Interleaved Recording of Auditory Evoked Potentials in Adults

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Abstract

The Auditory Brainstem Response (ABR) and the Cortical Auditory-Evoked Potential (CAEP) are auditory-evoked potentials used in the objective diagnosis of hearing loss and validation of paediatric amplification. They are far-field responses, meaning their acquisition can be time consuming complete due to their low signal-to-noise ratio, and therefore the larger number of response averages required for a clear response signal. A recent study of people with normal hearing discovered that eliciting the ABR using interleaved stimulation yields reliable results in half the time it takes to test each ear with typical sequential monaural stimulation (Bencito, 2020). The current study extends this work by exploring the efficacy of interleaved ABR and CAEPs in adults as compared with conventional monaural testing with a slow rate and monaural testing with a fast rate, with the underlying assumption that neural fatigue occurs in the peripheral auditory pathway, and therefore does not occur with bilateral interleaved stimulation. A total of 44 participants (27 females, 17 males) aged 18 to 63 years (M = 33, SD = 9.2) with symmetrical normal to mild sensorineural hearing loss underwent AEP testing under three conditions: interleaved, monaural slow and monaural fast. The measures for this study were Fsp, wave V latency and amplitude for click-evoked ABR, and the latency and amplitude of the P1-N1-P2 complex for 1 kHz tone-burst CAEP. Latency results showed no significant differences between the monaural slow and interleaved conditions, but significantly longer latencies in the monaural fast condition, for both ABR and CAEP testing. Fsp and amplitude measures revealed no significant difference for the ABR wave V and the CAEP P1 between the interleaved and monaural slow conditions. However, the P1-N1 and N1-P2 amplitudes and Fsp data for CAEP were significantly larger in the monaural slow condition as compared to the interleaved condition. Overall, these results support the efficacy of the interleaved technique for ABR testing, with potential benefits for CAEP as well, pending further exploration.

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I'd be remiss to not start by first outwardly expressing my gratitude to Allah (ﷻ) for His infinite blessings, including the opportunity and ability to embark on this next step in my education and career. I pray He increases me in beneficial knowledge, and benefits others with my knowledge.

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ABR	Auditory Brainstem Response
AEPs	Auditory Evoked Potentials
ALR	Auditory Late Latency Response
AMLR	Auditory Middle Latency Response
ASSR	Auditory Steady-State Response
BIC	Binaural Interaction Component
CAEP	Cortical Auditory-Evoked Potentials
dB	Decibels
dB HL	Decibels in Hearing Level
dB nHL	Decibels above Normal Adult Hearing Level
Fsp	Single-Point F-Ratio
Hz	Hertz
ISI	Inter-Stimulus Interval
IT5	Interaural Difference of Wave V
kΩ	Kilohms
MMN	Mismatch Negativity
ms	Milliseconds
µV	Microvolts
s	Seconds
SNR	Signal-to-Noise Ratio
SRR	Stimulus Repetition Rate

Chapter 1: Introduction

1.1 General Introduction: The Auditory Pathway

The auditory pathway begins peripherally at the outer, middle and inner parts of the ear, and spans to central structures including the brainstem, midbrain and auditory cortex (Aibara et al., 2001; Alvord & Farmer, 1997). Acoustic stimuli are transduced at the cochlea to electrical impulses which travel up the ascending auditory pathway via the auditory nerve, a branch of the VIIIth cranial nerve (also known as the vestibulocochlear nerve). Within this pathway is the systematic mapping of frequency characteristics to the place of maximum stimulation at each point in the pathway (Briley & Krumbholz, 2013). This is referred to as tonotopic organisation and begins at the level of the cochlea in the inner ear, continuing up the ascending auditory pathway into the cortex. This pathway is visually represented in Figure 1. A lesion anywhere in this pathway can lead to a hearing impairment (Ekdale, 2015; Hall, 2006).

