THE CLINICAL APPLICATION OF CORTICAL AUDITORY EVOKED POTENTIAL (CAEP) IN CHILDREN AT MALAYSIA TERTIARY HOSPITAL

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by

NURNAZEHA BINTI ISNAN

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LIST OF SYMBOLS

msec	Miliseconds
μV	Microvolts
P_1	Positive peak 100
N_1	Negative Peak 100
P_2	Positive Peak 200
N_2	Negative Peak 200
dB	Decibel
Hz	Frequency
d	Cohen Effect Size
r	Correlation
p	Significance value
%	Percentage

LIST OF ABBREVIATIONS

ABR	Auditory Evoked Response
AEP	Auditory Evoked Potentials
ASHA	American Speech-Language- Hearing Association
ASSR	Auditory Steady State Response
BSER	Brainstem Evoked Response
CAEP	Cortical Auditory Evoked Potential
CI	Cochlear Implant
FDA	Food and Drug Administration
HA	Hearing Aid
HRPZ II	Hospital Raja Perempuan Zainab II
IPS	Institut Pengajian Siswazah
JEPeM	Jawatankuasa Etika Penyelidikan Manusia USM
MDA	Medical Device Authority
MLR	Middle Latency Response
MREC	Medical Research and Ethic Committee
NIDCD	National Institute of Deafness and Other Communication Disorders
NMRR	National Medical Research Registry
SD	Standard Deviation
SLM	Sound Level Meter
SPSS	Statistical Package for Social Science
USM	Universiti Sains Malaysia
WHO	World Health Organization

LIST OF APPENDICES

APLIKASI KLINIKAL CETUSAN POTENSI AUDITORI KORTEKS (CAEP) DALAM KALANGAN KANAK-KANAK DARI HOSPITAL TERTIARI DI MALAYSIA

ABSTRAK

Kajian ini bertujuan untuk menentukan ujian cetusan potensi auditori korteks (CAEP) sebagai ujian objektif untuk menilai faedah alat bantu pendengaran pada kanak-kanak. Kajian ini dibahagikan kepada tiga fasa. Fasa I adalah mengenai menentukan kebolehpercayaan kajian rentas melalui orang dewasa dan kebolehlaksanaan CAEP apabila menguji kanak-kanak. Sebaliknya, fasa II memfokuskan pada membandingkan keputusan CAEP yang dihasilkan oleh montaj elektrod yang berbeza dan oleh keadaan pendengaran yang berbeza. Korelasi antara hasil CAEP, soal selidik ibu bapa (MAIS dan MUSS), dan tindak balas bantuan dalam kanak-kanak bermasalah pendengaran juga dinilai. Selepas itu, dalam fasa III, keputusan CAEP dibandingkan antara kanak-kanak normal dan kanak-kanak bermasalah pendengaran. Kajian ini merekrut 14 kanak-kanak bermasalah pendengaran dan 22 kanak-kanak normal berumur 4 hingga 12 tahun. CAEP direkodkan pada dua lokasi montaj elektrod (C_Z dan T_3) untuk kedua-dua kumpulan menggunakan empat rangsangan pertuturan, iaitu, /ba/, /m/, /g/, dan /t/. Didapati bahawa keputusan CAEP yang dihasilkan oleh semua rangsangan pertuturan mempunyai kebolehpercayaan yang baik (fasa I). Selain itu, ujian CAEP juga boleh direkodkan dengan mudah pada kanak-kanak normal dan bermasalah pendengaran. Dalam fasa II, keputusan CAEP didapati setanding merentas keadaan pendengaran (kiri, kanan dan binaural) ($p > 0.05$). Walaupun tiada korelasi ditemui antara CAEP dan ambang pendengaran berbantu ($p > 0.05$), beberapa parameter CAEP menunjukkan korelasi yang ketara dengan soal selidik MAIS dan MUSS ($p < 0.05$). Dalam fasa III,

tiada perbezaan ketara dalam amplitud CAEP ditemui antara dua kumpulan untuk kedua-dua montaj elektrod ($p > 0.05$). Untuk perbandingan latensi, kecuali latensi P_1 (C_Z dan T_3) dan N_1 (T_3), majoriti keputusan latensi CAEP didapati setanding antara kedua-dua kumpulan. Kesimpulanya, ujian CAEP sememangnya penilaian yang berguna untuk menentukan fungsi kortikal kanak-kanak bermasalah pendengaran secara objektif.

THE CLINICAL APPLICATION OF CORTICAL AUDITORY EVOKED POTENTIAL (CAEP) IN CHILDREN AT MALAYSIA TERTIARY HOSPITAL

ABSTRACT

This study aim to determine the usefulness of CAEP measurement as an objective tool to assess hearing aid benefits in children. This study was divided into three consecutive phases. Phase I was about determining the test-retest reliability in adults and studying the feasibility of CAEP when testing children. On the other hand, phase II focused on comparing CAEP results elicited by different electrode montages and by different listening conditions. The correlations between CAEP outcomes, parental questionnaires (MAIS and MUSS), and aided responses in hearing-impaired children were also assessed. Subsequently, in phase III, CAEP results were compared between normal children and hearing-impaired children. This study recruited 14 hearing-impaired children and 22 normal children aged 4 to 12 years. The CAEP was recorded at two points of electrode montages (C_Z and T_3) for both groups using four speech stimuli, i.e., /ba/, /m/, /g/, and /t/. It was found that CAEP results elicited by all stimuli had good test-retest reliability (phase I). The CAEP testing conveniently recorded in normal and hearing-impaired children. In phase II, CAEP results were found to be comparable across the listening conditions (left, right and binaural) ($p > 0.05$). While no correlations were found between CAEP and aided responses ($p > 0.05$), some CAEP parameters showed significant correlations with MAIS and MUSS questionnaires ($p < 0.05$). In phase III, no significant differences in CAEP amplitudes were found between the two groups for both electrode montages ($p > 0.05$). For latency comparisons, except for P1 latency (C_Z and T_3) and N1 latency (T_3), the majority of the

CAEP latency results were found to be comparable between the two groups. In conclusion, the CAEP testing is indeed a useful assessment to determine the cortical function of hearing-impaired children objectively.

