auditory Brain Stem Response (ABR). *Ear and Hearing*, 5(6), 361–365. <https://doi.org/10.1097/00003446-198411000-00008>
- Frisna, R. D. (2009). Age-related hearing loss. *Annals of the New York Academy of Sciences*, 1170, 708–717.
- Fobel, O. and Dau, T. (2004). Searching for the optimal stimulus eliciting auditory brainstem responses in humans, *Journal Acoustical Society America*. 116, 2213–2222.
- Fowler (1992) Fowler, C. G. Effects of stimulus phase on the normal auditory brainstem response. *Journal Speech Hearing Res.* 35(1):167-74. <https://doi:10.1044/jshr.3501.167>
- Fowler, C. G., and Nofsinger, D. (1983). Effect of stimulus repetition rate and frequency on the auditory brainstem response in normal, cochlea-impaired, and VIII nerve brainstem-impaired subjects. *Journal of Speech and Hearing Research*, 26, 560–567.
- Francois, M., Teissier, N., Barthod, G., and Nasra, Y., (2012). Sedation for children 2–5 years of age undergoing auditory brainstem response and auditory steady state responses recordings, *International Journal Audiology*, 51, 282–286.
- Galambos, R., and Hecox, K. E. (1978). Clinical applications of the auditory brain stem response. *Otolaryngologic Clinics of North America*, 11(3), 709-722.
- Gold, S., Cahani, M., Sohmer, H., Horowitz, M., and Shahar, A. (1985). Effects of body

temperature elevation on auditory nerve-brain-stem evoked responses and EEGs in rats. *Electroencephalography and Clinical Neurophysiology*, 60(2), 146-153.  
[https://doi.org/10.1016/0013-4694\(85\)90021-5](https://doi.org/10.1016/0013-4694(85)90021-5)

Gorga, M. P., Johnson, T. A., Kaminski, J. R., Beauchaine, K. L., Garner, C. A., and Neely, S. T. (2006). Using a Combination of Click- and

Tone Burst–Evoked Auditory Brain Stem Response Measurements to Estimate Pure-Tone Thresholds. *Ear & Hearing*, 27(1), 60–74.  
<https://doi.org/10.1097/01.aud.0000194511.14740.9c>

Gorga, M. P., and Thornton, A. R. (1989). The choice of stimuli for ABR measurements. *Ear Hear*, 10, 217–230.

Gøtsche-Rasmussen K., Poulsen T., and Elberling C. (2012). Reference hearing threshold levels for chirp signals delivered by an ER-3A insert earphone. *International Journal Audiology*, 51, 794 – 799.

Graham, E. H., Walker, E. A., Eastman, J. A., Frenzel, M. R., Joe, T. R., and McCreery, R. W. (2021). The impact of mild-to-severe hearing loss on the neural dynamics serving verbal working memory processing in children. *NeuroImage: Clinical* 30, 1-9.

Granade, G. L., Collet, L, and Morgon, A. (1994). Auditory-Evoked Brainstem Response Elicited by Maximum Length Sequences in Normal and Sensorineural Ears. *Audiology*, 33, 218-236.

Graven, S. N. and Browne, J. V. (2008). *Sensory Development in the Fetus, Neonate, and Infant: Introduction and Overview* Elsevier.  
<https://doi:10.1053/j.nainr.2008.10.007>

Grey, S., Sanz, C., Morgan-Short, K., and Ullman, M. T. (2018). Bilingual and monolingual adults learning an additional language: ERPs reveal differences in syntactic processing. *Bilingual Language Cognitive*, 21, 970–994.  
<https://doi.org/10.1017/S1366728917000426>

Gundogdu, O., Yaman, H., Karaaslan, P., and Serbetcioglu, M. B. (2022). Effect of General

- Anesthesia on Auditory Brainstem Response Testing. *Medeni Medical Journal*, 37(2), 145-149. [https://doi: 10.4274/MMJ.galenos.2022.25741](https://doi.org/10.4274/MMJ.galenos.2022.25741)
- Gullick, W. L. and Cutt, R. A. (1962). The relationship between response magnitude of first- and second-order auditory neurons. *The psychological record*, 12, 121-131.
- Hall, J. W., Susan, H. M., Eugenio, A. A., Mackey, J., and Robert, A. J. (1984). Neuro-otologic applications of simultaneous multi-channel auditory evoked response recordings. *Laryngoscope*, 94, 883–889.
- Hall, J. W. (1992). *Handbook of Auditory Evoked Responses*: Allyn and Bacon.
- Hall III, J. W. (2013). Application of ABR in Objective Assessment of Infant Hearing. Hamam, K., & Purnami, N. (2020). Newborns Hearing Screening with Otoacoustic Emissions and Auditory Brainstem Response. *Journal of Community Medicine and Public Health Research*, 1(1), 1–13. <https://doi.org/10.20473/jcmpshr.v1i1.20287>
- Harvey, L. A., Wilson, W. J., Darnell, R., Bradley, A. P., and Baker, F. C. (2006). The effect of sleep on the fast and slow components of the auditory brainstem response: a case study. *The Australian and New Zealand Journal of Audiology*, 28(2), 106–121. <https://search.informit.org/doi/10.3316/informit.813477665937999>
- Hashimoto, I., Ishiyama, Y., Yoshimoto, T., & Nemoto, S. (1981). Brain- Stem Auditory-Evoked Potentials Recorded Directly from Human Brain-Stem and Thalamus. *Brain*, 104(4), 841–859. <https://doi.org/10.1093/brain/104.4.841>
- Hayakawa, K., Konishi, Y., Matsuda, T., Kuriyama, M., Konishi, K., Yamashita, K., Okumura, R., and Hamanaka, D. (1989). Development and aging of brain midline structures: assessment with MR imaging. *Neuroradiology*, 172, 171-177.
- Hayes, D. (2003). Screening methods: Current status. *Mental Retardation and Developmental Disabilities Research Reviews*, 9(2), 65–72. <https://doi.org/10.1002/mrdd.10061>
- Hecox, K., and Burkard, R. (1982). Developmental dependencies of the human brainstem

- auditory evoked response. *Annual N Y Acad Science*, 388, 538-556. [https://doi: 10.1111/j.1749-6632.1982.tb50815.x](https://doi.org/10.1111/j.1749-6632.1982.tb50815.x). PMID: 62840
- Hecox, K., Galambos, R., and Jolla, L. (1974). Brain Stem Auditory Evoked Responses in Human Infants and Adults. <http://archotol.jamanetwork.com/>
- Hecox, K., Squires, N., and Galambos, R. (1976). Brainstem auditory evoked responses in man. I. Effect of stimulus rise-fall time and duration. *The Journal of the Acoustical Society of America* 60, 1187. <https://doi.org/10.1121/1.381194>
- Hood, L. (1998). Clinical Applications of the Auditory brainstem Response. *Singular Publishing Group*. Clifton Park, N.Y.
- Hrnčić, H. H., Goga, A., Glas, D. H. M. (2019). Does an early discharge of a newborn influence the success of the newborn hearing screening in developing countries? A hospital based study *Nermin* 16(2), 209-215. [https://doi: 10.17392/988-19](https://doi.org/10.17392/988-19)
- Holland et al., 1985 Holland, P. W., and Welsch, R. E. 1977. Robust regression using iteratively reweighted least-squares, 6, 813–827.
- Hughes, J. R., Fino, J., and Gagnon, L. (1981). The importance of phase of stimulus and the reference recording electrode in brain stem auditory evoked potentials. *Electroencephalography and Clinical Neurophysiology*, 51(6), 611–623. [https://doi.org/10.1016/0013-4694\(81\)90205-4](https://doi.org/10.1016/0013-4694(81)90205-4)
- Interacoustics(2010). Eclipse NB CE- LS Chirp Norms. <https://www.interacoustics.com/eclipse>
- Interacoustics(2017). How to Measure Residual Noise. <https://www.interacoustics.com/academy/evoked-potentials/abr-training/how-to-measure-residual-noise>
- Ismail, A. I., Majid, A. H. A., Zakaria, M. N., Abdullah, A. C., Hamzah, S. and Mukari, S. Z. M. (2018). Factors predicting health practitioners' awareness of UNHS program in Malaysian non-public hospitals. *International Journal of Pediatric Otorhinolaryngology*, 109, 78-84. <https://doi.org/10.1016/j.ijporl.2018.03.030>.

- Ito, T., Bishop, D.C., and Oliver, D.L. (2016). Functional organization of the local circuit in the inferior colliculus. *Anatomical Science International*, 91(1), 22-34. <https://doi.org/10.1007/s12565-015-0308-8>
- Jacobson, J. T. (1985). Normative aspects of the pediatric auditory brainstem response. *The Journal of otolaryngology*, 14, 7- 11.
- Jacobson, J. T. (1985). Normative aspects of the pediatric auditory brainstem response. *Journal of Otolaryngology*.
- Jacobson, J. T., and Jacobson, C. A. (1994). The effects of noise in transient EOAE newborn hearing screening. *International Journal of Pediatric Otorhinolaryngology*, 29, 235-248. [https://doi.org/10.1016/0165-5876\(94\)90170-8](https://doi.org/10.1016/0165-5876(94)90170-8)
- Jamal, F. N., Arafat Dzulkarnain, A. A., Shahrudin, F. A., and Marzuki, M. N. (2021). Test-Retest Reliability of Level-Specific CE-Chirp Auditory Brainstem Response in Normal-Hearing Adults. *Journal of Audiology and Otology*, 25(1), 14–21. <https://doi.org/10.7874/jao.2020.00073>
- Janssen, R.M., Usher, L., Stapells, D. R. (2010). The British Columbia's Children's Hospital tone-evoked auditory brainstem response protocol: how long do infants sleep and how much information can be obtained in one appointment? *Ear Hear*. 31, 722–724.
- Jerger, J., and Hall, J. (1980). Effects of Age and Sex on Auditory Brainstem Response. In *Arch Otolaryngol*,106. <http://archotol.jamanetwork.com/>
- Jerger, J. and Johnson, K. (1988). Interactions of age, gender, and sensorineural hearing loss on ABR latency. *Ear Hear*, 9(4), 168-76. <https://doi.org/10.1097/00003446-198808000-00002>
- Jewett, D. L. (1970). Volume-conducted potentials in response to auditory stimuli as detected by averaging in the cat. *Electroencephalography and Clinical Neurophysiology*, 28(6), 609–618. [https://doi.org/10.1016/0013-4694\(70\)90203-8](https://doi.org/10.1016/0013-4694(70)90203-8)
- Jewett, D. and Williston, J.S. (1971). Auditory-evoked far fields averaged from the scalp

of humans. *Brain*, 94, 681-696.

Jiang, Y., Samuel, O. W., Asogbon, M. G., Chen, S., and Li, G. (2021). Towards optimal selection of stimuli polarity method for effective evoking auditory brainstem responses *Journal of Integrative 2*. <https://doi.10.31083/j.jin2002029>

Johnson, J. L., White, K. R., Widen, J. E. (2005). A Multicenter Evaluation of How Many Infants with Permanent Hearing Loss Pass a Two-Stage Otoacoustic Emissions/Automated Auditory Brainstem Response Newborn Hearing Screening Protocol. *Pediatrics*, 116, 663-672.

Johnson, K. L., Nicol, T., Zecker, S. G., and Kraus, N. (2008). Developmental plasticity in the human auditory brainstem. *Journal of Neuroscience*, 28(15), 4000–4007. <https://doi.org/10.1523/jneurosci.0012-08.2008>

Joint Committee on Infant Hearing. (2000). JCIH Year 2000 Position Statement: Principles and Guidelines for Early Hearing Detection Intervention Programs. *American Speech- Language Hearing Association*, 2, 27–50.

Joint Committee on Infant Hearing. (2019). Year 2019 Position Statement: Principles and Guidelines for Early Hearing Detection and Intervention Programs. *Journal of Early Hearing Detection and Intervention*, 4(2).

Junius, D. and Dau, T. (2005). Influence of cochlear traveling wave and neural adaptation on auditory brainstem response. *Hearing Research*, 205(1-2), 53-67. <https://doi.org/0.1016/j.heares.2005.03.001>

Katbanna, B., Bennett, S. L., Dokler, P. A., and Metz, D. A. (1995). Effects of electrode montage on infant auditory brainstem response. *Scandinavian Audiology*, 24(2), 133-136.