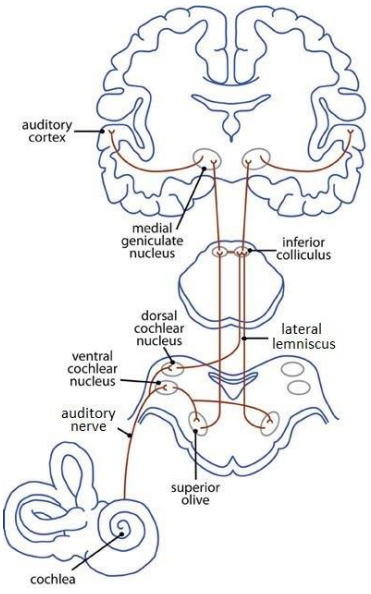


Figure 1

The Ascending Auditory Pathway from Cochlea to Cortex (Butler and Lomber (2013)

At various points in the auditory system, the electrophysiologic response to sound stimuli can be recorded using several subjective and objective tests. Auditory evoked

potentials (AEPs) are objective responses generated in the ascending auditory pathway, evoked by acoustic stimuli and recorded as electrophysiologic responses (Figure 2). AEPs provide valuable insight into the integrity and functioning of structures along the auditory pathway (Almeqbel & McMahon, 2015; Antonelli & Grandori, 1984; Sharma & Cardon, 2015). This objective data can be collected non-invasively using surface electrodes, hence AEPs have many uses in both clinical and research settings. Clinically, they are widely used in audiology for the identification of lesions along the auditory pathway and the diagnosis of hearing impairments (Bagatto et al., 2010). AEPs can also be used for the objective validation of audiological intervention (Bagatto et al., 2010; Hazzaa et al., 2016).

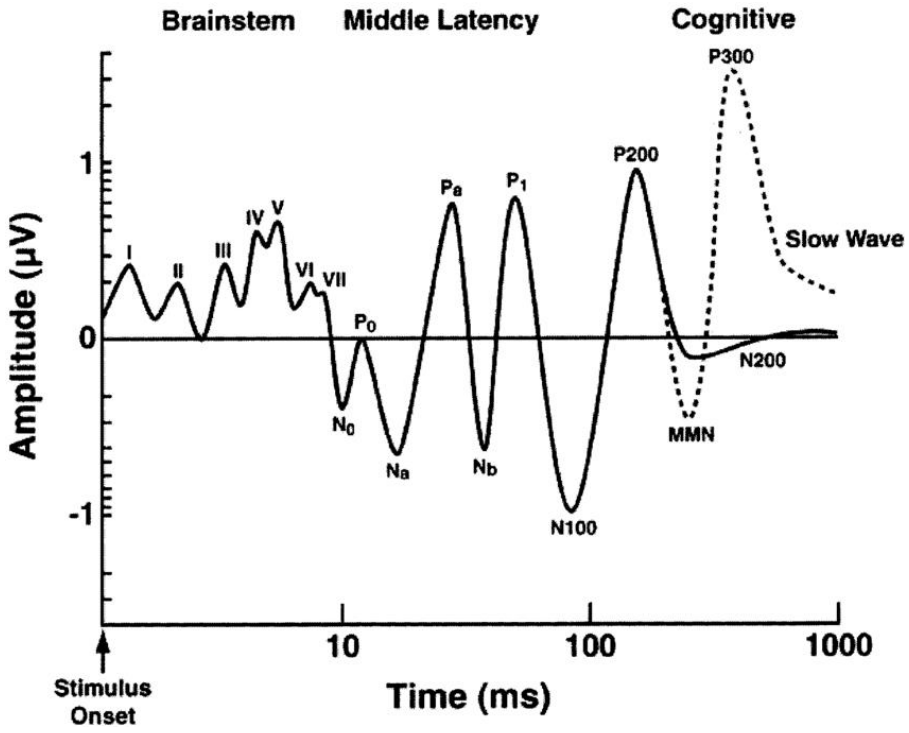


Figure 2

Auditory Evoked Potentials recorded from the scalp, shown with a logarithmic time axis

Picton et al. (1974).

AEPs are identified according to the latency with which they appear; that is: the time it takes, in milliseconds (ms) for the response to occur following the onset of a stimulus. Early AEPs typically take place between 0 and 10 milliseconds after the presentation of stimuli (Aoyagi, 2010). The Auditory Brainstem Response (ABR) is the most widely utilized

early electrical evoked potential, with applications in both adult and paediatric audiological diagnosis and management (Alhussaini et al., 2018).