CHAPTER 1

INTRODUCTION

1.1 Introduction

Chapter 1 outlines the research focus and presents the important issues that have garnered much attention in this research area. It briefly depicts the research background, clarifies the research problem, states the research purpose, points out the research questions, formulates the research aim and objectives to be addressed, identifies the research scope and highlights the research significance. This chapter further presents the research structure in the thesis outline and ends with an overall summary.

1.2 Research background

The prevalence of hearing impairment among children is a worldwide large-scale health concern, affecting millions of individuals globally. Moreover, the World Health Organization (2020) estimated that approximately 34 million children worldwide have disabling hearing with 40 percent of them unpreventable, making up around 5% of the global population of children. However, it is important to note that this prevalence can differ significantly in emerging nations. According to Joint Committee Infants Hearing, 1-6 of 1000 live births are diagnosed with permanent hearing loss (JCIH, 2019) Moreover, Center of Disease Control and Prevention (2020) states that birth defects related to hearing loss are more prevalent compared to eyes, heart, and spinal problems .The awareness has increased in detecting babies with hearing impairment. As mentioned by Berita Harian Online on 3 March 2022, the government is now focusing on increasing the detection rates in Universal Neonatal Hearing Screening up to 95% in Malaysia as the current percentage is less than 70% (Mat Ruzki & Muzamir, 2022) .

The advantage of high detection rates is that almost all congenital hearing impairment in newborns can be identified. Hearing impairment is defined as a decreased ability to hear sounds that ranges from mild to profound levels. Children (including newborns) with hearing impairment can have overwhelming and enduring consequences on their overall development, including speech and language acquisition, educational accomplishment, social interaction, and psychological and physical functioning (Keilmann et al., 2007). The reason for this is that the development of hearing began in the womb as early as 25 weeks of gestation (Dommelen et al., 2020). As such, the hearing screening procedure can be conducted as early as possible after birth as a primary tool in detecting hearing loss in newborns. Even though hearing loss is a permanent disability, it can be diagnosed and treated at a young age. The number of hearing-impaired individuals increases every year with the increase in birth rates. Moreover, *Jabatan Kebajikan Masyarakat* (2022) has reported there are 41,703 disabled registries and 3,572 of them are children (0-14 years old) in Malaysia. However, the figures did not reflect current data on the hearing-impaired population.

The data from the registry is one sign of the weaknesses of the health system in Malaysia due to limited sources, equipment, feasibility, and appropriate approaches in hearing loss detection. The significance of early detection and intervention is crucial for mitigating the adverse effects of hearing impairment, and hearing aids have been widely employed as a primary rehabilitative tool (Vos et al., 2019). However, the precise assessment of the benefit provided by hearing aids in children with hearing impairment remains a complex challenge (Billings et al., 2012).

The traditional methods used to evaluate the effectiveness of hearing aids in children have primarily relied on subjective measures, such as parental reports and clinician observations (Ching & Hill, 2007; Purdy et al., 2004).While these measures provide valuable insights into the functional outcomes of hearing aid use, they often lack objectivity and may not fully capture the subtle improvements or changes in auditory processing. To address this limitation, researchers have turned to objective neurophysiological measures, such as the Cortical Auditory Evoked Potential (CAEP), to assess the auditory processing capabilities of children with hearing impairment.

The CAEP is an electrophysiological response recorded from the scalp that reflects the neural activity in the auditory cortex in response to sound stimuli. It offers a direct measure of auditory processing, independent of the individual's ability to respond behaviorally or provide subjective feedback (Hall, 2007). By analyzing the CAEP waveform, researchers can objectively evaluate the effects of hearing aid use on neural processing, providing valuable insights into the functional benefits and cortical changes associated with auditory stimulation.

The present study aims to investigate the efficacy of CAEP in children population as an objective measure.. By comparing the CAEP responses of children between normal and hearing-impaired children, we can quantify the neural changes induced by hearing aid use and determine the extent to which hearing aids improve auditory processing capabilities in children with hearing impairment. The findings from this study can contribute to a more comprehensive understanding of the benefits of hearing aids and inform evidence-based clinical practices for the management of pediatric hearing impairment.

In this thesis, a comprehensive overview of the prevalence, etiology, and consequences of hearing impairment and management in children with hearing impairment will be disccussed. We then discuss the current approaches to hearing aid evaluation, highlighting. The subsequent chapters present the results, followed by a discussion of the implications and clinical significance of the findings. The limitations of our research and propose directions for future studies to advance the understanding of hearing aid benefits in children with hearing impairment also will be highlighted.

In summary, this study seeks to contribute to the growing body of research on hearing aid effectiveness in children with hearing impairment. By employing the aided CAEP as an objective measure of auditory processing, we hope to provide valuable insights into the functional benefits and neural changes associated with hearing aid use in this population. The development of objective evaluation technique would enhance the accuracy of measuring the benefits of hearing aids, informs evidence-based clinical practices, and ultimately leads to better outcomes and improved well-being for children with hearing loss.

1.3 Problem Statement

There are many subjective audiological test used to evaluate the hearing aids benefits in children such as, behavioural aided responses and speech outcome test. Different from others audiological test, the CAEP test is useful as an objective tool to observe and monitor hearing thresholds in adults (Lightfoot & Kennedy, 2006). More notably, it can be used as an objective method to assess whether amplified speech sounds are detectable in infants and children wearing hearing aids (Golding et al., 2007; A. Sharma et al., 2005).