Kaveh, M. S., Shariat, M., and Zarkesh, M. R. (2021). Perinatal factors influencing the neonatal hearing screening results. *Pediatrics*, 21, 15

<https://doi.org/10.1186/s12887-020-02476-0>

Kato, T., Shiraishi, K., Eura, Y., Shibata, K., Sakata, T., Morizono, T., and Soda, T. (1998).

A 'Neural' Response with 3-ms Latency Evoked by Loud Sound in Profoundly Deaf Patients. *Audiology and Neurotology*, 3(4), 253-264. <https://doi.org/10.1159/000013797>

Kaynakoğlu, B., and Ceyhan, S. (2023). Which stimulus should be used for auditory brainstem response in newborns; CE-Chirp® level specific versus Click stimulus.

*International Journal Pediatric Otorhinolaryngology*, 170, 111597. [https://doi: 10.1016/j.ijporl.2023.111597](https://doi.org/10.1016/j.ijporl.2023.111597)

Khan, Y.T., Tsompanidis, A., Radecki, M., Dorfschmidt, L., Consortium, A., Austin, T., Suckling, J., Allison, C., Lai, M. C., Bethlehem, R. A. I., and Baren-Cohen, S. (2024). Sex Differences in Human Brain Structure at Birth. *Biol Sex Differ* 15, 81 <https://doi.org/10.1186/s13293-024-00657-5>

Kenna, M. A. (2003). Neonatal Hearing Screening. *Pediatrics Clinic North American*, 50(2), 301-313. [https://doi.org/10.1016/s0031-3955\(03\)00023-3](https://doi.org/10.1016/s0031-3955(03)00023-3)

Kerneis, S., Caillauda, E., and Bakhos, D. (2023). Technical note Auditory brainstem response: Key parameters for good-quality recording. *European Annals of Otorhinolaryngology, Head and Neck diseases* 140, 181–185. <https://doi.org/10.1016/j.anorl.2023.04.003> 1879-7296

Kevanishvili, Z., and Aphonchenko, V. (1979). Frequency composition of brain-stem auditory evoked potentials. *Scandinavian Audiology*, 8(1), 51–55. <https://doi.org/10.3109/01050397909076301>

Klaassen, M. (2016). Air- and bone-conducted brainstem evoked response audiometry collection of normative data for the new-developed level-specific CE-Chirp stimulus in normal-hearing adults. Radboud University Nijmegen.

Khatoun, M., Nighute, S., Nighute, S., Singh, R., Singh, R., Awari, A., Awari, A., Ishaque, M., and Ishaque, M. (2013). Maturation of Brainstem Auditory Evoked Potential from Full Term Infants & Children to Young Adult. *International Journal of Biomedical Research*, 3(12), 439. <https://doi.org/10.7439/ijbr.v3i12.585>

Kirkim, G., Serbetcioglu, B., Erdag, T. E., and Ceryan, K. (2008). The frequency of

- auditory neuropathy detected by universal newborn hearing screening program. *International Journal of Pediatric Otorhinolaryngology*, 72,(10), 1461-1469. <https://doi.org/10.1016/j.ijporl.2008.06.010>
- Kohshi, K., and Konda, N. (1990). Human auditory brain stem response during induced hyperthermia. *Journal of Applied Physiology*, 1419-1422.
- Konrad-Martin, D., Marilyn F. D., McMillan, G., Griest, G., McDermott, D., Fausti, S. A., and Austin, D. F. (2012). Age-related changes in the auditory brainstem response. *Journal of American Academy of Audiology*, 23(1), 18–35. <https://doi.org/10.3766/jaaa.23.1.3>
- Kristensen, S. G. B., & Elberling, C. (2012). Auditory brainstem responses to level-specific chirps in normal-hearing adults. *Journal of the American Academy of Audiology*, 23(9), 712–721. <https://doi.org/10.3766/jaaa.23.9.5>
- Kullgren, J. and Sibella, M. (2004) Calculating your costs per visit. *American Academy of Family Physician*, 41-45.
- Kumar, K., Bhat, J. S., D’Costa, P. E., Srivastava, M., and Kalaiah, M. K. (2013). Effect of stimulus polarity on speech evoked auditory brainstem response. *Audiology Research*, 3, 8.
- Lasky, R. E., Rupert, A., and Waller, M. (1987). Reproducibility of auditory brain-stem evoked responses as a function of the stimulus, scorer and subject. *Electroencephalography and Clinical Neurophysiology/Evoked Potentials Section*, 68(1), 45–57. [https://doi.org/10.1016/0168-5597\(87\)90069-4](https://doi.org/10.1016/0168-5597(87)90069-4)
- Łęski, J. M. (2002). Robust weighted averaging. *IEEE Transactions on Biomedical Engineering*, 49(8), 796–804. <https://doi.org/10.1109/TBME.2002.800757>
- Lev, A., and Sohmer, H. (1972). Sources of averaged neural responses recorded in animal and human subjects during cochlear audiometry (Electro-Cochleogram). *Archiv Für Klinische Und Experimentelle Ohren- Nasen- Und Kehlkopfheilkunde*, 201(2), 79–90. <https://doi.org/10.1007/BF00341066>
- Levit, Y., Himmelfarb, M., and Dollberg, S. (2015). Sensitivity of the automated auditory

- brainstem response in neonatal hearing screening. *Pediatrics*, 136(3), 641–647. <https://doi.org/10.1542/peds.2014-3784>
- Lewis, J. D., Kopun, J., Neely S. T., Schmid, K. K., and Gorga, M. P. (2015). Tone-burst auditory brainstem response wave V latencies in normal-hearing and hearing-impaired ears. *Acoustical Society of America*, 3210-3219. <http://doi.org/10.1121/1.4935516>
- Lv, J., Simpson, D. M., and Bell, S. L., (2007). Objective detection of evoked potentials using a bootstrap technique. *Medical Engineering and Physics*, 29(2): 191–198. <https://doi.org/10.1016/j.medengphy.2006.03.001>
- Maloff, E. S. and Hood, L. J. (2014) A comparison of auditory brain stem responses elicited by click and chirp stimuli in adults with normal hearing and sensory hearing loss. *Ear and Hearing*, 35(2), 271-282. <https://doi.org/10.1097/aud.0b013e3182a99cf2>
- Marcoux, A. M. (2011). The manipulation of auditory brain stem response data to predict the behavioral audiogram during infancy. *Seminars in Hearing*, 32(2), 156–162. <https://doi.org/10.1055/s-0031-1277237>
- Marsh, R. R., Yamane, H., and Potts, W. P. (1984). Auditory brain-stem response and temperature: relationship in the guinea pig. *Electroencephalography and Clinical Neurophysiology*, (57)3, 289- 293. [https://doi.org/10.1016/0013-4694\(84\)90130-5](https://doi.org/10.1016/0013-4694(84)90130-5)
- Maruthy, S., Gnanateja, G., Ramachandran, R., and Thuvassery, P. (2015). Characterizing Muscle Artifact Interference in AEP Recording. *Journal of Hearing Science*, 5(3), 33–44. <https://doi.org/10.17430/895269>
- Maslin (2017) and Mellor, D. H. (1984). Brain-stem, middle latency and late cortical evoked potentials in children with speech and language disorders. *Electroencephalography and Clinical Neurophysiology/ Evoked Potentials*, 59(4), 297–309. [https://doi.org/10.1016/0168-5597\(84\)90047-9](https://doi.org/10.1016/0168-5597(84)90047-9)
- Mauk, G. W., Behrens, T. R., & Ph, D. (1993). Historical, Political, And Technological Context Associated with Early Identification of Hearing Loss. *Seminars in Hearing*, 14(1), 1–17. <https://doi.org/10.1055/s-0028-1085101>

- Maurer, K., Schäfer, E., and H Leitner, H. (1980). The effect of varying stimulus polarity (rarefaction vs. condensation) on early auditory evoked potentials (EAEPs), *Electroencephalography and Clinical Neurophysiology*, 50, 3–4,332-334, [https://doi.org/10.1016/0013-4694\(80\)90162-5](https://doi.org/10.1016/0013-4694(80)90162-5)
- McKearney, R. M. and MacKinnon, R. C. (2019). Objective auditory brainstem response classification using machine learning. *International Journal of Audiology*, 58(4), 224–230. <https://doi.org/10.1080/14992027.2018.1551633>
- McKnight et al (2018) Rosemary J McKnight<sup>1</sup>, Hannah Glick<sup>2</sup>, Garrett Cardon<sup>3</sup>, Anu Sharma<sup>4</sup>, The Effects of Stimulus Rate on ABR Morphology and its Relationship to P1 CAEP Responses and Auditory Speech Perception Outcomes in Children with Auditory Neuropathy Spectrum Disorder: Evidence from Case Reports *Intractable & Rare Diseases Research*. 2019; 8(3), 179-186. <https://10.5582/irdr.2019.01073>
- Megha, K. N., Divyashree, K. N., Lakshmi, A., Adithya, S., Keerthana, K. P., Pushpalatha, Z. V., Konadath, S. (2018). Narrow-band chirp and tone burst auditory brainstem response as an early indicator of synaptopathy in industrial workers exposed to occupational noise. *Hearing Balance Communication*, 16(1): 1–12. <https://doi:10.1080/21695717.2017.1418803>
- Miller, A. R. and Jannetta, P. (1985). Neural generators of the ABR. In: Jacobson JT, The auditory brainstem response, 13-31.
- Malaysia Ministry of Health Hearing Screening Committee. (2014a). Report of The Evaluation of the Implementation of the High Risk Neonatal Hearing Screening in the Ministry of Health , Malaysia for the year of 2013-2014.
- Malaysia Ministry of Health Hearing Screening Committee. (2014a). Report of The Evaluation of the Implementation of the High Risk Neonatal Hearing Screening in the Ministry of Health, Malaysia for the year of 2013-2014.
- Ministry of Health Malaysia Hearing Screening Committee. (2014). Guidelines for neonatal hearing screening (Issue September). <http://www.moh.gov.my/english.php/pages/view/532>

- Mizrahi, E. M., Maulsby, R. L., and Frost, J. D. (1983). Improved wave V resolution by dual-channel brain stem auditory evoked potential recording. *Electroencephalography and Clinical Neurophysiology*, 55(1), 105–107. [https://doi.org/10.1016/0013-4694\(83\)90153-0](https://doi.org/10.1016/0013-4694(83)90153-0)
- Mobley, K. J. and Gibson, E. (2000). Tone burst evoked potentials: clinical applications. <https://www.audiologyonline.com/articles/tone-burst-evoked-potentials-clinical-1279>
- Mochizuki, Y., Go, T., Ohkubo, H., and Motomura, T. (1983). Development of human brainstem auditory evoked potentials and gender differences from infants to young adults. *Neurobiology*. [https://doi.org/10.1016/0301-0082\(83\)90005-9](https://doi.org/10.1016/0301-0082(83)90005-9)
- Mokotoff, B., Schulamn-Galambos, C., and Galambos, R. (1977). Brain Stem Auditory Evoked Responses in Children. *Archives of Otolaryngology*. 103(1), 38-43. <https://doi:10.1001/archotol.1977.00780180076010>
- Moeller, M. P. (2000). Early intervention and language development in children who are deaf and hard of hearing. *Pediatrics*, 106(3). <https://doi.org/10.1542/peds.106.3.e43>
- Moller, A. (2006). *Hearing: Anatomy, Physiology, and Disorders of the Auditory System* (2nd edn.). Academic Press.
- Moller, A. R. (2003). *Sensory systems: anatomy and physiology*. Amsterdam: Academic Press.
- Moller, A. R., and Jannetta, P. J. (1983). Interpretation of brainstem auditory evoked potentials: Results from intracranial recordings in humans. *Scandinavian Audiology*, 12(2), 125–133. <https://doi.org/10.3109/01050398309076235>
- Moller, A. R. and Jannetta, P. J. (1982a). Auditory evoked potentials recorded intracranially from the brainstem in man. *Experimental Neurology*, 74, 862-874.
- Moller, A. R. and Jannetta, P. J. (1985). Neural generators of the auditory brainstem response. *The Auditory Brainstem Response*, 13-31.
- Møller, A. R., Jannetta, P. J., and Sekhar, L. N. (1988). Contributions from the auditory

nerve to the brain-stem auditory evoked potentials (BAEPs): results of intracranial recording in man. *Electroencephalography and Clinical Neurophysiology/ Evoked Potentials*, 71(3), 198–211. [https://doi.org/10.1016/0168-5597\(88\)90005-6](https://doi.org/10.1016/0168-5597(88)90005-6)

Møller, A. R., Jho, H. D., Yokota, M., and Jannetta, P. J. (1995). Contribution from crossed and uncrossed brainstem structures to the brainstem auditory evoked potentials: A study in humans. *Laryngoscope*, 105(6), 596–605.