Middle AEPs occur between 10 and 50-100 ms and include the Auditory Steady-State Response (ASSR) and the Auditory Middle-Latency Response (AMLR) (Aoyagi, 2010). Much like the ABR, the ASSR and AMLR can be clinically used to estimate hearing thresholds, with the ASSR also utilized to validate audiological interventions with hearing aids (Sardari et al., 2015; Vlastarakos et al., 2017). Later AEPs are classified as responses occurring from 100 ms and onwards after stimulus onset. These include the Auditory Late Latency Response (ALR), Cortical Auditory-Evoked Potentials (CAEP) and the Mismatch Negativity (MMN) repsonse (Cone-Wesson & Wunderlich, 2003). Unlike previously mentioned AEPs, the MMN response uses an "oddball" stimulus to interrupt a sequence of repetitive acoustic stimuli, providing assessment of perception and cognitive functioning (Fitzgerald & Todd, 2020; Garrido et al., 2009).

AEPs are considered far-field responses as they are recorded using surface-electrodes on the scalp, at a significant distance from the anatomical site where they are produced (i.e. their generators) (Bardy et al., 2016; Hall, 2006). As such, the potential for noise interference is high due to environmental and myogenic noise (Burkard, 1991). Hence, large number of response averages are required in order to identify a clear response (Bataillou et al., 1995). Additionally, the stimulus repetition rates are typically slow to avoid neural fatigue and maintain clarity of responses (Leski & Henzel, 1999). Together, these factors increase testing time, which decreases the feasibility of using these tests in clinical settings. This study aims to explore a new technique that greatly reduces the time it takes to obtain these responses while maintain a high degree of response quality.

1.2 The Auditory Brainstem Response

The Auditory Brainstem Response (ABR) is an electrical cortical evoked potential produced at the brainstem in response to acoustic stimuli. The ABR uses transient evoked stimuli and measures the response of the VIIIth nerve and the ascending auditory pathway to these stimuli (Alhussaini et al., 2018). It is an early evoked potential, meaning it occurs shortly after the presentation of a stimulus, approximately within 10 ms (Starr, 1976). This response is presented as a series of peaks and troughs, in waveform, recorded and labelled as seven wave responses.

1.2.1 Uses of the ABR

Among its many applications, the ABR is most extensively used as an objective audiological test with infants, children, and adults to identify and diagnose hearing loss (Elberling & Don, 2010; Galambos & Hecox, 1978; Galambos et al., 1984). Two of its main uses consist of threshold estimation and neurological assessment with both the adult and paediatric populations (Bagatto et al., 2010; Gorga et al., 2006; Schulman-Galambos & Galambos, 1979). The efficacy of ABR has been proven several times in identifying neural lesions, particularly in adults (Cueva, 2004; Elberling & Parbo, 1987; Jewett & Williston, 1971).In addition to these clinical applications, the ABR has also been used for identifying and diagnosing cochlear synaptopathy and retrocochlear lesions on the VIIIth cranial nerve, intra-operative audiological monitoring, diagnosis of central nervous system diseases such as multiple sclerosis, among many other uses (Abramovich, 1987; Acioly et al., 2010; Acioly et al., 2013; Bagatto et al., 2010; Bauch et al., 1990; Mehraei et al., 2016; Prasher & Gibson, 1980a; Sato et al., 2015).

1.2.2 ABR Pathway

The ABR spans the response of the VIIIth cranial nerve and the ascending auditory pathway (Figure 3, DNLL: dorsal nucleus of the lateral lemniscus; IC: inferior colliculus; MGB: medial geniculate body; VNLL: ventral nucleus of the lateral lemniscus). Starting peripherally, acoustic stimuli travel from the outer and middle ears to the inner ear, stimulating the basilar membrane in the cochlea (Britt & Rossi, 1980). The signal is then converted to bioelectrical action potentials, transmitted via the ipsilateral vestibulocochlear nerve along the ascending auditory pathway to the cochlear nuclei and to the central auditory processing system in the brain (Britt & Rossi, 1980; Hall, 2006). The signal then crosses the midline to the contralateral superior olivary complex, lateral lemniscus, inferior colliculi and medial geniculate nuclei, ultimately ending at the inferior colliculus (Hall, 2006; Hood, 2015).