There are many ways to measure the hearing aid benefits either subjectively or objectively (Amri et al., 2019). Considering its potential, the CAEP testing is not widely used to evaluate the higher central auditory processing in Malaysia. The role of CAEP in assessing the benefits of hearing aids and cochlear implant in infants and toddlers should be explored. Mehta et al. (2017) found that there was a significant reduction in the age of hearing aid fitting in children who underwent the unaided CAEP measurement in the study to determine the impact on patient management of introducing CAEP assessments into the audiological pathway. This population is at a critical period of hearing and speech development at an early age (Chomsky, 1965). In conjunction with the extensive development of Malaysia's Neonatal Hearing Screening Program, the coverage rate is improving in order to identify the population with hearing impairment at the earliest possible age.

The fitting of hearing aids during an early childhood facilitates access to the enriched speech input critical for characterizing auditory development. Still, our capacity to reliably validate sufficient benefits from early amplification in children less than 6 months remains inadequate. The audiological outcome verification continues to emphasize behavioural testing which can be highly variable based on a child's age, cognitive maturity, and attention capability (Wunderlich et al., 2006).

The CAEP results are influenced by brain activities evoked by complex sounds such as speech stimuli (Cone-Wesson & Wunderlich, 2003; Wunderlich & Cone-Wesson, 2001). The types of natural speech sound syllables and the acclimatization of hearing aids may play important aspects in obtaining clearer waveforms in hearing aid users. In this regard, the use of various speech stimuli is advantageous in recording CAEP in hearing-impaired children.

The CAEP responses are dependent on the stimulus parameters and the site of the generators to retrieve clearer waveforms and morphology. In term of speech processing, it is dependent on many factors including the optimum hearing aid functions. In this regard, hearing aid benefits can be measured using subjective and objective responses. Even though some CAEP studies have been conducted in this field, more research is required, particularly among different populations. Hazzaa et al. (2016) found that non-linear frequency compression (NLFC) had an influence on P1 of CAEP in children with hearing aids compared to the control group. Furthermore, children who did not have NLFC had less detectable P1 CAEP. Other studies showed N1 to be the most reproducible peak that was correlated with behavioural aided responses(Ching et al., 2016) Leite et al. (2018) concluded that the transformation in the central auditory pathways can be identified using P1-N1 and P2-N2 amplitude components, and the presence of these components increases after a short period of auditory stimulation or hearing aids usage.

Previous findings emphasize the importance of using the CAEP components to monitor the neuroplasticity of the central auditory nervous system in hearing aid users (Fitzpatrick, 2015). For example, one of the neurophysiological markers, the P1 peak, revealed statistically significant results (Koravand et al., 2012).

Moreover, the performance of amplification in hearing-impaired children at the cortical level requires further research, which is the focus of the proposed study. There are also persisting questions surrounding which specific cortical response features (e.g., latency, amplitude) and their maturation over time may provide optimal indicators of amplification benefit. Furthermore, the relationship between aided CAEP outcomes with gold-standard measures of behavioural hearing performance remains unclear.

Most studies have been restricted by small sample sizes and varied methodologies, which precludes generalizable knowledge regarding normative response trends. There is a pressing need for aided CAEP research that systematically analyses electrode placement, stimulus parameters, and testing conditions to produce evidence-based procedural guidelines tailored to children. A bigger exploration of comparisons with both subjective and objective hearing aid benefits is also critical. In Malaysia, the current practice of using functional measures is called Evaluation of Audiological Responses to Speech (EARS), which has components known as

Meaningful Auditory Integration Scale (MAIS) and Meaningful Use of Speech Scale (MUSS) (both are in Malay language). These scales are among the subjective measurements to validate the benefits of hearing aids in children. Additionally, CAEP characteristics or changes may correspond with emerging skills measured through parental reports in hearing-impaired children.

There is limited evidence regarding the comparison of cortical responses between normal dan hearing-impaired groups. The gold-standard protocol based on CAEP has not been thoroughly characterized in order to obtain appropriate audiological expectations. Besides, substantial knowledge gaps restrict comprehensive implementation towards optimizing clinical hearing aid fitting using the electrophysiological measures.

In summary, significant gaps remain in the optimal application of CAEP testing to improve functional monitoring in hearing aid amplification from early intervention in hearing-impaired pediatric patients. It is essential to conduct research that focuses on clarifying developmental response patterns and audiological relationships in order to improve utilization and maximize the benefits received by children.

1.4 Research Questions

The following are the research questions to be answered in the present study:

i) What is the best and optimum CAEP protocol?

ii) Is it possible to conduct CAEP in children?

iii) Are there any differences in response rate, amplitudes, and latencies in different electrode montages in measuring CAEP in normal children?

iv) Are there any differences in listening conditions in hearing-impaired children between monaural and binaural conditions?

v) Are there any differences in response rate, amplitudes and latencies in different electrode montages in measuring CAEP in hearing-impaired children?

vi) Does CAEP correlate with parental questionnaires (MAIS and MUSS) in hearing-impaired children?

vii) Does CAEP correlate with an aided threshold in hearing-impaired children?

viii) Are there differences in CAEP between normal-hearing children and hearing-impaired children in terms of response rate, amplitudes, and latencies?

1.5 Research aims and objectives

The main aim of the present study was to evaluate the response rates, amplitudes, and latencies in processing speech sounds using the CAEP test in hearing-impaired children who were hearing aid users.