<https://doi.org/10.1288/00005537-199506000-00007>

Moore, J. K. (1987). The human auditory brain stem as a generator of auditory evoked potentials. *Hearing Research*, 29, 33-43.

Moore, J. K., Ponton, C. W., Eggermont, J. J., Wu, B. J.-C., and Huang, J. Q. (1996). Perinatal maturation of the auditory brain stem response: changes in path length and conduction velocity. *Ear and Hearing*, 17, 411-418.

Morimoto, T., Fujisaka, Y., Okamoto, Y., and Irino, T. (2019). Rising-frequency chirp stimulus to effectively enhance wave-I amplitude of auditory brainstem response. *Hearing Research*, 377, 104-108. <https://doi.org/10.1016/j.heares.2019.03.016>

Morton, C. C., & Nance, W. E. (2006). Newborn Hearing Screening — A Silent Revolution. *The New England Journal of Medicine*, 354(20), 2151–2164.

Muhler R, Mentzel K, Verhey J. (2012). Fast Hearing-Threshold Estimation Using Multiple Auditory Steady-State Responses with Narrow-Band Chirps and Adaptive Stimulus Patterns. *Scientific World Journal*, 192178.

Muhler, R., Rahne, T., and Verhey, J. L. (2013). Auditory brainstem responses to broadband chirps: Amplitude growth functions in sedated and anaesthetised infants. *International Journal of Pediatric Otorhinolaryngology*, 77(1), 49–53. <https://doi.org/10.1016/j.ijporl.2012.09.028>

Muse, C., Harrison, J., Yoshinaga-Itano, C., Grimes, A., Brookhouser, P. E., Epstein, S., Buchman, C., Mehl, A., Vohr, B., Moeller, M. P., Martin, P., Benedict, B. S., Scoggins, B., Crace, J., King, M., Sette, A., & Martin, B. (2013). Supplement to the JCIH 2007 Position Statement: Principles and Guidelines for Early Intervention

After Confirmation That a Child Is Deaf or Hard of Hearing. *Pediatrics*, 131(4), e1324– e1349. <https://doi.org/10.1542/peds.2013-0008>

Musiek (2015) Auditory Brainstem Response Differential Diagnosis. In: Katz, J., Ed., *Handbook of Clinical Audiology*, Lippincott Williams & Wilkins, Philadelphia, 13, 231-248.

NHSP (2013). Guidance for Auditory Brainstem Response testing in babies. Sutton, G., Lightfoot, G., Contributors: Stevens, J., Booth, R., Brennan, S., Feirn, R., and Meredith, R.

Ness, D. A. (2009). Normative data for neurodiagnostic auditory brainstem response testing (ABR). Louisiana Tech University.

Northern, J. L., & Downs. P. (2002). *Hearing in Children*. <https://books.google.com.my/books?id=1CUFXsBbBgoC&pg=PA293&lpg=PA293&dq=Roeser+RJ+and+Northern+JL.+Screening+for+hearing+loss+and+middle+ear+disorders.+In+Roeser+RJ+and+Downs+MP,+Eds.+Auditory+Disorders+in+School+Children&source=bl&ots=HXF11lgEzh&sig=ACfU>

Ocal, F.C.A., Karacayli, C., Coban, V.K., and Satar, B. (2021). Can Narrow Band Chirp Stimulus Shake the Throne of 500 Hz Tone B, 98-103. [https://doi: 10.7874/jao.2020.00486](https://doi.org/10.7874/jao.2020.00486)

Ormundo, D. S. and Lewis, D. R. (2021). Auditory brainstem response with click and CE-Chirp® Level Specific stimuli in hearing infants. *International Journal of Pediatric Otorhinolaryngology*, 147, 1-6.

Ormundo, D. S., Favero, M. L., and Lewis, D. R. (2024). Audiogram Estimation by Auditory Brainstem Response with NB CE-Chirp LS stimulus in Normal Hearing Infants. *International Archives Otorhinolaryngology*, 28(2), 294-300.

Osterhammel, P. A., Shallop, J. K., and Terkildsené, K. (1985). The effect of sleep on the auditory brainstem response (ABR) and the middle latency response (MLR). *Scandinavian Audiology*, 14(1), 47–50. <https://doi.org/10.3109/01050398509045921>

- Ota, T., Nin, F., Choi, S., Muramatsu, S., Sawamura, S., Ogata, G., Sato, M. P., Doi, K., Doi, K., Tsuji, T., Kawano, S., Reichenbach, T., & Hibino, H. (2020). Characterisation of the static offset in the travelling wave in the cochlear basal turn. *Pflügers Archives European Journal of Physiology*, 472(5), 625–635. <https://doi.org/10.1007/s00424-020-02373-6>
- Paludetti, G., Conti, G., Nardo, W. D., Corso, E. D., Rolesi, R., Picciotti, P.M., and Fetoni, A. R. (2012). Infant Hearing Loss: From diagnosis to therapy official report of XXI conference of Italian Society of Pediatric Otorhinolaryngology. *Acta Otorhinolaryngologica Italica*, 32(6), 347-370.
- Papping et al (2022) Pathak, R. D., and Deshpande, S. S. (2021). Awareness of newborn hearing screening in pediatricians and gynaecologists in Maharashtra, India. *International Journal of Otorhinolaryngology and Head and Neck Surgery*, 7(6), 938- 945. <https://doi.org/10.18203/issn.2454-5929.ijohns20211940>
- 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 of the American Academy of Audiology*, 9(2), 134–140. <https://doi.org/10.1121/1.414070>
- Parving, A., Elberling, C. and Salomon, G. (1981). Slow cortical responses and the diagnosis of central hearing loss in infants and young children. *Audiology*, 20, 465-479.
- Pathak, R.D. and Deshpande, S. S. (2021). Awareness of newborn hearing screening in pediatricians and gynaecologists in Maharashtra, India. *International Journal of Otorhinolaryngology and Head and Neck Surgery*, 7(6), 938-945. <https://www.ijorl.com/index.php/ijorl/article/view/3003>
- Pathak, R. D., Deshpande, S. S., Patterson, J. V., Michalewski, H. J., Thompson, L. W., Bowman, T. E., and Litzelman, D.K. (1981). Age and Sex Differences in the Human Auditory Brainstem Response. *Journal of Gerontology*, 36(4), 455–462. <https://doi.org/10.1093/geronj/36.4.455>
- Petoe, M. A. and Bradley, A. P., and Wilson, W. J. (2010). On chirp stimuli and neural

- synchrony in the suprathreshold auditory brainstem response. *Journal Acoustical Soc. American*, 128, 235-246.
- Petoe, M. A., Bradley, A. P., and Wilson, W. J. (2007). A system to generate patient-specific stimuli for use with the auditory brainstem response test. *Proceedings of the 29th Annual International Conference of the IEEE Engineering in Medicine and Biology Society*.
- Pimperton, H. and Kennedy, C. R. (2012). The impact of early identification of permanent childhood hearing impairment on speech and language outcomes. *Arch Dis Child*, 97, 648–653. <https://doi:10.1136/archdischild-2011-301501>
- Picton, T. W. and Hillyard, S.A. (1974). Human auditory evoked potentials. Ii. Effects of attention. *Electroencephalogr Clinical Neurophysiology*, 36, 191–199. [https://doi:10.1016/0013-4694\(74\)90156-4](https://doi:10.1016/0013-4694(74)90156-4)
- Pinto, F. R., and Matas, C. G. (2007). A comparison between hearing and tone burst electrophysiological thresholds. *Brazilian Journal of Otorhinolaryngology*, 73(4), 513–522. [https://doi.org/10.1016/S1808-8694\(15\)30103-8](https://doi.org/10.1016/S1808-8694(15)30103-8)
- Polonenko, M. J., and Maddox, R. K. (2019). The Parallel Auditory Brainstem Response. *Trends in Hearing*, 23. <https://doi.org/10.1177/2331216519871395>
- Ponton, C. W., Moore, J. K., and Eggermont, J. J. (1996). Auditory brain stem response generation by parallel pathways: differential maturation of axonal conduction time and synaptic transmission. *Ear and Hearing*, 17, 402-410. <https://doi.org/10.1097/00003446-199610000-00006>
- Poonual, W., Navacharoen, N., Kangsanarak, J., Namwongprom, S., (2017). Outcome of Early Identification and Intervention on Infants with Hearing Loss Under Universal Hearing Screening Program. *Journal Medical Association Thailand*, 100(2), 197-206.
- Pushpalatha, Z. V., and Konadath, S. (2016). Auditory Brainstem Responses for Click and CE-Chirp Stimuli in Individuals with and without Occupational Noise Exposure. *Noise Health*, 18(84), 260–265. <https://doi.org/10.4103/1463-1741.192477>

- Rasetshwane, D. M., Argenyi, M., Neely, S. T., Kopun, J. G., and Gorga, M. P. (2013). Latency of tone-burst-evoked auditory brain stem responses and otoacoustic emissions: level, frequency, and rise-time effects. *The Journal of the Acoustical Society of America*, 133(5), 2803-2817. <https://doi.org/10.1121/1.4798666>
- Reichmuth, C., Mulsow, J., Finneran, J. J., Houser, D. S., and Supin, A. Y. (2007). Measurement and Response Characteristics of Auditory Brainstem Responses in Pinnipeds. *Aquatic Mammals*, 33(1), 132-150, <https://doi.org/10.1578/am.33.1.2007.132>
- Ribeiro, F. M. and Carvalho, R. M. Tone evoked ABR in normal hearing neonates. *International Journal Audiology*, 47, 21–29.
- Rissman, B. (2006). The road to diagnosis and post-school life. *Medical and Educational Perspectives on Nonverbal Learning Disability in Children and Young Adults*, 20.
- Roncagliolo, M., Benítez, J., and Eguibar, J. R. (2000). Progressive Deterioration of Central Components of Auditory Brainstem Responses during Postnatal Development of the Myelin Mutant taiep Rat. *Audiol Neurootology*, 5, 267–275.
- Rodrigues, G. R. I., and Lewis, D. R. (2012). Comparison of Click and CE-Chirp Stimuli on Brainstem Auditory Evoked Potential Recording, *Rev. Soc. Bras. Fonoaudiol.* 17(4), 412–416.
- Rodrigues, G. R. I., Ramos, N., and Lewis, D. R. (2013). Comparing auditory brainstem responses (ABRs) to tone burst and narrow band CE-chirp® in young infants. *International Journal of Pediatric Otorhinolaryngology*, 77(9), 1555–1560. <https://doi.org/10.1016/j.ijporl.2013.07.003>
- Rohfls, A- K., Wiesner, T., Drews, H., Müller, F., Breitfuß, A., Schiller, R., and Hess, M. (2010). Interdisciplinary approach to design, performance, and quality management in a multicenter newborn hearing screening project. *European Journal of Pediatrics*, 169, 1453–1463. <https://doi.org/10.1007/s00431-010-1229-0>
- Rosenhamer et al (1980) Rosenhammer. H. 1981. The auditory evoked brainstem response (ABR) in cochlear hearing loss. *Scandinavian Audiology*, 13, 83-93.