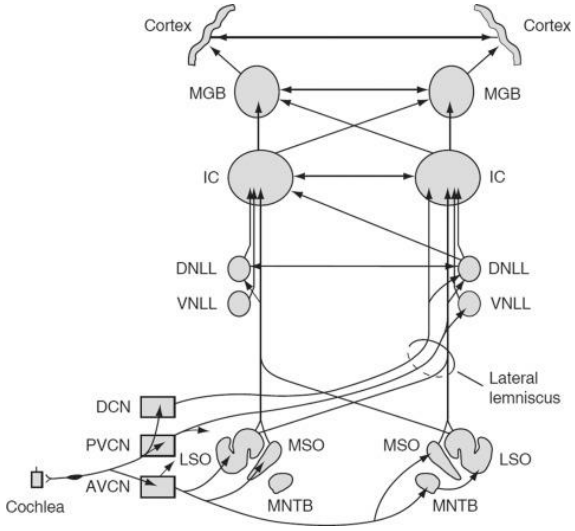


Figure 3

The Main Ascending Pathways of the Brainstem (Pickles, 2015)

1.2.3 ABR Neural Generators

At each point in the ascending auditory pathway, a peaked wave response is generated during ABR in response to stimuli. It was previously thought that each peak response was the result of the successive activation of different nuclei points in the ascending auditory pathway (Allen & Starr, 1978; Arezzo et al., 1975; Buchwald & Huang, 1975; Davis et al., 1952; Jewett, 1970; Pratt et al., 1992). In 1980, Achor and Starr recorded ABR in four adult cats and performed spatial and temporal analyses. They used click-ABR on the anaesthetised cats at a rate of 25 clicks per second (s). A structure was considered a generator of a response if the evoked activity at the site was at or above the 50% criterion level, as set by the authors. The research findings showed multiple generation sites of responses (measured in microvolts of peaks and troughs) along the ascending auditory pathway, particularly for components three onwards (equivalent to wave III in more recent research). The authors deducted that the activation process of the ascending auditory pathway is more intricate than previously thought, wherein the activation of one nucleus in the pathway may contribute to one or more peak responses of the ABR (Achor & Starr, 1980). Through various other animal-centred experiments in the late 1900s, Achor and Starr's (1980) findings were confirmed by multiple studies with human participants of various pathologies, using surface electrodes and intracranial recording during neurosurgical operations exposing the auditory nerve (Martin et al., 1995; Møller et al., 1994; Møller et al., 1981).

The generation sites of waves I and II have been proven to be at the ipsilateral (i.e., same side as the ear which received the stimulus) peripheral and central portions of the VIIIth auditory nerve, respectively. Consequently, waves III and V are thought to be the sum of multiple bilateral generation sites in the brainstem (Britt & Rossi, 1980; Møller & Jannetta, 1983). Surrounded by these multiple activation sites, waves III and IV are most likely produced in the lower portion of the brainstem, with activation of the cochlear nucleus and the superior olivary complex contributing to the generation of wave III (Britt & Rossi, 1980). Thus far, the signal activates the ipsilateral ascending auditory pathway. From here, the signal crosses the midline, activating the contralateral side of the pathway. Wave IV is generated bilaterally at the superior olivary complex, with evidence also showing contribution from the lateral lemniscus (Durrant et al., 1994; Parkkonen et al., 2009). Next, wave V is generated in the upper region of the brainstem at the level of the superior olivary complex and the inferior colliculus (Parkkonen et al., 2009). Unlike the previous wave responses, wave V is uniquely generated by the structures contralateral to the stimulus ear, with little contribution from the ipsilateral side. For example, if an ABR stimulus is presented to the right ear, the corresponding wave V response is largely generated by the superior olivary complex and the inferior colliculus in the left.

1.3 Cortical Auditory-Evoked Potentials

Cortical evoked potentials are late evoked potentials occurring at the level of the cortex. Most of these potentials can be evoked by several modalities of stimuli, such as auditory and visual stimulation (Tremblay & Clinard, 2015). Unlike the ABR, which is a result of an action potential in the brainstem leading to synchronous firing, cortical auditory-evoked potentials (CAEPs) are stimulus-locked potentials, happening post-synaptically within apical dendrites of neurons in the cerebral cortex (Aoyagi, 2010). Eggermont (2001) described how these extracellular currents spread through the conductive tissue in the brain, travelling to the cerebrospinal fluid, skull and skin, generating voltage differences which can be recorded using electrodes at the scalp surface.