1.5.1 Specific objectives

i) To determine the test-retest reliability of CAEP

ii) To determine the feasibility of CAEP recording among normal and hearing-impaired children

iii) To compare CAEP response rates, amplitudes and latencies (elicited by 4 speech stimuli) between two electrode montages (C_Z versus T_3) among normal-hearing children (within-group comparisons)

iv) To compare CAEP amplitudes and latencies (elicited by /ba/ stimulus) between different listening conditions (left, right and binaural) among normal-hearing children (within-group comparisons)

v) To compare CAEP response rates, amplitudes and latencies (elicited by 4 speech stimuli) between two electrode montages (C_Z versus T_3) among hearing-impaired children (within-group comparisons)

vi) To determine the correlation between aided CAEP amplitudes and latencies (elicited by 4 speech stimuli) with parental questionnaire scores (MAIS and MUSS) among hearing-impaired children (within-group comparisons)

vii) To determine the correlation of CAEP amplitudes and latencies (elicited by 4 speech stimuli) with aided thresholds at 500 Hz,1000 Hz, 2000 Hz and 4000 Hz among hearing-impaired children (within-group comparisons)

viii) To compare cortical auditory evoked potential (CAEP) response rates, amplitudes, and latencies (elicited by 4 speech stimuli) between normal and hearing-impaired groups (within and between-group comparisons)

1.6 Research Scope

The present study mainly focused on measuring CAEP in children by creating speech stimuli using speech samples from native speakers in Malay language. The children population with the age scope from 4 years to 12 years old children would be selected in this study.

1.7 Research Significance

The research outcome may become a preliminary design protocol in developing the CAEP test as a new assessment or intervention for audiology professionals.

1.8 Theoretical framework

The development of hearing aids fitting, verification, and validation protocols includes a variety of methods in order to obtain the ultimate ways. The process needs a logical pathway that will lead to reliable and optimum responses. Here is the importance of frameworks to be chosen to enhance confidence of audiologists by referring to the guidelines.

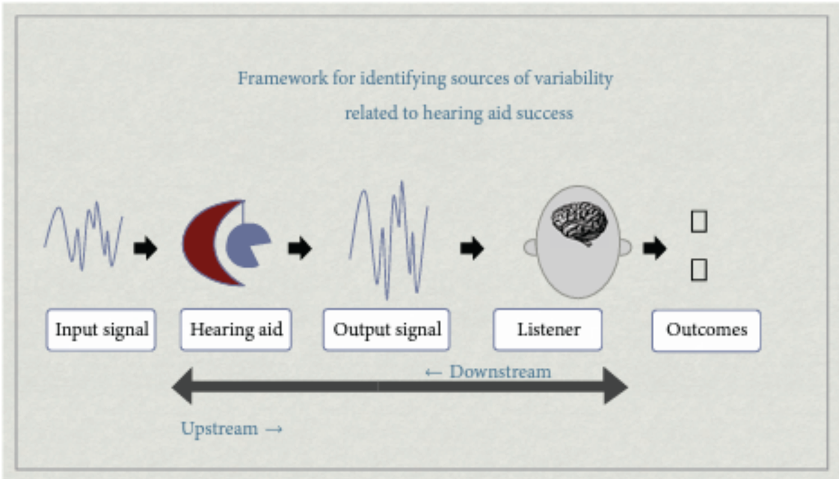

Figure 1.1 Framework for identifying sources of variability related to hearing aid success

Figure 1.1 shows the process of hearing aid success, and to measure hearing aid outcomes, there are two categories of test procedures involved in the process: (i) subjective measures, which require active participation by the patient (e.g., pure-tone threshold estimation, speech testing, and self-report questionnaires), and (ii) objective measures, where behavioural responses are not required (e.g., probe microphone electroacoustics and unaided electrophysiology). The application of electrophysiology is to determine if brain measures can be used as an objective measure to estimate aided thresholds by quantifying hearing aid transduced signals in the brain (Tremblay et al., 2014).

Moreover, the purpose of electrophysiology is to use as a guided device fitting and/or to assess the suprathreshold representation of amplified auditory signals in the brain so that it can estimate perceptual performance and/or the related cognitive resources involved. This expanded use of objective measures is relevant to patients of all ages but is particular to the pediatric population where the use of behavioral tools is limited. As described by Jenstad et al. (2003), behavioural threshold information is not usually available before age 6 months (and often later), speech testing is unavailable, and subjective questionnaires are limited to caregiver observation of behaviours. Thus, there is greater trust on objective procedures to measure the effects of amplification beyond the tympanic membrane in infants and young children. One such measure is the use of auditory evoked potential (Tremblay et al., 2014).

Souza & Tremblay (2006) adapted another framework for the stage of hearing aids toward speech recognition. It has strong theoretical foundations in the field of measuring hearing aids' benefits.

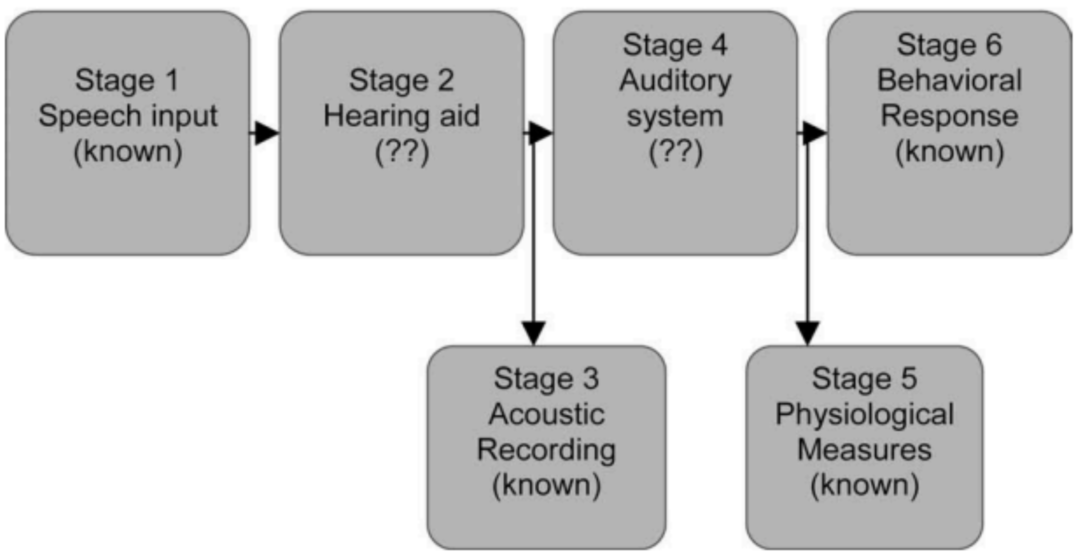

Figure 1.2 Framework of hearing aids to speech recognition in a series of linked stages

Souza & Tremblay (2006) were the first to present a framework approach by illustrating the process among hearing aid users. The contribution of hearing aid to speech recognition is viewed as a series of linked stages (Figure 1.2). The stages are specifically explained in Table 1.1.