- Rouillon, I., Parodi, M., Denoyelle, F., and Loundon, N. (2016). How to perform ABR in young children. *Otorhinolaryngology Head Neck Diseases*, 133(6), 431-435. <https://doi.org/10.1016/j.anorl.2016.05.004>
- Rowe III, M. J. (1978). Normal variability of the brain-stem auditory evoked response in young and old adult subjects. *Electroencephalography and Clinical Neurophysiology*, 44(4), 459–470. [https://doi.org/10.1016/0013-4694\(78\)90030-5](https://doi.org/10.1016/0013-4694(78)90030-5)
- Ruth, R. A., Hildebrand, D. L., and Cantrell, R. W. (1982). A Study of Methods Used to Enhance Wave I in the Auditory Brain Stem Response. *Otolaryngol Head Neck Surgery*, 90(5), 635-640.
- Roger, A., Hildebrand, D. L., and Cantrell, R. W. (1982). Annual Meeting of the American Academy of Otolaryngology—Head and Neck Surgery, 9(5). <https://doi.org/10.1177/019459988209000524>
- Sabo, D. L., Durrant, J. D., Curtin, H. B., Robert, J., and Rood, S. (1992). Correlations of Neuroanatomical Measures to Auditory Brain Stem Response Latencies. *Ear and Hearing*, 13(4), 213-222.
- Salamy, A. and McKean, C. M. (1975). Postnatal Development of Human Brainstem Potentials During the First Year Of Life Brain-Behavior. *Electroencephalography and Clinical Neurophysiology*, 40, 418—426.
- Sand, T. (1991). Clinical correlates of brain-stem auditory evoked potential variables in multiple sclerosis. Relation to click polarity. *Electroencephalography and Clinical Neurophysiology/Evoked Potentials Section*, 80(4), 292-297. [https://doi.org/10.1016/0168-5597\(91\)90112-B](https://doi.org/10.1016/0168-5597(91)90112-B).
- Sasmal, A. and Grosh, K. (2019). Unified cochlear model for low- and high-frequency mammalian hearing. *Proceedings of National Academy of Sciences of the United States of America*, 116 (28), 13983-13988. <https://doi.org/10.1073/pnas.190069511>
- Schwartz, D. M., Morris, M. D., Spydell, J. D., Brink, C. T., Grim, M. A., Schwartz, J. A. (1990). Influence of click polarity on the brain-stem auditory evoked response (BAER) revisited, *Electroencephalography and Clinical Neurophysiology/Evoked*

Potentials Section, 77(6), 445-457, [https://doi.org/10.1016/0168-5597\(90\)90005-X](https://doi.org/10.1016/0168-5597(90)90005-X).

Severn, M. S., Searchfield, G. D., & Huggard, P. (2012). Occupational stress amongst audiologists: Compassion satisfaction, compassion fatigue, and burnout. *International Journal of Audiology*, 51(1), 3–9. <https://doi.org/10.3109/14992027.2011.602366>

Sharma, M., Bist, S. S., & Kumar, S. (2016). Age-Related Maturation of Wave V Latency of Auditory Brainstem Response in Children. *Journal of Audiology and Otology*, 20(2), 97–101. <https://doi.org/10.7874/jao.2016.20.2.97>

Sinclair, J. L., Fischl, M. J., Alexandrova, O., Heb, M., Grothe, B., Leibold, C., Kopp-Scheinflug, C. (2017). Sound-evoked activity influences myelination of brainstem axons in the trapezoid body. *Journal of Neuroscience*. 37(34), 8239-8255. <https://doi.org/10.1523/jneurosci.3728-16.2017>

Sininger YS. Filtering and spectral characteristics of averaged auditory brain-stem response and background noise in infants. *J Acoust Soc Am*, 98(04), 2048–2055.

Sininger, Y. S., Abdala, C., Cone-Wesson, B. (1997). Auditory Threshold Sensitivity of Neonate as Measured by the Auditory Brainstem Response, *Hear. Res.* 104, 27–38.

Sininger, Y. S. (2016). Technology Advances to Meet the Needs of Pediatric Electrophysiologic Assessments: The Use of CE-Chirp Stimuli for Pediatric Electrophysiology. *A Sound Foundation Through Early Amplification CE-Chirp® stimuli for pediatric electrophysiology.*

Sininger, Y. S., Cone-Wesson, B., Folsom, R. C., Gorga, M. P., Vohr, B. R., Widen, J. E., Ekelid, M., and Norton, S. J. (2000). Identification of neonatal hearing impairment: auditory brain stem responses in the perinatal period. *Ear & Hearing*, 21, 383-399. <https://doi.org/10.1097/00003446-200010000-00006>

Skoe, E., Krizman, J., Anderson, S., and Kraus, N. (2015). Stability and Plasticity of Auditory Brainstem Function Across the Lifespan. *Cerebral Cortex*, 25(6), 1415–1426. <https://doi.org/10.1093/cercor/bht311>

- Sleifer, P., da Costa, S. S., Coser, P.L., Goldani, M. Z., Dornelles, C., Weiss, K. (2007). Auditory brainstem response in premature and full-term children. *Journal of Pediatric Otorhinolaryngology*, 71, 1449-1456. <http://www.elsevier.com/locate/ijporl>
- Sloan, T. B. (2006). *Electrophysiological Monitoring. Foundations of Anesthesia, Basic Sciences for Clinical Practice*. Elsevier Health Sciences.
- Sohmer, H. and Feinmesser, M. (1967). Cochlear action potentials recorded from the external ear in man. *Annals of Otology, Rhinology and Laryngology*, 76(2), 427-435. <https://doi.org/10.1177/000348946707600211>
- Speidel, D. P. (2016). *The Level Specific CE-Chirp* ©. 2015, 1–5.
- Spitzer, E., White-Schwoch, T., Carr, K. W., Skoe, E., and Kraus, N. (2015). Continued maturation of the click-evoked auditory brainstem response in preschoolers. *J Am Acad Audiol*. 26(1), 30-35. <https://doi:10.3766/jaaa.26.1.4>.
- Spivak, L. G. (1993). Spectral composition of infant auditory brainstem responses: implications for filtering, *Audiology*, 32, 185–194.
- Stapells, D. R. (2000). Frequency-specific evoked potential audiometry in infants. In R. C. Seewald (Ed.), *A Sound Foundation Through Early Amplification*, 13 – 22.
- Stapells, D. R., and Oates, P. 1997. Estimation of the pure tone audiogram by the auditory brainstem response: A review. *Audiology and Neurotology* 2, 257–280.
- Starr, A. and Achor L. J. (1975). Auditory Brain Stem Responses in Neurological Disease. *Arch Neurology*, 32, 761-768.
- Starr, A. (1976). Auditory brain-stem responses in evaluating brain-death. *Brain*, 99, 543-554.
- Starr, A., & Squires, K. (1982). Distribution Of Auditory Brainstem Potentials Over the Scalp and Nasopharynx in Humans. *Annals of the New York Academy of Sciences*, 388, 427–442. <https://doi.org/10.1111/j.1749-6632.1982.tb50807.x>
- Stipdonk, L. W., Weisglas-Kuperus, N., Franken, M. C. J., Nasserinejad, K., Dudink, J.,

- and Goedegebure, A. (2016). Auditory brainstem maturation in normal-hearing infants born preterm: a meta-analysis. *Developmental Medicine and Child Neurology*, 58(10), 1009-1015. <https://doi.org/10.1111/dmcn.13151>
- Stockard, J. E., Stockard, J. J., and Westmoreland, B., and Corfits, J. (1979). Brainstem auditory-evoked responses; normal variation as a function of stimulus and subject characteristics. *Archives Neurology*, 36, 823-831.
- Stockard, J. E., and Curran, J. S. (1990). Transient Elevation of Threshold of the Neonatal Auditory Brain Stem Response. *Ear and Hearing*, 11(1), 21–28. <https://doi.org/10.1097/00003446-199002000-00006>
- Stuart, A., and Yang, E. Y. (1994). Effect of high-pass filtering on the neonatal auditory brainstem response to air- and bone-conducted clicks, *J. Speech Lang. Hear. Res.* 37, 475–479.
- Suleman, S. (2021). Auditory brainstem response elicited by CE - Chirps and an investigation of their time-frequency properties. thesis for the degree of Doctorate of Clinical Practice.
- Talaat, H.S., Hammad, A., and El Abedein, A.M.Z. (2020). Hearing Threshold Evaluation in Children Using Narrow Band Chirp Auditory Brainstem Response and Tone Burst Auditory Brainstem Response. *International Journal of Otolaryngology and Head & Neck Surgery*, 9, 30-37. <https://doi.org/10.4236/ijohns.2020.91005>
- Tafti, F. M., Gharib, K., and Teimuri, H. (2007). Study of age effect on brainstem auditory evoked potential waveforms. *Journal Medical Science*, 7(8), 1362-1365.
- Taylor, D. J., and Mencher, G. T. (1972). Neonate Response: The Effect of Infant State and Auditory Stimuli. *Archives of Otolaryngology*, 95(2), 120–124. <https://doi.org/10.1001/archotol.1972.00770080208006>
- Thodi, C., and Katbamna, B. (1993). Binaural Interaction in the Auditory Brainstem Response: Multichannel Recordings. *Scandinavian Audiology*, 22(3), 205-208. <http://doi.org/10.3109/01050399309047470>
- Thornton, A. R. D., and Slaven, A. (1993). Auditory brainstem responses recorded at fast

stimulation rates using maximum length sequences. *British Journal of Audiology*, 27(3), 205–210. <https://doi.org/10.3109/03005369309076694>

Thayer, J. F., Ahs, F., Fredrikson, M., Sollers, J. J. 3rd, and Wager, T. D. (2012) A meta-analysis of heart rate variability and neuroimaging studies: implications for heart rate variability as a marker of stress and health. *Neurosci Biobehav Rev* 36, 747–756.

Trott, S., Cline, T., Weihing, J., Beshear, D., Bush, M., Shinn, J. (2019). Hormones and hearing: central auditory processing in women. *Journal American Academy Audiology*, 30, 493–501. [10.3766/jaaa.17123](https://doi.org/10.3766/jaaa.17123)

Trune, D. R., Mitchell, C., and Phillips, D. S. (1988). The relative importance of head size, gender and age on the auditory brainstem response. *Hearing Research*, 32(2–3), 165– 174. [https://doi.org/10.1016/0378-5955\(88\)90088-3](https://doi.org/10.1016/0378-5955(88)90088-3)

UNESCO - United Nations Educational, Scientific and Cultural Organization. International Organizations. Retrieved from the Library of Congress, <https://www.unesco.org/en/sdgs>

Van Dyk, M., Swanepoel, D. W., and Hall III, J. W. (2019). Outcomes with OAE and AABR screening In The first 48 Hours–Implications For Newborn hearing screening in developing Countries. *International Journal of Pediatric Otorhinolaryngology*, 1-24, <http://doi.org/doi:10.1016/j.ijporl.2015.04.021>

Verhulst, S., Jagadeesh, A., Mauermann, M., & Ernst, F. (2016). Individual differences in auditory brainstem response wave characteristics. *Trends in Hearing*, 20, 1-20. <https://doi.org/10.1177/2331216516672186>

Vidler, M., and D. Parker, D. (2004). Auditory Brainstem Response Threshold Estimation: Subjective Threshold Estimation by Experienced Clinicians in a Computer Simulation of the Clinical Test. *International Journal of Audiology*, 43(7), 417– 429. <https://doi:10.1080/14992020400050053>

Wang, X., Xia, Z., and Hu, Y. (2023). Normal reference values of low frequency specific air-conducted auditory brainstem responses among normal hearing children of

- different ages: A retrospective observational study. *International Journal of Pediatric Otorhinolaryngology*, 164. <https://doi.org/10.1016/j.ijporl.2022.111409>.
- Weber, B. A. (1983). Pitfalls in Auditory Brain Stem Response Audiometry. *Ear and Hearing* 4(4), 179-184.
- Weber, B. A. and Roush, P. A. (1993). Application of maximum length sequence analysis to auditory brainstem response testing of premature newborns. *Journal of American Academy Audiology*. 4(3), 157-162.
- Wegner, O., and T. Dau, T. (2002). Frequency specificity of chirp-evoked auditory brain stem responses, *J. Acoust. Soc. Am.* 111, 1318–1329.
- World Health Organization. *World report on hearing*. Geneva: World Health Organization; 2021.
- Wroblewska-Seniuk, K., Greczka, G., Dabrowski, P., Szyfter-Harris, J., & Mazela, J. (2017). Hearing impairment in premature newborns —Analysis based on the national hearing screening database in Poland. *PLoS ONE*, 12(9). <https://doi.org/10.1371/journal.pone.0184359>
- Xu, Z. M., Cheng, W. X., and Yao, Z. H. (2014). Prediction of frequency-specific hearing threshold using chirp auditory brainstem response in infants with hearing losses. *International Journal of Pediatric Otorhinolaryngology*, 78(5), 812-816. <https://doi.org/10.1016/j.ijporl.2014.02.020>
- Yamada, O., Ashikawa, H., Kodera, K., and Yamane, H. (1983). Frequency-selective auditory brainstem response in newborns and infants, *Arch. Otolaryng* 109, 7–82.
- Year 2019 Position statement: principles and guidelines for early hearing detection and intervention programs. *Journal of Early Hearing Detection and Intervention (EHDI)*, 4(2).
- Year 2019 Recommended stimulus reference level for ABR systems (2019). *British Society of Audiology*.
- Year 2021 Report on Neonatal Hearing Screening Statistics in Malaysia. *Malaysia*

Neonatal Hearing Screening Committee.

Yoshinaga-Itano, C., Sedey, A. L., Coulter, D. K., and Mehl, A. L. (1998). Language of early- and later-identified children with hearing loss. *Pediatrics*, 102(5), 1161–1171.