1.3.1 Uses of CAEP

CAEPs are used clinically in the diagnosis of hearing impairment, the estimation of hearing thresholds and the assessment of speech detection and discrimination (Agung et al., 2006; Alvarenga et al., 2013; Baydan et al., 2019; Ching et al., 2016; Hall, 2006). They have

also been reportedly used in the assessment of Auditory Neuropathy Syndrome Disorder (ANSD) and in children with Auditory Processing Disorder (APD) for the assessment and measurement of intervention outcomes (Pearce et al., 2007; Sharma & Cardon, 2015; Sharma, Purdy, et al., 2014). The presence of CAEPs is used to indicate whether the presented stimuli is adequate enough to elicit neural activity at the level of the auditory cortex, from which audibility of the signal is inferred (Pearce et al., 2007; Purdy et al., 2013; Sharma et al., 2002). As such, CAEPs are also widely used in paediatric screening protocols for the objective validation of paediatric hearing aid fittings (Ching et al., 2016; Golding et al., 2007; Mehta et al., 2017; Punch et al., 2016).

In addition to the validation of acoustic amplification, CAEPs have been used in the programming and validation of cochlear implants and in the functional assessment of maturation of the auditory system following insertion of a cochlear implant (Brown et al., 2015; Sharma et al., 2015; Sharma et al., 2002; Silvaa et al., 2014). CAEPs also have various applications in the field of clinical and research psychology, as well as being a potential counselling tool for parents of children with hearing loss (Barker et al., 2017; Brown et al., 2017; Brown & Musiek, 2013; Kasper et al., 1988; Mehta et al., 2020).

1.3.2 CAEP Pathway

Much like the ABR, CAEPs follow the same route up the ascending auditory pathway. However, where the ABR ends at the level of the inferior colliculus, the CAEP response continues to the medial geniculate body and up into the auditory cortex (Shaw, 1995). Zouridakis et al. (1998) attempted to establish the pathway of activation for monaural stimulation using pure tones, musical tones and words. They found the majority of activation initially occurred at the level of the auditory cortex, but as the response progressed, greater pathway activation extended to the superior surface of the temporal lobes, with occurrences in the ipsilateral and contralateral hemispheres. More specifically, the trajectory of activation spread from posterior to anterior, medial to lateral and superior to inferior regions, bilaterally. While both hemispheres were stimulated, an asymmetry in the distribution of activation was observed, with larger stimulation occurring in the right hemisphere (Zouridakis et al., 1998). It can therefore be concluded that, in addition to the crossover in the auditory pathway at the superior olivary complex and the inferior colliculus (as observed in the ABR in response to acoustic stimuli), further crossover takes place in CAEP at the level of the cortex in the temporal lobes.

1.3.3 CAEP Neural Generators

CAEPs have been widely proven to originate from the primary auditory cortex in the temporal lobe. The generation sites for mature CAEPs in adults differs from that in the paediatric population, with activation becoming more central as neural pathways mature (Bakhos et al., 2012; Bruneau et al., 1997; Ponton et al., 2002). The P1 peak response of CAEP is believed to originate from the primary auditory cortex, with specific influence from the hippo campus, planum temporal and the lateral temporal cortices (Howard et al., 2000; Lightfoot, 2016). Research by Lütkenhöner and Steinsträter (1998) explored the dipole organisation of the auditory cortex in adults with a neuromagnetic study. They found the planum temporale within the Sylvian fissure (located posteriorly to the auditory cortex) gave rise to the N1 response, while P2 was generated more centrally near Heschl's gyrus. Their findings were consistent with similar studies, such as that of Pantev et al. (1988) and Cansino et al. (1994), among others (Engelien et al., 2000; Howard et al., 2000; Pantev et al., 1991). Picton et al. (1999) and Zouridakis et al. (1998) also found evidence of contralateral stimulation in their CAEP recordings. CAEPs are seen as a sequence of overlapping temporal wave responses, the sum of which is recorded as a response on the scalp surface (Näätänen & Picton, 1987; Pratt & Lightfoot, 2012; Wunderlich & Cone-Wesson, 2006). Therefore, while the key generator is the primary auditory cortex, CAEPs represent input from various cortical locations (Čeponien et al., 1998; Wunderlich & Cone-Wesson, 2006).