Table 1.1 The contribution of hearing aids to speech recognition

Stages	Process
Stage 1	Representation of the acoustic content of the incoming signal
Stage 2	Modification of the signal by the processing parameters of the hearing aid
Stage 3	Interaction between sound at the output of the hearing aid and the listener's ear
Stage 4	The integrity of the peripheral and central auditory system
Stage 5	Coding of available acoustic cues by the listener's auditory system
Stage 6	Correct identification of the speech sound by the listener

1.9 Conceptual Framework

The primary framework by Tremblay et al. (2014) is about variability in hearing aid success. It identifies variability that guides hearing aid success by considering the individual factors that influence HA outcomes. It differentiates physiological and perceptual roles of outcomes in hearing aids success. Another framework by Souza and Tremblay (2006) is hearing aids to speech recognition. It is designed by breaking the process into linked stages to obtain understandable figures from sound input to the speech detection process. The integration of the conceptual framework in Figure 1.3 for the present study has actually combined the idea of the previous framework by introducing aided CAEP as a key element in measuring HA benefits that are specifically designed for children in this study.

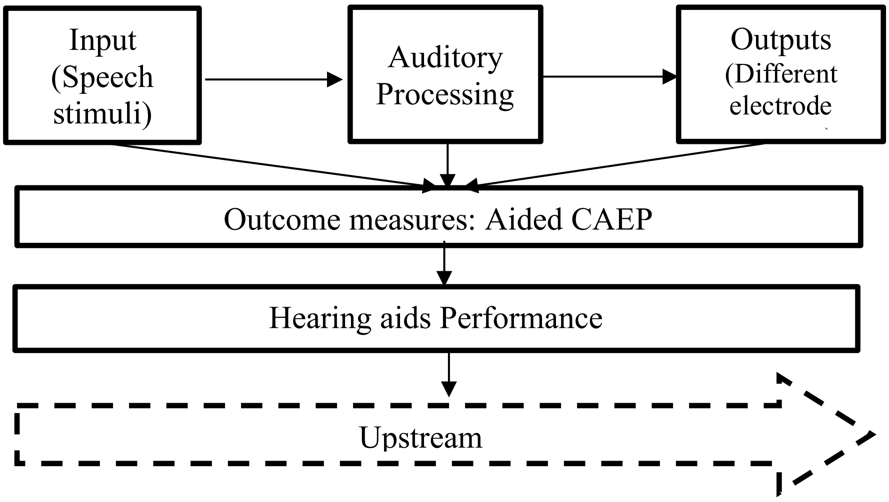

Figure 1.3 The conceptual framework of the present study

1.10 Operational Definitions

Operational terms used in the present study are defined in the following sections.

1.10.1 Hearing Impairment

Hearing impairment or hearing loss is the inability of a person to hear sounds. World Health Organization (2021) defined hearing impairment as "a person who is not able to hear as well as someone with normal hearing (hearing thresholds of 20 dB or better in both ears)". Hearing impairment ranges from mild-moderate-severe and profound levels. Theoretically, it is categorized into 3 types, which are conductive, sensorineural, and mixed hearing loss. Conductive hearing loss affects the outer and middle ear, while sensorineural hearing loss occurs because of inner ear damage or problem with the nerve pathways that lead to permanent hearing loss. Mixed hearing loss is a combination of both conductive and sensorineural hearing loss (American Speech & Hearing Association, ASHA).

1.10.2 Hearing Aids

According to United State Food & Drug Administration (FDA), hearing aids are sound-amplifying devices designed to help people who have hearing loss. Most hearing aids share several similar electronic components; i) A microphone that picks up sound, ii) Amplifier circuitry that makes the sound louder, iii) A miniature loudspeaker (receiver) that delivers the amplified sound into the ear canal iv) Batteries that power the electronic parts.

Hearing aids are varied by design, technology used to achieve amplification (analog or digital), and features such as wireless connectivity and software applications. There are different hearing aids that have earmolds or earpieces to direct the flow of sound into the ear and enhance sound quality. Hearing aid selection is based on the type and severity of hearing loss, listening needs, lifestyle, and age factors. Hearing aids are managed by Medical Device Authoriy (MDA) in Malaysia to ensure the product safety and effectiveness. Moreover, this authority body is important to review and authorize the advancement of technologies to ensure regulatory compliance, protocols and requirements for the industry.

1.10.3 Hearing Aids Benefits

Hearing aid benefits can be defined as the improvement of hearing impairment after being fitted with the devices as described by National Institute of Deafness and Other Communication Disorders. It makes the sound louder so that children with hearing impairment are able to hear, listen, communicate, and speak in daily activities. It highly depends on rehabilitation factors and critical period intervention for good prognosis especially in children with congenital hearing loss.

1.10.4 Aided CAEP

Aided CAEP is an evoked potentials recorded from individuals while wearing their hearing aids, may be of use to evaluate hearing aid fittings, as well as experience-related plasticity associated with amplification (Billings et al., 2011).

1.11 Thesis Outline

This thesis consists of six (6) chapters, as described in the following:

Chapter 1 presents a general outlook on CAEP usage as tool in measuring hearing aid benefits in Malaysia. This chapter begins with an introduction, research background, research problem, research questions, research aim and objectives, the research scope, research significance, theoretical frameworks and conceptual frameworks used in the study. The operational definitions are then explained at the end of chapter 1.

Chapter 2 draws up a comprehensive review of the contributors in CAEP. This chapter includes academic writing on CAEP, the implementation of CAEP and the contributors that influence CAEP. Systematic literature review also is included in this chapter. Next, the following section defines the key components of the framework using CAEP tools in measuring HA benefits.