Yoshinaga-Itano, C., and Gravel, J. S. (2001). The Evidence for Universal Newborn Hearing Screening. *American Journal of Audiology*, 10, 62-

64.[https://doi.org/10.1044/1059-0889\(2001/013\)](https://doi.org/10.1044/1059-0889(2001/013))

Yoshinaga-Itano, C., Sedey, A. L., Wiggin, M., & Chung, W. (2017). Early hearing detection and vocabulary of children with hearing loss. *Pediatrics*, 140(2). <https://doi.org/10.1542/peds.2016-2964>

Yoshinaga-Itano, C., Sedey, A. L., Wiggin, M., & Mason, C. A. (2018). Language outcomes improved through early hearing detection and earlier cochlear implantation. *Otology and Neurotology*, 39(10), 1256–1263. <https://doi.org/10.1097/MAO.0000000000001976>

Young, A., Cornejo, J., and Spinner, A. (2022). Auditory brainstem response. Treasure Island (FL): StatPearls Publishing. Retrieved from <https://www.ncbi.nlm.nih.gov/books/NBK564321>.

Zakaria et al (2022) Zakaria, M. N., Wahab, N. A. A., Nashrah Maamor, N., Jalaei, B., and Dzulkarnain, A. A. A. (2019). Auditory brainstem response (ABR) findings in males and females with comparable head sizes at supra-threshold and threshold levels. *Neurology, Psychiatry and Brain Research*, 32, 4-7, <https://doi.org/10.1016/j.npbr.2019.03.001>.

Zhou, G., Dornan, B., and Hinchion, W. (2012). Clinical experience of auditory brainstem response testing on pediatric patients in the operating room. *International Journal Otolaryngology*.<https://doi.org/10.1155/2012/350437>

Zirn, S., Louza, J., Reiman, V., Wittlinger, N., Hempel, J. M., and Schuster, M. (2014). Comparison between ABR with click and narrow band chirp stimuli in children. *International Journal of Pediatric Otorhinolaryngology*, 78(8), 1352- 1355.

## APPENDIX I

### PARTICIPANT INFORMATION SHEET

I.D. NO.: 

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### PARTICIPANT INFORMATION SHEET

**Title** : **Auditory Brainstem Response to Narrow Band Level Specific CE-Chirp in Infants**  
**Researcher** : **Amnah binti Mohamad Noor Master Student Kulliyah of Allied Health Sciences International Islamic University Malaysia**  
**Supervisor** : **Prof. Dr. Ahmad Aidil Arafat bin Dzulkarnain Dean (KAHS) / Lecturer (Audiology) Kulliyah of Allied Health Sciences International Islamic University Malaysia**

Thank you for your interest to join this study. This information sheet is about a study to explore the new sound stimulus for hearing assessment in infants. Please read all information in this sheet. For further information, please contact the researcher; Amnah binti Mohamad Noor.

#### **Purpose of study**

The current Master works aims to investigate the ABR using NB LS CE-Chirp stimulus among infants. The knowledge is important to better understand the new stimulus and provides reference for clinical practice in Malaysia.

#### **Background of Study**

This study will be divided into two phases. The first phase (Phase 1) is the screening stage. In the screening stage, the preliminary audiological routine tests will be conducted to the infants. The caregiver will have to fill in a pediatric history form. The outer ear, middle ear, and hearing test will be conducted. Participants who failed the screening will be excluded from the study and referred to related professionals for further management. The next stage will be conducted after infants pass the screening stage. The second phase (Phase 2) is the main study which is the Auditory Brainstem Response (ABR) assessment. The

ABR is an assessment for hearing threshold estimation before any intervention given especially among infants under the age of six months. The ABR assessment is will be done using to types of stimuli which are narrow band level specific (NB LS) CE-Chirp and tone burst. All of the assessments will be used are non-invasive procedures. The estimation time for the study session is about 1.5 hours.

Information in this Participant Information Sheet will be focusing on Phase 2 of the study.

### **Eligibility of participation**

For infants subjects, the inclusion criteria are as follows;

1. Healthy newborn
2. Aged 6 months old and below
3. Type A tympanogram
4. “PASS” automated auditory brainstem response (AABR) screening

However, the participation will be excluded if the infant has otological problem, middle ear problem or upper respiratory tract infection (URTI), and high risk factors for hearing loss.

### **Procedures**

Phase 2 of the study consists of 1 stage; hearing assessment. Participants need to undergo this stage to complete the study. Participants who decides to take part will be expected to complete the consent form and return it to the researcher; Amnah binti Mohamad Noor before they can proceed to the Screening stage.

In the ABR hearing assessment stage, the infants just need to be in a relax state and if possible, sleep on the bed or on caretaker’s lap during the recording session to reduce muscle or movement artifact. No sedatives will be used. ABR will be recorded using four electrodes. Before placing the electrode, the subject will be prepared by scrubbing the respective places for electrodes placement using NuPrep Skin Preparation electrode gel. This session will be held at the IIUM Hearing Clinic, SASMEC IIUM, and Audiology unit, ORL Department, Hospital Tengku Ampuan Afzan.

### **Participation in the study**

Your participation is voluntary and based on your own free will. You have the right to withdraw from the study at any time you wish to do so with no adverse effect. At the point when you withdraw from the study, any data and information that you provided by then will be permanently destroyed.

### **Risks and Benefits**

There can be a minimal discomfort during the Auditory Brainstem Response (ABR) examination when removal of electrodes from the skin. However, the examination will be conducted by a trained audiologists whom will ensure the safety of the procedure. The benefit of participating in this study is that the information gathered from this study will be useful in universal newborn hearing screening (UNHS) program and hearing status information of the participants itself.

### **Confidentiality and Anonymity**

Your data will be anonymized and treated confidentially. Hard copies of the consent forms and participant response sheets will be stored separately in locked filing cabinets in the department's office, while the soft copies will be saved in a password-protected computer. Collected data will be analysed and used in the production and presentation of the thesis. Moreover, a soft copy of the anonymised will be identified with numbering as master list and the data may be preserved and where appropriate used as teaching materials.

### **Inquiries**

Any inquiries, concerns, or reports regarding your rights as a research subject, please contact;

**Researcher:**

Amnah binti Mohamad Noor

[annahmn@yahoo.com](mailto:annahmn@yahoo.com)

010-2319427

**Supervisor:**

Prof. Dr. Ahmad Aidil Arafat bin Dzulkarnain

[ahmadaidil@iium.edu.my](mailto:ahmadaidil@iium.edu.my)

09-5706400 Ext: 5402

## APPENDIX II

### MAKLUMAT KAJIAN

I.D. NO.:					
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### MAKLUMAT KAJIAN

- Tajuk** : **Tindak Balas Batang Otak Auditori kepada Tahap Spesifik Jalur Picik CE-Ciapan pada Bayi**
- Penyelidik** : **Amnah binti Mohamad Noor Pelajar Ijazah Sarjana Kulliyah Sains Kesihatan Bersekutu Universiti Islam Antarabangsa Malaysia**
- Penyelia** : **Prof. Dr. Ahmad Aidil Arafat bin Dzulkarnain Dekan (KSKB) / Pensyarah (Audiologi) Kulliyah Sains Kesihatan Bersekutu Universiti Islam Antarabangsa Malaysia**

Terima kasih kerana berminat untuk menyertai kajian ini. Lembaran ini bertujuan untuk menerangkan mengenai kajian berkenaan tajuk di atas. Untuk maklumat lebih lanjut, sila hubungi penyelidik; Amnah binti Mohamad Noor.

#### **Tujuan Kajian**

Kajian ini bertujuan untuk memperoleh pengetahuan mengenai ujian pendengaran bayi menggunakan bunyi stimuli baharu. Ilmu pengetahuan ini penting untuk memahami fenomena ini dengan lebih baik dan memberikan rujukan untuk amalan klinikal di Malaysia.

#### **Latar Belakang Kajian**

Kajian ini akan dibahagikan kepada dua fasa. Fasa 1 melibatkan fasa saringan pendengaran. Fasa saringan ini bertujuan menyaring bayi berpendengaran normal sahaja untuk keperingkat seterusnya. Fasa 2 ialah fasa kajian utama iaitu ujian pendengaran bayi. Kesemua ujian dan prosedur yang akan dijalankan terhadap bayi-bayi adalah bukan invasif. Jangka masa prosedur kajian dijangka selama 1.5 jam. Maklumat kajian ini berfokus kepada Fasa 2.

## **Kriteria Penyertaan**

Kriteria penyertaan bagi bayi baru lahir adalah seperti berikut.

1. Bayi sihat
2. Berusia 6 bulan dan ke bawah
3. Timpanogram jenis A
4. “LULUS” ujian saringan pendengaran bayi

Bayi yang telah didiagnos dengan masalah telinga luar, telinga Tengah atau jangkitan pada telinga, hidung, dan tekak, dan bayi yang berisiko untuk mengalami masalah pendengaran.

## **Prosedur**

### **Penyertaan dalam Kajian**

Penyertaan anda adalah sukarela dan berdasarkan kehendak bebas anda sendiri. Anda mempunyai hak untuk menarik diri dari kajian ini pada bila-bila masa anda mahu melakukannya tanpa apa-apa kesan buruk. Pada saat anda menarik diri dari kajian, data dan maklumat yang anda berikan pada masa itu akan dimusnahkan secara kekal.

### **Risiko dan Manfaat Kajian**

Mungkin terdapat sedikit ketidakselesaan semasa ujian pendengaran bayi di mana Ketika pengeluaran wayar perakam dari kulit bayi. Walaubagaimanapun, pemeriksaan akan dilakukan oleh audiologis terlatih yang akan memastikan keselamatan prosedur ini. Maklumat yang dikumpulkan dari kajian ini akan berguna dalam mendiagnos tahap pendengaran bayi lebih cepat dan spesifik.

### **Kerahsiaan dan Anonimiti**

Data anda akan disimpan tanpa nama dan dijaga kerahsiaannya. Salinan boring persetujuan dan kertas maklumbalas peserta akan disimpan secara berasingan di cabinet pemfailan yang terkunci di pejabat, sementara Salinan cetak akan disimpan dalam komputer yang dilindungi kata laluan. Data yang dikumpulkan akan dilabel dengan nombor sahaja pada senarai utama. Data ini akan dianalisis dan digunakan dalam penghasilan dan pembentangan tesis. Salinan lembut data tanpa nama mungkin akan disimpan lama dan

sekiranya esuai, akan digunakan sebagai bahan pengajaran dengan mengambilkira aspek kerahsiaan.

### **Pertanyaan**

Sebarang pertanyaan, kebimbangan, atau laporan mengenai hak anda sebagai subjek penyelidikan, sila hubungi;

<b>Penyelidik:</b> Amnah binti Mohamad Noor <a href="mailto:amnahmn@yahoo.com">amnahmn@yahoo.com</a> 010-2319427	<b>Penyelia:</b> Prof. Dr. Ahmad Aidil Arafat bin Dzulkarnain <a href="mailto:ahmadaidil@iium.edu.my">ahmadaidil@iium.edu.my</a> 09-5706400 Ext: 5402
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## APPENDIX III

### PARTICIPANT CONSENT FORM

I.D. NO.: 

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### PARTICIPANT CONSENT FORM

**Title : Auditory Brainstem Response to Narrow Band Level Specific CE-Chirp in Infants**  
**Researcher : Amnah binti Mohamad Noor Master Student Kulliyyah of Allied Health Sciences International Islamic University Malaysia**  
**Supervisor : Prof. Dr. Ahmad Aidil Arafat bin Dzulkarnain Dean (KAHS) / Lecturer (Audiology) Kulliyyah of Allied Health Sciences International Islamic University Malaysia**

If you understand the content described in the Participant Research Information Sheet and agree to participate in this research, please sign in the space provided below.

1. I have read and been explained on all the information in the Participant Information Sheet and Participant Consent Form including any information regarding the risks involved in the study.
2. I have been given sufficient time to consider the information and understand the researcher will have the right to answer my queries only before or after the study session.
3. I give permission for my child to take part in the above research project at the Hearing and Speech Clinic, International Islamic University Malaysia, Kuantan Pahang
4. I understand that my participation and that of my child's are voluntary and that I am free to withdraw my consent at any time without giving a reason.
5. I give permission for the video and/or audio recordings collected for this study to be stored, securely and confidentially, for longer than the duration of the study.