A review by Näätänen and Picton (1987) elaborated further on this concept, concluding that a minimum of six cerebral processes per hemisphere can contribute to the generation of an N1 wave response, which is the biggest deflection recorded from CAEP recordings. This concept has been corroborated by several studies around the same time period, such as that of Wolpaw and Wood (1982) and Scherg and Von Cramon (1985), with more recent research also supporting these findings (Alcaini et al., 1994; Giard et al., 1994; Woods, 1995; Zouridakis et al., 1998). The supratemporal plane, lateral aspect of the temporal and parietal cortices and the motor and premotor cortices are considered 'true' N1 components and are influenced by both endogenous and exogenous factors. The remaining processes outlined in the review included both temporal and frontal components of negativity processing, similar to those found in the MMN response (Garrido et al., 2009; Picton et al., 1999). These components were found to last much longer than the aforementioned 'true' components of the N1, leading to overlapping of these processes (Näätänen & Picton, 1987).

1.4 Neural Adaptation

As AEPs are recorded far-field and the voltage of response signals is relatively small, numerous repetitions of the signal are needed to obtain reliable responses. The large number of repetitions needed prove challenging to the auditory system due to adaptation (Reichenbach et al., 2016). Neural adaptation refers to the decay in neural responses as a result of repeated, consecutive and/or prolonged stimulus presentations (Lanting et al., 2013). Numerous studies have observed adaptation in auditory responses at the level of the cortex (Eliades et al., 2014; Lanting et al., 2013).

While the exact process contributing to adaption is not entirely understood, three key models have been suggested to explain the mechanisms of adaptation, as discussed in Grill-Spector et al. (2006). The first of these models is the fatigue model, which proposes a reduction in neural sensitivity to the stimulus, leading to a depletion of neurotransmitter. Secondly, the sharpening model suggests those neurons which are responsive to the presented stimuli become more sharply tuned to the stimulus, thus leading to a reduction in those responsive neurons and a subsequent decrease in the overall response. Finally, the facilitation model assumes that stimulus repetition causes faster processing, which in turn leads to shorter durations of neural firing.

Earlier studies, such as those by Desimone (1996), Wiggs and Martin (1998) and Henson and Rugg (2003), indicate the cause of adaption to be a reduction in the number of responsive neurons reflecting nerual sharpening, as explained by the sharpening model. In contrast, a more recent experiment by Briley and Krumbholz (2013) investigated which of these models applies to adaption in the human auditory cortex by measuring auditory late latency potentials, including the N1-P1-P2 complex of CAEP, with puretone stimuli. They concluded the fatigue model best explains the neural adaptation observed in their data. These findings were consistent to that of several studies (Don et al., 1977; Lanting et al., 2013). Regardless of the underlying mechanism, the stimulus repetition rate has a significant effect on neural adaptation. As each neural firing caused by the stimulus takes to time to transmit and recover before the next transmission can occur, a stimulus rate faster than the recovery period would not yield optimal results (Thornton & Coleman, 1975). Optimal stimulus repetition rates for the ABR and CAEP are further discussed below.

1.4.1 The Binaural interaction Component

The binaural interaction component (BIC) is a measure of interaction during the presentation of simultaneous stimuli, representing the sum of neural activity from the brainstem and midbrain (Laumen et al., 2016). The BIC is the difference between the sum of monaurally evoked responses in the right and left ears, individually, and the sum of binaurally evoked responses (Dean & Grose, 2020). In other words, the BIC represents the discrepancy between responses obtained via monaural and binaural stimulation (Tolnai & Klump, 2020). The BIC is likely generated at the superior olivary complex, and is a measure mostly used with ABR, although it has potential applications with middle and late AEPs (Benichoux et al., 2018; Fowler, 2004; Tolnai & Klump, 2020).

The evidence and research around the BIC support the hypothesis that although crossover is present in the auditory pathway, it does not significantly influence ipsilateral responses (Fowler, 2004; Stollman et al., 1996; Van Yper et al., 2015). Ainslie and Boston (1980), for example, examined the BIC in the ABR of normal hearing adults. They found no significant differences in the wave V amplitude of the sum of monaural responses versus binaural responses, confirming the assumption that significant interactions typically occur peripherally rather than centrally (Ainslie & Boston, 1980; Prasher & Gibson, 1980b). It is important to note that the BIC has been explored for simultaneous binaural stimulation and is therefore unlikely to be present during interleaved stimulation when the left and right pathways are activated in rapid succession rather than simultaneously.