Chapter 3 The research framework is discussed first, followed by a description of the research design that explains the research methods used in conducting the study Then, this chapter further presents a description of the three phases involved in the study, namely Phase I (Developing speech stimulus), Phase II (Validating speech stimuli in normal hearing adults) and Phase III (Measuring CAEP in normal children and hearing-impaired children).

Chapter 4 presents the outcomes retrieved from the quantitative approach. Detailed and step-by-step explanations are provided for the results and data analysis. It begins with an introduction, then goes into detail about the results and analysis of the main contributors that influence disputes, and concludes with a summary.

Chapter 5 discusses the overall research outcomes in accordance with each phase. This chapter is divided into phases and written in response to the research objectives and questions.

Chapter 6 outlines the overall research findings, which are concluded by looking into the framework development, significant findings, the contributions offered in this study, and several recommendations for future studies.

CHAPTER 2

LITERATURE REVIEW

2.1 Introduction

The study aims to investigate the use of Cortical Auditory Evoked Potential (CAEP) to assess hearing aid benefits in hearing-impaired children. It will examine the response rates, latencies, amplitudes, and interactions of CAEP components as indicators of hearing aid benefits at the auditory cortex level. Additionally, the study will explore the association between subjective parental observation reports and CAEP component measures.

This chapter starts by describing the optimum CAEP protocol used in adults and children to obtain good CAEP components (P_1, N_1, P_2 and N_2) from various studies. This information is useful to audiologists for quantifying the best practice and novel emerging methods for applying CAEP in clinical practice. This literature review aims to provide an overview of the current state of knowledge regarding CAEP. It explores the underlying mechanisms of CAEP generation, factors influencing CAEP responses, and various paradigms and methodologies employed in CAEP research. This is a well-recognized subject that necessitates a better approach to explore the use of CAEP as an effective method to be measured in adults and children with and without hearing impairment.

Based on the above indication, this chapter attempts to situate the current research within its broader context. In this process, it hopes to coherently connect this study with both related research in the area and theories that underpin it. Moreover, the key aim is to conduct an in-depth literature review focusing on CAEP studies in children. This review synthesizes and analyses existing research findings concerning the cortical responses elicited by auditory stimuli in the developing brains of children.

By examining a range of studies conducted across different age groups and populations, the chapter aims to elucidate the intricate developmental routes of cortical auditory processing in children, particularly in late latency responses in cortical areas physiologically. Furthermore, this review aims to explore the implications of these findings for our understanding of auditory system maturation, sensory integration, and cognitive development during the critical period in children based on CAEP findings. The ultimate goal is to provide a comprehensive overview of the current state of knowledge in this field and identify gaps and inconsistencies that could pave the way for research directions and possible applications in clinical settings.

On top of that, CAEP variables such as i) response rates, ii) amplitudes, and iii) latencies that are affected by electrode montage and abnormality in children are also discussed in this chapter. The above variables are the main core of findings and are summarized and synthesized on the contributing factors that will imply the CAEP components outcomes. These components can be elicited by various auditory stimuli, including tones, speech sounds, and complex auditory patterns. Researchers have made substantial progress in characterizing the different components of CAEP, such as the P_1, N_1, P_2, and N_2 each representing specific stages of auditory processing.

2.2 Auditory Evoked Potential (AEP)

Auditory Evoked Potential (AEP) is one of the objective measurements that falls under the electrophysiology category. Electrophysiology is the biomedical study of the body's electrical activity. In general, it is the study of electrical activity generation and its effects on the body (Carter & Shieh, 2010; Bell et al., 2007).

By inducing electrical changes in the human body, it is possible to measure any difference in the presence of stimulating factors based on responses in microvolts (V) and miliseconds (ms). There are many types of AEPs generated along the auditory pathway, which are the brainstem, midbrain and auditory cortex. The AEP is stimulated by acoustic stimuli that cause neuron depolarization along the auditory pathway which then triggers neural responses. This scalp-recorded signal is obtained from specific electrode placement at the head area (Edmonds, 2008).

The scalp recording in AEP can be named into different types; i) early latency recording (auditory brainstem responses / brainstem evoked responses), ii) mid-latency recording (mid latency responses, mismatch negativity), iii) late-latency recording (cortical auditory evoked potential, P300) based on Figure 2.1. These recordings can also be divided into subject states and attention, which may require a related event to stimulate the brain waves using the AEP device (Crivelli & Balconi, 2017).