6. I give permission for video and/or audio recordings of my child and myself to be used for teaching purposes.
7. I give permission for video recordings and/or audio recordings of my child and myself to be included in scientific presentations at conferences and meetings with other academics and professionals working in related area.
8. I understand that the video recordings and written information about my child and me will be given a code to keep us anonymous and our names will not be disclosed.

Participant's Name:	Participant's MyKid No:
Signature:	Date:
Parent's/Caregiver's Name:	Parent's /Caregiver's MyKad No:
Signature:	Date:
Researcher's Name:	
Signature:	Date:

## APPENDIX IV

### BORANG KEIZINAN PESERTA

I.D. NO.:

### BORANG KEIZINAN PESERTA

**Tajuk :** Tindak Balas Batang Otak Auditori kepada Tahap Spesifik Jalur Picik CE- Ciapan pada Bayi

**Penyelidik :** Amnah binti Mohamad Noor Pelajar Ijazah Sarjana  
Kulliyah Sains Kesihatan Bersekutu Universiti Islam Antarabangsa Malaysia

**Penyelia :** Prof. Dr. Ahmad Aidil Arafat bin Dzulkarnain Dekan (KSKB) /  
Pensyarah (Audiologi)  
Kulliyah Sains Kesihatan Bersekutu Universiti Islam Antarabangsa Malaysia

Sekiranya anda memahami kandungan yang dijelaskan dalam lembaran Maklumat Kajian dan bersetuju untuk mengambil bahagian dalam penyelidikan ini, sila masuk ke ruangan yang disediakan di bawah.

1. Saya telah membaca serta diberikan penjelasan mengenai semua maklumat dalam Lembaran Maklumat Kajian dan Borang Keizinan Peserta. Ini termasuk sebarang maklumat mengenai risiko yang terlibat dalam kajian ini.
2. Saya telah diberikan masa yang secukupnya untuk mempertimbangkan maklumat tersebut, dibenarkan untuk bertanya soalan sebelum dan selepas kajian, dan memahami penyelidik berhak untuk menjawab hanya sebelum atau selepas kajian dijalankan.
3. Saya membenarkan anak saya untuk mengambil bahagian dalam projek penyelidikan di atas yang bertempat di Klinik Pendengaran dan Pertuturan, Universiti Islam Antarabangsa Malaysia, Kuantan, Pahang.
4. Saya faham bahawa penyertaan anak saya adalah sukarela dan bahawa saya bebas menarik balik kebenaran saya pada bila-bila masa tanpa perlu memberikan alasan.
5. Saya memberi kebenaran agar rakaman video dan / atau audio yang dikumpulkan untuk kajian ini disimpan secara selamat dan rahsia lebih lama daripada tempoh kajian ini.

6. Saya memberi kebenaran untuk rakaman video dan / atau audio anak saya dan saya digunakan untuk tujuan pengajaran dan pembelajaran.
7. Saya memberi kebenaran agar rakaman video dan / atau rakaman audio anak saya dan saya disertakan dalam persembahan ilmiah di persidangan saintifik dan perjumpaan dengan ahli akademik dan profesional lain yang bekerja di bidang berkaitan.
8. Saya faham bahawa rakaman video dan maklumat bertulis mengenai anak saya dan saya akan diberi kod untuk memastikan kami tidak dikenali dan nama kami tidak akan didedahkan.

Nama Peserta :	Nombor MyKid Peserta:
Tandatangan:	Tarikh:
Nama Iubapa/Penjaga:	Nombor MyKad Iubapa/Penjaga:
Tandatangan:	Tarikh:
Nama Penyelidik:	
Tandatangan:	Tarikh:

## APPENDIX V

### DEMOGRAPHIC DATA FORM

I.D. NO.:

Version: 1.0

Date: 14<sup>th</sup> March 2023

#### DEMOGRAPHIC DATA FROM

ID No.: \_\_\_\_\_

Gender: MALE/ FEMALE

Date of Birth: \_\_\_\_\_

Race: \_\_\_\_\_

<b>ANTENATAL/ PRENATAL HISTORY</b>			
Gestational age	_____ weeks		
Mode of birth delivery	Normal (SVD): <input type="checkbox"/>	C-Section Operation: <input type="checkbox"/>	
	Vacuum: <input type="checkbox"/>	Forceps: <input type="checkbox"/>	
Prenatal/ Antenatal medical history	Yes No <input type="checkbox"/>	If Yes, What _____	
	<input type="checkbox"/>		
Consanguinity	Yes No <input type="checkbox"/>	If Yes, What _____	
	<input type="checkbox"/>		
Family history of hearing loss	Yes <input type="checkbox"/>	If Yes, Who _____	
	No <input type="checkbox"/>		

**POSTNATAL HISTORY**

APGAR scores dan birth weight	APGAR scores: _____ Birth weight: _____ kg		
Medical illnesses (Please CIRCLE one: Yes or No)	i)	Ear pain	Yes / No
	ii)	Ear discharge (watery/pus)	Yes / No
	iii)	History of ear operation	Yes / No
	iv)	Meningitis	Yes / No
	v)	Epilepsy or seizure	Yes / No
	vi)	Neonatal Jaundice	Yes / No
	vii)	Head/ Neck injury	Yes / No
	viii)	Physical and nerves impairment	Yes / No
	ix)	Others	
	Please stated here _____		
Syndrome	Yes	<input type="checkbox"/>	If Yes, What _____
	No	<input type="checkbox"/>	
Hearing screening results	i)	Right ear:	<input type="checkbox"/> Pass <input type="checkbox"/> Pass <input type="checkbox"/> Refer <input type="checkbox"/> Refer
	ii)	Left ear:	<input type="checkbox"/> <input type="checkbox"/>

## APPENDIX VI

### BORANG DATA DEMOGRAFI

I.D. NO.:

Version: 1.0 Date: 14<sup>th</sup> March 2023

### BORANG DATA DEMOGRAFI

No. Kajian: \_\_\_\_\_ Jantina: L/ P  
 Tarikh lahir: \_\_\_\_\_ Bangsa: \_\_\_\_\_

<b>SEJARAH ANTENATAL/ PRENATAL:</b>			
Tempoh mengandung	_____ minggu		
Mod kelahiran	Normal (SVD):	<input type="text"/>	Pembedahan (C-Section):
	Vakum:	<input type="text"/>	Forsep:
Masalah mengandung/ melahirkan anak	Ya	<input type="text"/>	Sekiranya Ya, Nyatakan _____
	Tidak	<input type="text"/>	
Anda dan suami mempunyai hubungan persaudaraan	Ya	<input type="text"/>	Sekiranya Ya, Nyatakan _____
	Tidak	<input type="text"/>	
Ahli keluarga bermasalah pendengaran sejak lahir	Ya	<input type="text"/>	Sekiranya Ya, Nyatakan siapa _____
	Tidak	<input type="text"/>	

SEJARAH POSTNATAL						
Skor APGAR dan berat semasa lahir	Skop APGAR: _____		Berat: _____ kg			
Masalah kesihatan lain (Silax bulatkan salah satu: Ya atau Tidak)	x)	Sakit telinga	Ya / Tidak			
	xi)	Keluar cecair dari telinga	Ya / Tidak			
	xii)	Pembedahan telinga	Ya / Tidak			
	xiii)	Jangkitankuman pada otak	Ya / Tidak			
	xiv)	Sawan	Ya / Tidak			
	xv)	Demam kuning / jaundis	Ya / Tidak			
	xvi)	Kecederaan di kepalaatauleher	Ya / Tidak			
	xvii)	Perkembanganfizikal&saraf	Ya / Tidak			
	xviii)	Lain-lain	Ya / Tidak			
	Nyatakan .....					
Sindrom	Ya	<input type="checkbox"/>	Sekiranya Ya, Nyatakan			
	Tidak	<input type="checkbox"/>	_____			
Keputusan ujian saringan pendengaran	iii)	Telinga kanan:	<input type="checkbox"/>	Lulus	<input type="checkbox"/>	Gagal
	iv)	Telinga kiri:	<input type="checkbox"/>	Lulus	<input type="checkbox"/>	Gagal

**APPENDIX VII**  
**CASE REPORT FORM**

I.D. NO.:				
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Version: 1.0 Date: 14<sup>th</sup> March 2023



AUDIOLOGY CLINIC



**CASE REPORT FORM**

ID No.: \_\_\_\_\_

Gender: MALE/ FEMALE

Date of Birth: \_\_\_\_\_

Race: \_\_\_\_\_

**PRELIMINARY TESTINGS:**

**OTOSCOPE EXAMINATION:**

Right Ear	
Left Ear	

**TYMPANOMETRY EXAMINATION:**

Right Ear	
Left Ear	

**HEARING SCREENING ASSESSMENT (AABR):**

Right Ear	
Left Ear	

**RESEARCH:**

**HEARING ASSESSMENT (ABR):**

*Stimulus 1: Narrow band level specific (NB LS) CE- Chirp*

	Right ear			Left ear		
<b>Frequencies (Hz)</b>	<b>500</b>	<b>1000</b>	<b>4000</b>	<b>500</b>	<b>1000</b>	<b>4000</b>
<b>decibels (dB)</b>						

*Stimulus 2: Tone burst*

	Right ear			Left ear		
<b>Frequencies (Hz)</b>	<b>500</b>	<b>1000</b>	<b>4000</b>	<b>500</b>	<b>1000</b>	<b>4000</b>
<b>decibels (dB)</b>						

**Summary:**

<b>Right Ear</b>	
<b>Left Ear</b>	

**Audiologist,**

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(PEGAWAI PEMULIHAN PERUBATAN(PENDENGARAN))

**APPENDIX VIII**  
**BORANG LAPORAN PESAKIT**

I.D. NO.: 

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**VERSION: 1.0**

Date: 14<sup>th</sup> March 2023



KEMENTERIAN KESIHATAN  
MALAYSIA

AUDIOLOGY CLINIC

**BORANG LAPORAN PESAKIT**

No. Kajian: \_\_\_\_\_

Jantina: L/ P

Tarikh lahir: \_\_\_\_\_

Bangsa: \_\_\_\_\_

PRA KAJIAN:

**UJIAN OTOSKOPI:**

Telinga kanan	
Telinga kiri	

**UJIAN TIMPANOMETRI:**

Telinga kanan	
Telinga kiri	

**UJIAN SARINGAN PENDENGARAN (AABR):**

Telinga kanan	
Telinga kiri	

**KAJIAN:**

**UJIAN PENDENGARAN BAYI (ABR):**

*Stimuli 1: Narrow band level specific (NB LS) CE- Chirp*

	Telingakanan			Telingakiri		
Frekuensi (Hz)	500	1000	4000	500	1000	4000
desiBel (dB)						

*Stimuli 2: Tone burst*

	Telingakanan			Telingakiri		
Frekuensi (Hz)	500	1000	4000	500	1000	4000
desiBel (dB)						

**Kesimpulan:**

Telinga kanan	
Telinga kiri	

**Audiologis,**

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(PEGAWAI PEMULIHAN PERUBATAN(PENDENGARAN))

# APPENDIX IX

## KPGRC

 <p><b>الجامعة الإسلامية العالمية ماليزيا</b> <b>INTERNATIONAL ISLAMIC UNIVERSITY MALAYSIA</b> بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ Garden of Knowledge and Virtue</p>	<p><b>LEADING THE WAY</b> KHALIFAH - AMANAH - IZQA - RAHMATAN UL ALAMIN</p> <p><b>SUSTAINABILITY INSTITUTION OF THE YEAR</b></p>
<p>Our Ref.: IIUM/310/14/11/2 Date: 28<sup>th</sup> March 2023</p>	
<p>PROF. DR. AHMAD AIDIL ARAFAT DZULKARNAIN Department of Audiology and Speech-Language Pathology (DASLP) Kulliyah of Allied Health Sciences (PG Student: Sr. Amnah binti Mohamad Noor – G2217364)</p>	
<p>السَّلَامُ عَلَيْكُمْ وَرَحْمَةُ اللَّهِ وَبَرَكَاتُهُ</p> <p>Dear Dr.,</p>	
<p><b>ID NUMBER : KAHS 44/23</b> <b>PROJECT TITLE : AUDITORY BRAINSTEM RESPONSE TO NARROW BAND LEVEL SPECIFIC CE-CHIRP IN INFANTS</b></p>	
<p>May this letter reach you in the best of <i>Iman</i> and health by the grace of <i>Allah Subhanahu Wa Ta'ala</i>.</p>	
<p>Please be informed that the study protocol was tabled and discussed in the Kulliyah Postgraduate and Research Committee [KPGRC] Meeting No. 2/2023 on the 27<sup>th</sup> March 2023. After due deliberation, the decisions of the Committee are as follows:</p>	
<p>1. <b>Approved.</b></p>	<input checked="" type="checkbox"/>
2. Approved subject to modifications that do not require resubmission.	<input type="checkbox"/>
3. Approved subject to modifications that require resubmission. [Conditional approval]	<input type="checkbox"/>
4. Resubmission of application form and all relevant materials.	<input type="checkbox"/>
5. Rejected.	<input type="checkbox"/>
<p>Thank you. وَالسَّلَامُ</p>	
<p> ASSOC. PROF. DR. MUHAMMAD BIN IBRAHIM Deputy Dean Kulliyah Postgraduate and Research Committee (KPGRC)</p>	
<p>Copy to : Head of Research, Kulliyah of Allied Health Sciences : KPGRC File</p>	
<p>KULLIYAH OF ALLIED HEALTH SCIENCES (KAHS) International Islamic University Malaysia, Jalan Sultan Haji Ahmad Shah, Bandar Indera Mahkota, 25200 Kuantan, Pahang Darul Makmur (Company No: 101067-P) Tel: +609 571 6400 Fax: +609 571 6776 Website: <a href="http://www.iium.edu.my/kahs">www.iium.edu.my/kahs</a></p>	
	