1.4.2 Peripheral versus Central Adaptation

The source of neural adaptation was presumed to originate centrally at the level of the cortex (Sagalovich & Melkumova, 1981), however this premise has been disproven. Don et al. (1977) explored this concept by recording the ABR wave V latency in response to a presentation of a train of 20 clicks at a stimulus rate of 100 clicks per second at different intensities to adults with normal hearing. The first click was presented to participants' right ears, followed by 18 clicks to the left ear and the 20th click presented at the right ear (Figure 4). They found no shifts in the wave V latency of the two clicks presented to the right ear, whereas the wave V latency increased and the amplitude decreased in the left ear following the presentation of the 18 consecutive clicks. If adaptation did indeed occur centrally, an increase in wave V latency in the 20th click would have recorded due to the neural adaptation resulting from the consecutive clicks in the left ear. Therefore, these results refute the notion

that adaptation occurs centrally. Consequently, it can be concluded that adaptation likely occurs peripherally at the VIIIth cranial nerve rather than centrally at the level of the brainstem (Don et al., 1977), with these outcomes being supported in the literature (Eggermont & Odenthal, 1974).

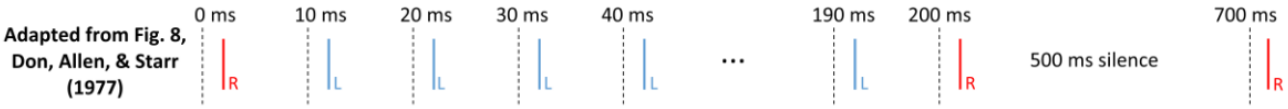


Figure 4

The Schematic Diagram Adapted from Figure 8 of Don et al. (1977)

Although points of crossover and interaction between the left and right pathways exists, evidence has demonstrated that adaptation is restricted to the ipsilateral pathway of the stimulated ear with little to no signifcant influence from contralateral stimulation (Don et al., 1977; Eggermont & Odenthal, 1974; Thornton & Coleman, 1975). Based on the evidence surrounding adaptation and interaction, it is assumed that interleaved stimuli presented to each ear will not be affected by the contralateral stimuli presentation of the opposite ear. For this research project, this assumption is extended to and will be examined for both ABR and CAEPs.

1.5 Signal-to-Noise Ratio

The signal-to-noise ratio (SNR) refers to the strength to which an electrophysiologic signal carries interference of unwanted information (Billings & Grush, 2016). The SNR largely determines how long AEP testing will take (Billings & Grush, 2016; Shetty et al., 2014). In the context of this project, the signal is the ABR and CAEP responses, and the unwanted interference is that of noise, which is the main factor influencing SNR. Myogenic noise and movement artifact caused by the individual undergoing AEP testing has a significant impact on the response signal. External noise, such as environmental acoustic noise and electrical interference from equipment, can also be a factor (Marcoux & Kurtz, 2012).

There are three ways to improve SNR: increasing the signal, decreasing the noise, or a combination of both. A clear signal is needed to determine whether a wave response is

present or absent, and thus for diagnostic interpretation. An improvement in SNR means recording a higher number of signals, leading to better quality wave responses for diagnostic interpretation. Replicating each wave response is one method to prove the presence of a signal (Elsayed et al., 2015). As noise is aperiodic, it appears in wave recordings as random peaks and troughs not linked to a time constant (Leski, 2002). In contrast, the signal is periodic and time locked, therefore we expect the replication of a signal to elicit the same response, proving it to be a true response to the stimulus.

Noise can also be reduced by the individual's state and posture during testing, with best results achieved with a relaxed posture, natural sleep or sedation for ABR. CAEPs are more resilient to myogenic noise than earlier evoked potentials, such as the ABR. Therefore, participants' alert status can be awake and quiet for CAEPs (Robier et al., 1983; Small et al., 2018). Apart from these physical adjustments, SNR can also be improved by utilizing more qualitative methods, such as signal averaging, noise rejection and electrode impedance, discussed further below (Marcoux & Kurtz, 2012).