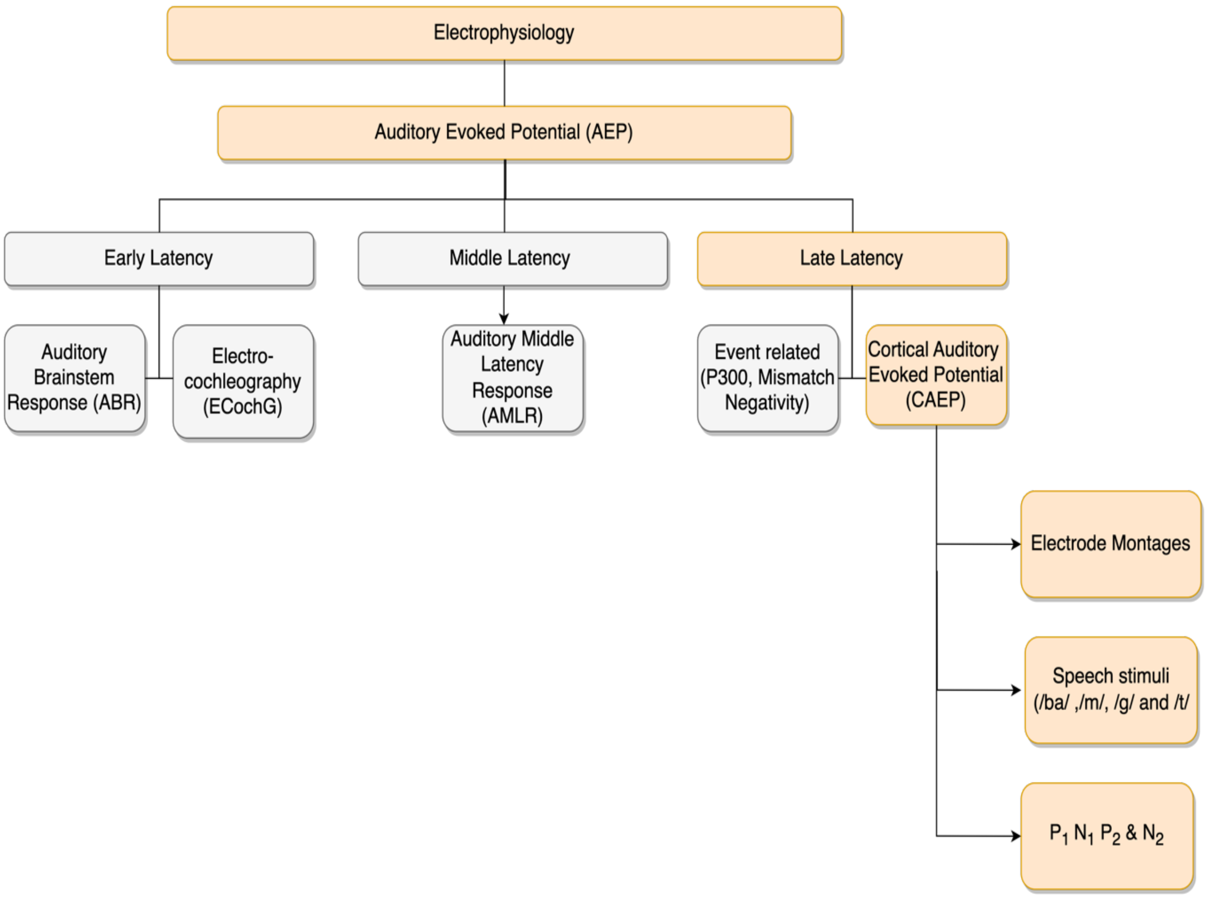

Figure 2.1 Types of electrophysiological tests

2.3 AEP Neurophysiologic properties

The AEP components/waveforms are influenced by the location of the recording electrode (i.e., near-field recording or far-field recording) as it increases the distance between the recording electrode and voltage sources. The spatial and temporal characteristics affect the volume conduction of the AEP responses due to the polarity of the activated neurons (Wood & Allison, 1981). The AEP is accepted as a clinical procedure due to its non-invasive recording, that is painless as no usage of any needle or catheter into the body (Hall, 2007).

The type of AEP that is tremendously used in clinical practice is Auditory Brainstem Responses (ABR). It is specifically used for diagnostic hearing threshold and retro-cochlear pathology detection. The ABR is an early latency response that is derived from the auditory pathways up to the brainstem at the first of 10 milliseconds (ms). It has several peaks and plotted in Roman numbers (I, II, III, IV, and V) (Figure 2.2).

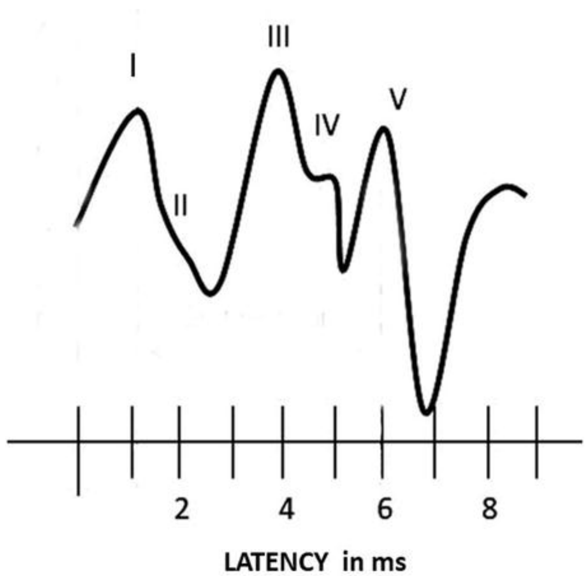

Figure 2.2 Auditory Brainstem Response (ABR) waveforms

The peaks are generated by specific areas of the auditory system; i) Wave I – Eight cranial nerve, ii) Wave II – Cochlear Nucleus, iii) Wave III – Superior Olivary Complex, iv) Wave IV- Lateral lemniscus, and v) Wave V- Inferior Colliculus (Hall, 2007).

Subsequently, the middle latency of AEP, known as Middle Latency Response (MLR) is typically observed from 12 to 50 ms post-stimulus and is considered to represent the subcortical activation (Crivelli & Balconi, 2017). The middle-latency component mainly represents electrical potentials from medial geniculate and polysensory nuclei within the thalamus and the primary auditory cortex (Picton et al., 1973). Figure 2.3 shows the waveform peaks for MLR (Bell et al., 2004).

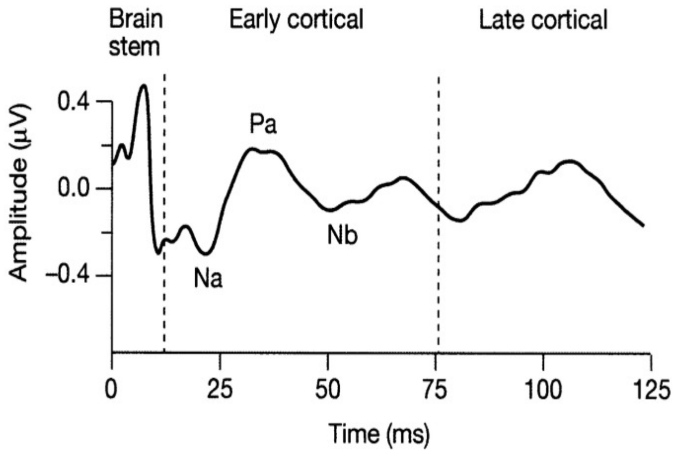

Figure 2.3 Peaks of Middle Latency Response (MLR)

The MLR is elicited with the presence of sounds to evaluate the auditory function in hearing-impaired patients in order to identify auditory limits and to investigate the latency duration and amplitude values associated with diverse deflections.