# APPENDIX X

## IREC

I.D. NO.: 

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الجامعة الإسلامية العالمية ماليزيا  
INTERNATIONAL ISLAMIC UNIVERSITY MALAYSIA  
بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ  
Garden of Knowledge and Virtue

**LEADING THE WAY**  
KHALIFAH · AMANAH · IGHRA' · RAHMATAN UL-ALAMIN

**SUSTAINABILITY INSTITUTION OF THE YEAR**

### RESEARCH MANAGEMENT CENTRE (RMC)

Our Ref. : IIUM/504/14/11/2/ IREC 2023-065  
Date : 17 April 2023

Prof. Dr. Ahmad Aidil Arafat bin Dzulkarnain (Principal Investigator)  
Kulliyah of Allied Health Sciences  
IIUM Kuantan Campus  
25200 Kuantan Pahang

Dear Prof. Dr.,




The IIUM Research Ethics Committee (IREC) has reviewed your study protocol as mentioned below:-

<b>ID NO.</b>	: IREC 2023-065
<b>RESEARCH TITLE</b>	: Auditory Brainstem Response To Narrow Band Level Specific CE-CHIRP In Infants
<b>REGISTRATION DATE</b>	: 28 Mar 2023
<b>CO-INVESTIGATOR</b>	: 1. Asst. Prof. Dr. Saiful Adli bin Jamaluddin 2. Asst. Prof. Dr. Sarah binti Rahmat
<b>STUDENT</b>	: Amnah Binti Mohamad Noor
<b>STUDY SITE</b>	: 1. Audiology Unit, Otorhinolaryngology Department, Sultan Ahmad Shah Medical Centre (SASMEC)IIUM, Jalan Sultan Haji Ahmad Shah, Bandar Indera Mahkota, 25200 Kuantan, Pahang 2. IIUM Hearing and Speech Clinic, Jalan Hospital Campus, 25100 Kuantan, Pahang
<b>SAMPLE SIZE</b>	: 238 ears
<b>ETHICAL EXPIRY DATE</b>	: 16 April 2024


The IIUM Research Ethics Committee (IREC) operates in accordance to the Declaration of Helsinki, International Conference of Harmonization Good Clinical Practice Guidelines (ICH-GCP), Malaysia Good Clinical Practice Guidelines and Council for International Organizations of Medical Sciences (CIOMS) International Ethical Guidelines

The following documents have been received and reviewed to the above study:-


1. Study Proposal/Protocol: Version 1, dated 17 Mar 2023
2. Informed Consent Form (ICF) –
  - i. Information Sheet (English) – Version 1, dated 14 Mar 2023
  - ii. Consent Form (English) - Version 1, dated 14 Mar 2023
  - iii. Information Sheet (Malay) – Version 1, dated 14 Mar 2023
  - iv. Consent Form (Malay) - Version 1, dated 14 Mar 2023
3. Case Report Form - Version 1, dated 14 Mar 2023
4. Approval Letter from Kulliyah of Allied Health Sciences, IIUM
5. Principal Investigator's CV


WINNER  
2020 SUSTAINABILITY  
INSTITUTION OF THE YEAR




GREATER GOOD  
2020 SUSTAINABILITY  
INSTITUTION OF THE YEAR




UNITED NATIONS  
UNIVERSITY




RECIPIENT  
AL-KHAWARIZMI  
EDUCATION AWARD 2021




Premier  
Digital Tech  
University



MOC  
MALAYSIA  
OFFICE OF  
COMMISSIONER  
OF  
MORALITY



Research Management Centre  
International Islamic University Malaysia, Jalan Gombak, 53100 Kuala Lumpur  
Telephone: (+603) 6421 5002 / 5010 | Fax: (+603) 6421 4862  
Email: rescentre@ium.edu.my | Website: https://www.ium.edu.my/centre/rmc



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# APPENDIX XI

## MREC

I.D. NO.: 

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**JAWATANKUASA ETIKA & PENYELIDIKAN PERUBATAN  
(MEDICAL RESEARCH & ETHICS COMMITTEE)  
KEMENTERIAN KESIHATAN MALAYSIA  
MINISTRY OF HEALTH MALAYSIA**  
Kompleks Institut Kesihatan Negara (NIH)  
No.1, Persiaran Setia Murni U13/52,  
Seksyen U13 Setia Alam,  
40170 Shah Alam, Selangor.



Tel.: +(6)03-33628888/ 33628205

Ruj.Kami/ Ref: 23-01821-J12  
Tarikh/ Date : 27-09-2023

**AMNAH BINTI MOHAMAD NOOR  
INTERNATIONAL ISLAMIC UNIVERSITY MALAYSIA (IIUM)- Kuantan Campus**

Dato'/ Dr/ Tuan/ Puan,

**SURAT KELULUSAN ETIKA/ LETTER OF ETHICAL APPROVAL:**

**NMRR ID-23-01821-J12 (IIR)**  
**AUDITORY BRAINSTEM RESPONSE TO NARROW BAND LEVEL SPECIFIC CE-CHIRP IN INFANTS**

Dengan hormatnya perkara di atas adalah dirujuk.

*This letter is made in reference to the matter above.*

2. Bersama dengan surat ini dilampirkan surat kelulusan saintifik dan etika bagi projek ini. Segala rekod dan data subjek adalah SULIT dan hanya digunakan untuk tujuan kajian dan semua isu serta prosedur mengenai *data confidentiality* mesti dipatuhi. Kebenaran daripada Pengarah Hospital / Institusi di mana kajian akan dijalankan mesti diperolehi terlebih dahulu sebelum kajian dijalankan. Dato'/ Tuan/ Puan perlu akur dan mematuhi keputusan tersebut dan undang-undang lain yang berkaitan.

*The Medical Research and Ethics Committee (MREC), Ministry of Health Malaysia (MOH) has provided ethical approval for this study. Please take note that all records and data are to be kept strictly **CONFIDENTIAL** and can only be used for the purpose of this study. All precautions are taken to maintain data confidentiality. Permission from the District Health Officer / Hospital Administrator/ Hospital Director and all relevant heads of departments /units where the study will be carried out must be obtained prior to the study. You are required to follow and comply with their decision and all other relevant regulations.*

3. Penyelidik- penyelidik dan lokasi penyelidikan yang terlibat ialah:

*The investigators and sites involved in this study are:*

**Hospital Tengku Ampuan Afzan, Kuantan**

Amnah Binti Mohamad Noor (Penyelidik Utama/ *Principal Investigator*)  
Wan Mohd Ashrul Bin Wan Mahamad Lokman

**International Islamic University Malaysia (IIUM)- Kuantan Campus**

Amnah Binti Mohamad Noor (Penyelidik Utama/ *Principal Investigator*)  
Ahmad Aidil Arafat Bin Dzulkarnain  
Saiful Adli Bin Jamaluddin  
Sarah Binti Rahmat

**Sultan Ahmad Shah Medical Centre (SAS Medical Centre)**

Amnah Binti Mohamad Noor (Penyelidik Utama/ *Principal Investigator*)

.../4-

Ruj.Kami/ Ref: 23-01821-J12

4. Dokumen- dokumen kajian berikut telah diterima dan disemak dengan merujuk kepada kajian di atas:

*The following study documents have been received and reviewed with reference to the above study:*

**Senarai dokumen yang diterima dan disemak/ List of documents received and reviewed:**

1. Surat iringan kepada JEPP  
*Cover letter to MREC*  
(Versi/ Version 1.2, bertarikh/ dated 05-09-2023)
2. Pengisytiharan Konflik Kepentingan  
*Declaration of Conflict of Interest (COI)*  
(Versi/ Version 5, bertarikh/ dated 05-09-2023)
3. Protokol  
*Protocol*  
(Versi/ Version 1.2, bertarikh/ dated 05-09-2023)
4. Borang persetujuan ibu bapa  
*Parental agreement form*  
Versi Bahasa Inggeris/ *English version* (Versi/ Version 1.2, bertarikh/ dated 05-09-2023)  
Versi Bahasa Melayu/ *Malay version* (Versi/ Version 1.2, bertarikh/ dated 05-09-2023)
5. Borang pengumpulan data  
*Data collection form*  
(Versi/ Version 1.1, bertarikh/ dated 14-07-2023)
6. Borang soal selidik  
*Questionnaire*  
Versi Bahasa Inggeris/ *English version* (Versi/ Version 1.1, bertarikh/ dated 14-07-2023)  
Versi Bahasa Melayu/ *Malay version* (Versi/ Version 1.1, bertarikh/ dated 14-07-2023)
7. Carta Gantt  
*Gantt Chart*  
(Versi/ Version 1.2, bertarikh/ dated 05-09-2023)
8. Borang IA-HOD-IA, *Curriculum Vitae (CV)* dan sijil *Good Clinical Practice (GCP)*  
*IA-HOD-IA form, Curriculum Vitae (CV) and Good Clinical Practice (GCP) certificate of:*
  - Amnah Binti Mohamad Noor
  - Wan Mohd Ashrul Bin Wan Mahamad Lokman
9. *Curriculum Vitae (CV)*  
*Curriculum Vitae (CV) of:*
  - Ahmad Aidil Arafat Bin Dzulkarnain
  - Saiful Adli Bin Jamaluddin
  - Sarah Binti Rahmat

5. Adalah dimaklumkan bahawa kelulusan ini adalah sah sehingga **26-09-2024**. Tuan/ Puan perlu menghantar dokumen-dokumen seperti berikut selepas mendapat kelulusan etika. Borang-borang berkaitan boleh dimuat turun daripada laman web *National Medical Research Registry (NMRR)*.

*Please note that the approval is valid until 26-09-2024. The following are to be reported upon receiving ethical approval. Required forms can be obtained from the National Medical Research Registry (NMRR) website.*

- i. **Continuing Review Form** harus dihantar kepada JEPP selewat-lewatnya dalam tempoh 2 bulan (60 hari) sebelum tamat tempoh kelulusan ini bagi memperbaharui kelulusan etika.

*Continuing Review Form has to be submitted to MREC within 2 months (60 days) prior to the expiry of ethical approval.*

- ii. **Study Final Report (Closure Notification)** harus dihantar kepada JEPP pada penghujung kajian.

*Study Final Report (Closure Notification) has to be submitted to MREC upon study completion.*

- iii. Mendapat kelulusan etika sekiranya terdapat **pindaan ke atas sebarang dokumen kajian/ lokasi kajian/ penyelidik**. Pihak JEPP mempunyai hak untuk menarik balik kelulusan etika sekiranya terdapat perubahan dokumen kajian yang tidak diisytiharkan.

*Ethical approval is required in the case of amendments/ changes to the study documents/ study sites/ study team. MREC reserves the right to withdraw ethical approval if changes to study documents are not completely declared.*

- iv. **Kajian berkenaan intervensi klinikal sahaja:** Laporan mengenai **all Serious Adverse Events (SAEs), Suspected Unexpected Serious Adverse Reaction (SUSARs)** dan **Protocol Deviation/Violation** di lokasi kajian yang diluluskan oleh JEPP jika berkenaan. SAE perlu dilaporkan dalam tempoh 15 hari kalender dari kesedaran kejadian (*awareness of event*) oleh penyelidik. Laporan awal SUSAR perlu dikemukakan seawal mungkin tapi tidak melewati 7 hari calendar dari kesedaran kejadian oleh penyelidik, disusuli dengan laporan lengkap dalam tempoh tambahan 8 hari kalender.

*Applicable for Clinical interventional Studies only: Report occurrences of all Serious Adverse Events (SAEs), Suspected Unexpected Serious Adverse Reaction (SUSARs) and Protocol Deviation/Violation at all MREC approved sites to MREC. SAEs are to be reported within 15 calendar days from awareness of event by investigator. Initial report of SUSARs are to be reported as soon as possible but not later than 7 calendar days from awareness of event by investigator, followed by a complete report within 8 additional calendar days.*

6. Bilangan **subjek/ pesakit/ responden** yang akan terlibat dalam kajian ini di Malaysia adalah seramai **119 orang**.

*There will be 119 subjects/ patients/ respondents involved in this study within Malaysia.*

7. Sila ambil maklum bahawa sebarang urusan surat-menyurat berkaitan dengan penyelidikan ini haruslah dinyatakan nombor rujukan surat ini untuk melicinkan urusan yang berkaitan.

*Please take note that the reference number of this letter must be stated in all future correspondence related to this study to facilitate the administrative processes.*

Ruj.Kami/ Ref. 23-01821-J12

8. Jawatankuasa Etika & Penyelidikan Perubatan, Kementerian Kesihatan Malaysia, beroperasi mengikut *Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use (ICH)*. Mana-mana ahli JEPP yang terlibat dalam kajian/ projek yang dinilai tidak akan mengambil bahagian dalam kelulusan kajian/ projek.

*The Medical Research & Ethics Committee, Ministry of Health Malaysia, operates in accordance to the International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use (ICH). Any member of the MREC who is involved in the study/ project under review will not participate in the approval of the study/ project.*

Lokasi kajian/ *Project Sites:*

**HOSPITAL TENGGU AMPUAN AFZAN, KUANTAN  
INTERNATIONAL ISLAMIC UNIVERSITY MALAYSIA (IIUM) - KUANTAN CAMPUS  
SULTAN AHMAD SHAH MEDICAL CENTRE (SAS MEDICAL CENTRE)**

Keputusan Jawatankuasa Etika & Penyelidikan Perubatan/  
*Decision by Medical Research & Ethics Committee:*

(  ) Lulus/ *Approved*  
(  ) Tidak lulus/ *Disapproved*

Tarikh Kelulusan Etika/ *Date of Ethical Approval:* **27-09-2023**

Sekian terima kasih.  
*Thank you.*

**"MALAYSIA MADANI"**

**"BERKHIDMAT UNTUK NEGARA"**

Saya yang menjalankan amanah,  
*I who carry out the trust,*



.....  
**DR. NURAIN BINTI MOHD NOOR**

Pengerusi/ *Chairperson*

Jawatankuasa Etika & Penyelidikan Perubatan/ *Medical Research & Ethics Committee*  
Kementerian Kesihatan Malaysia/ *Ministry of Health Malaysia*  
(No. MPM/ MMC No: 31576)

# APPENDIX XII

## SASMEC APPROVAL



Ref : IUM/413/013/14/11/1/IIR23-25  
 Date : 21 July 2023

**Prof. Dr. Ahmad Aidil Arafat Bin Dzulkarnain**  
 Department of Audiology and Speech- Language Pathology  
 Kulliyah of Allied Health Sciences  
 International Islamic University Malaysia

Dear Prof. Dr.

### APPROVAL TO CONDUCT RESEARCH AT SULTAN AHMAD SHAH MEDICAL CENTRE @IUM

May this email reached you in the best of health.

The above matter is kindly referred.

We would like to inform you that your student's application to conduct research activities in Sultan Ahmad Shah Medical Centre @IUM has been approved.

The details of the research study as below:

- Name : Amnah Binti Mohamad Noor
- Research Title : Auditory Brainstem Response to Narrow Band Level Specific Ce-Chirp in Infants
- Focus of research :
  1. Department of Ear, Nose & Throat
  2. Department of Obstetrics & ~~Gynaecology~~
- Duration of research : 28 July 2023 until 28 July 2024

If you have any inquiry, please do not hesitate to contact:

- 1) Sr. Amira Farhana Mohd Maizam 09-591 2581/  
[amiramaizam@ium.edu.my](mailto:amiramaizam@ium.edu.my)
- 2) Sr. Nur Hanis Aseerah Bt Rostam 09-591 2500, ext 1115/  
[hanisaseerah@ium.edu.my](mailto:hanisaseerah@ium.edu.my)

Your kind attention is highly appreciated.



## APPENDIX XIII

### ESTIMATION COST FOR ABR TO TONE BURST PER PATIENT

No.	Steps	Notes	Calculations (RM)
1	<b>Define the unit of service:</b>	ABR to Tone Burst in infants	
2	<b>Determine the number of units of service provided in the define time period:</b>	10000 infants in 2024	
3	<b>Calculate the direct costs:</b>		
a	Audiologist cost:	Salary and benefits of RM 74 400 per year ÷ 37 work weeks per year ÷ 40 work hours per week ÷ 60 minutes per hour = RM 0.87 per minute x 180 minutes required	156.60
b	Assistant nurse cost:	Salary and benefits of RM 21 600 per year ÷ 37 work weeks per year ÷ 40 work hours per week ÷ 60 minutes per hour = RM 0.18 per minute x 15 minutes required	2.70
c	Receptionist cost:	Salary and benefits of RM 72 0000 per year ÷ 37 work weeks per year ÷ 40 work hours per week ÷ 60 minutes per hour = RM 0.30 per minute x 10 minutes required	3.00
c	Disposable resources:	Per practice	30.00
	TOTAL direct costs per unit of service		192.30
4	<b>Calculate the indirect costs:</b>		
	Rent, utilities, etc:	Electricity	20000/year
	Other:		2000.00
	TOTAL:		22000.00
	Basis of allocation:	Percentage of total visits	
	Allocation rate:	20 % of patients visit in 2024 are ABR in infants	$10000 \times 0.2 = 2000$
	Number of units of service provided:	From step 2, above	$10000 \div 2000$
	TOTAL indirect costs per unit of service:		5.00
5	<b>Calculate depreciation and the value of donated goods and services:</b>		
	Initial cost of equipment associated with the service:		100000.00
	Resale value at the end of its useful life:		-60000.00

TOTAL:		40000.00
Estimated years the practice will use the equipment:		
Basis of allocation:	Ratio of total visits	$40000 \div 10$ years=4000
Allocation rate:	20 % of patients visit in 2024 are ABR in infants	$4000 \times 0.20 =$ 800
Number of units of service provided:	From step 2, above	$800 \div 2000$
TOTAL depreciation per unit per service:		0.40
Donated goods:	Calculate depreciation in the same manner as above	
Volunteer time:	Market value x allocation rate ÷ number of units of service	
TOTAL depreciation and donated goods and services per unit per service:		0.40
<b>6 Calculate the unit cost:</b>		
Total from step 3:		192.30
Total from step 4:		5.00
Total from step 5:		0.40
<b>TOTAL cost per unit of service:</b>	<b>RM</b>	<b>197.70</b>

## APPENDIX XIV

### ESTIMATION COST FOR ABR TO NB LS CE-CHIRP PER PATIENT

No.	Steps	Notes	Calculations (RM)
1	<b>Define the unit of service:</b>	ABR to NB LS CE-Chirp in infants	
2	<b>Determine the number of units of service provided in the define time period:</b>	10000 infants in 2024	
3	<b>Calculate the direct costs:</b>		
a	Audiologist cost:	Salary and benefits of RM 74 400 per year ÷ 37 work weeks per year ÷ 40 work hours per week ÷ 60 minutes per hour = RM 0.87 per minute x 60 minutes required	52.20
b	Assistant nurse cost:	Salary and benefits of RM 21 600 per year ÷ 37 work weeks per year ÷ 40 work hours per week ÷ 60 minutes per hour = RM 0.18 per minute x 15 minutes required	2.70
c	Receptionist cost:	Salary and benefits of RM 72 0000 per year ÷ 37 work weeks per year ÷ 40 work hours per week ÷ 60 minutes per hour = RM 0.30 per minute x 10 minutes required	3.00
c	Disposable resources:	Per practice	30.00
	TOTAL direct costs per unit of service		87.90
4	<b>Calculate the indirect costs:</b>		
	Rent, utilities, etc:	Electricity	20000/year
	Other:		2000.00
	TOTAL:		22000.00
	Basis of allocation:	Percentage of total visits	
	Allocation rate:	20 % of patients visit in 2024 are ABR in infants	10000 x 0.2 =

			2000
	Number of units of service provided:	From step 2, above	$10000 \div 2000$
	TOTAL indirect costs per unit of service:		5.00
<b>5</b>	<b>Calculate depreciation and the value of donated goods and services:</b>		
	Initial cost of equipment associated with the service:		100000.00
	Resale value at the end of its useful life:		-60000.00
	TOTAL:		40000.00
	Estimated years the practice will use the equipment:		
	Basis of allocation:	Ratio of total visits	$40000 \div 10$ years=4000
	Allocation rate:	20 % of patients visit in 2024 are ABR in infants	$4000 \times 0.20 =$ 800
	Number of units of service provided:	From step 2, above	$800 \div 2000$
	TOTAL depreciation per unit per service:		0.40
	Donated goods:	Calculate depreciation in the same manner as above	-
	Volunteer time:	Market value x allocation rate $\div$ number of units of service	-
	TOTAL depreciation and donated goods and services per unit per service:		0.40
<b>6</b>	<b>Calculate the unit cost:</b>		

Total from step 3:		87.90
Total from step 4:		5.00
Total from step 5:		0.40
<b>TOTAL cost per unit of service:</b>	<b>RM</b>	<b>93.30</b>



## APPENDIX XV

### RISK INDICATORS ASSOCIATED WITH PERMANENT CONGENITAL, DELAYED-ONSET, OR PROGRESSIVE HEARING LOSS IN CHILDHOOD LOSS ACCORDING TO JCIH (2019)

#### Perinatal Risk Indicators

##### Birth and Family History Section of Risk Assessment Form

1. A history of family members of early progressive or delayed onset, permanent hearing loss in childhood.
2. Neonatal Intensive care of more than five days.
3. Hyperbilirubinemia requiring exchange transfusion.
4. Aminoglycoside administration greater than 5 days duration.
5. Asphyxia and or hypoxic ischemic encephalopathy.
6. Extracorporeal membrane oxygenation (ECMO.)
7. In-utero infections such as herpes, rubella, syphilis, and toxoplasmosis.
8. In-utero infections with cytomegalovirus (CMV)
9. Mother + Zika and infant with laboratory findings of Zika - clinical findings

#### CHILD AND FAMILY HEARING HISTORY AND

##### \* JCIH RISK A SSESSMENT 2

1. Certain birth conditions or findings:
2. Craniofacial anomalies including microtia, atresia, ear dysplasia, white forelock, and microphthalmia.
3. Congenital microcephaly, congenital or acquired hydrocephalus.
4. Temporal bone anomalies
5. Over 400 syndromes have been identified with atypical hearing thresholds for more information refer to Hereditary Hearing Loss ([hereditaryhearingloss.org](http://hereditaryhearingloss.org)).

##### Summary of genes identified to date\*

1. Alport Syndrome
2. Branchio-Oto-Renal Syndrome

3. CHARGE Syndrome
4. Heimler Syndrome
5. Jervell & Lange-Nielsen Syndrome
6. Norrie Disease
7. Pendred Syndrome
8. Perrault Syndrome
9. Stickler Syndrome
10. Treacher Collins Syndrome
11. Usher Syndrome
12. Waardenburg Syndrome

Total nonsyndromic hearing loss associated genes: 154

Autosomal dominant nonsyndromic hearing loss associated genes: 63  
Autosomal recessive nonsyndromic hearing loss associated genes: 87  
Sex-linked nonsyndromic hearing loss associated genes: 7  
Mitochondrial nonsyndromic hearing loss associated genes: 9  
Auditory neuropathy associated genes: 5

i. **Postnatal Risk Factors**

**Child's Postnatal History Section of Risk Assessment Form**

1. Culture-positive infections associated with sensorineural hearing loss (meningitis, encephalitis) including viral infections such as varicella or herpes
2. Events associated with hearing loss
3. Significant head trauma especially basal skull/ temporal bone fracture
4. Chemotherapy
5. Family/caregiver concern