Finally, late latency responses that occur between 50 to 1000 ms and are represented by peaks such as P_1, N_1, P_2, and N_2 (Figure 2.3) are called cortical auditory evoked potential (CAEP) or auditory late latency response (ALLR). The CAEP has been used to assess the functions of the central auditory system in children with language disorders, learning disabilities, and hearing loss (Hall, 2007), intervention outcomes and management of pediatric hearing-impaired (Campbell et al, 2013).

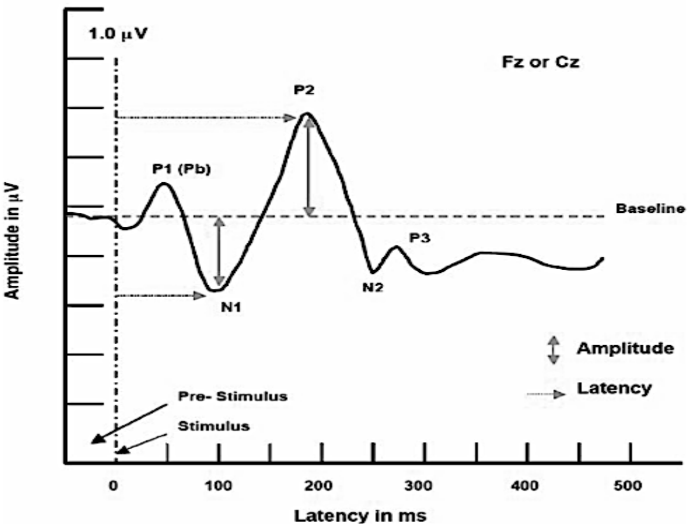

Figure 2.4 Auditory Late Latency Responses (Hall, 2007)

The CAEP components of P_1, N_1, P_2, and N_2 are believed to originate from different areas of primary and secondary auditory cortex. The comprehensive clinical use of CAEP can be associated with detection, discrimination, and developmental plasticity in humans (Hall, 2007). The present study is particularly interested in CAEP because it is useful to observe brain responses in an awake state, which can be conducted in children.

2.4 Fundamental History of CAEP

THE CAEP research has witnessed significant advancements over the years, with key contributions from prominent scientists in the field. Donald Jewett's ground breaking work in the 1960s and 1970s paved the way for the study of auditory evoked potentials. His collaboration with Williston led to the publication of a seminal paper in

1971, elucidating the scalp-recorded far-field auditory responses in humans (Jewett & Williston, 1971). This laid the foundation for subsequent research on CAEP that outlined the evaluation of components in human auditory evoked potentials, which became instrumental in subsequent studies (Picton et al., 1973).

In the following decades, David Stapells emerged as a key figure in CAEP research, particularly in pediatric populations. His work in the 1980s and 1990s focused on the assessment and interpretation of CAEPs, contributing significantly to the field's clinical applications. Stapells' studies provided valuable insights into the electrically evoked auditory response in adults, highlighting the potential diagnostic utility of CAEP (Stapells & Picton, 1981). Their work emphasized the distinct neural processes involved in generating CAEP responses and expanded our understanding of the auditory pathway's functioning.

The collective contributions have propelled the field of CAEP forward, evolving our understanding of the underlying mechanisms and clinical applications. Their work laid the groundwork for subsequent research, which further refined recording techniques, improved signal processing algorithms, and expanded the scope of clinical applications. More current studies focus on exploring the potential of CAEP as a diagnostic tool for various auditory disorders (Sharma et al., 1997) and as an objective measure for evaluating the effectiveness of interventions such as hearing aids and cochlear implants (Pantelemon et al., 2019). Ongoing advancements in CAEP research hold promise for enhancing the assessment and management of auditory disorders, ultimately improving the quality of life for individuals affected by hearing impairments.

The historical development of CAEP research has demonstrated the collaborative efforts of scientists worldwide, each building upon the contributions of their predecessors. The integration of various disciplines, including audiology, neuroscience, and clinical practice, has enriched our understanding of CAEP and its applications. Additionally, technological advancements in recording equipment and data analysis techniques have enhanced the accuracy and reliability of CAEP measurements.

2.5 Cortical Auditory Evoked Potential (CAEP)

In CAEP, the general "late response" time frame extends approximately from 50 to 1000 msec after the transmission of acoustic stimuli. These potentials can be interpreted based on response rates, amplitude, latency, and morphology. The prominent peaks generated by CAEP are P_1 (a small positive wave around 50 msec), N_1 (a strong negative wave around 100 msec), P_2 (a large positive wave around 175 msec) and N_2 (a small negative wave around 200 ms) (Figure 2.5). These peaks are assumed to be stimulated at different levels within the auditory cortex, which is a complex network of neural cells and fibers. Davis (1965) noted there are variations in the amplitude between subjects as peak voltages to loud clicks range anywhere between 10 and 100 microvolts, incidentally, sequential varied responses obtained in subjects in multiple recording.

The latency of CAEP was found to be prolonged in infants due to neural immaturity (Cone & Whitaker, 2013). In this regard, the maturity of CAEP was affected by age and site of electrode montage, as a study revealed a large positive peak (P_1) easily identified at the frontal sites across all ages, whereas N_2 emerged after 6 months of age and the following P_2 between 8 and 30 months of age (Shafer et al., 2015). Some studies found that P_1 latency remained stable between 0 and 6 years and reported that this finding is consistent with the maturation of neural generators of P_1 in the primary auditory cortex, while some reported a decrease in the latency of P_1 only after 5 years