1.5.1 Statistical Techniques for Response Quality Recognition

The SNR of wave responses can be statistically determined with various techniques. The single-point F-ratio (Fsp) is a commonly used measure when recording AEPs (Sininger, 1993; Sinkiewicz et al., 2017). First introduced by Elberling and Don (1984), the Fsp is a variance ratio measure used to determine the degree of confidence in the presence of a wave repsonse. It's calculated by dividing the magnitude of the response when the stimulus (representing the signal) is present, by the magnitude of the response when the stimulus is absent (representing noise). Therefore, it compares the variance of the averaged waveform to the variance of the background noise level (Hall, 2006). The higher the Fsp value, the greater the response compared to background noise and the greater the confidence of a clear response. A similar measure using multiple-point F-ratio (Fmp) was later introduced, however Fsp remains the main tool used in determining the SNR during AEP testing (Don & Elberling, 1994). An Fsp of 2.1 or greater indicates the presence of a signal/response (Hall, 2006). Typically, an Fsp of 3.1 is the target measure during ABR recordings, which corresponds to an SNR of 1.2 (Elberling & Parbo, 1987; Sininger, 1993).

Another widely used statistical measure, widely used for CAEP responses, is the Hotelling's T^2 statistic (Bardy et al., 2020; Golding et al., 2007). This test is an extension of the conventional one-sample t-test and assesses the hypothesis that the averages of cortical

responses are each identical to an independent value (Golding et al., 2009; Oliveira et al., 2019). It calculates the probability that the mean value of any linear combination is significantly different from zero (Munro et al., 2020; Van Dun et al., 2015). In the context of AEPs, the mean value refers to the peak responses. The Hotelling's T^2 test has been evidenced to have accurate sensitivity and specificity in identifying CAEP wave responses (Carter et al., 2010; Golding et al., 2007).

1.5.2 Signal Averaging

Signal averaging is the process by which information from a single periodic signal is stored and summed with information from successive signals. This sum total is then divided by the number of cycles to generate an average (Bataillou et al., 1995; Marcoux & Kurtz, 2012). These cycles are referred to as sweeps (i.e., the number of presentations of a stimuli), with several thousand sweeps collected for each presentation of the stimulus for ABR, and several hundred sweeps for CAEP (Bagatto et al., 2010; Mehta et al., 2017).

Because the signal of interest is relatively small and the responses recorded are far-field, signal averaging is an essential approach used during AEP testing. The goal of signal averaging is to highlight the signal while de-emphasizing noise and reducing its impact on the recordings. As discussed earlier, the signal is time locked to the stimulus, so the same response is able to be elicited upon replication. Conversely, noise is random by nature and aperiodic, so when signals are averaged, the responses group together and become separate from the noise. Noise with a high frequency spectrum is typically due to electrical interference from equipment, whereas noise with low frequency emphasis is commonly seen with myogenic muscle noise (Marcoux & Kurtz, 2012).

Various averaging techniques exist for the purpose of achieving the best SNR. One such method is the robust averaging method, discussed by Leski (2002), based on mathematical algorithms. The robust averaging method involves recording and retaining both signal and noise tracings, with less weighting given to the noisy traces. The Kalman and Bayesian weighted averaging techniques follow a similar concept, giving less emphasis to noisy traces when averaging (Elsayed et al., 2015; Marcoux & Kurtz, 2012; Sanchez & Gans, 2006). This is in contrast to conventional averaging techniques, which account for all sweeps regardless of their noise content (Burkard, 1991; Leski, 2002; Zhaoxia & Tao, 1991). The above averaging methods, as well as multiple others, are all based on conventional averaging techniques, and are widely used in numerous protocols (Bataillou et al., 1995; Elsayed et al.,

2015; Leski & Henzel, 1999; National Screening Unit, 2016; Rennert et al., 2012; Zhaoxia & Tao, 1991).

The number of averages needed to yield the best possible SNR depends on the amount of noise present in the wave response (Zhaoxia & Tao, 1991). The improvement in SNR due to averaging is proportional to the square root of the number of averages (SNR $\propto \sqrt{n}$, n = number of sweeps), meaning the SNR does not improve exponentially as the number of averages increases, as a plateau is eventually reached. Consequently, setting an especially large number of target averages is not only time consuming, but it also does not necessarily guarantee an ideal improvement in the SNR, particularly if there is a high amount of noise present (Bataillou et al., 1995). Additionally, estimating the averages needed may lead to over averaging in the instance of high signal or low noise, thus leading to unnecessarily time-consuming testing (Leski, 2002). As such, it is not possible to determine the number of averages needed for an ideal SNR before testing begins. This dilemma can be resolved by implementing a stop criterion for averaging (Elsayed et al., 2015).

A stop criterion is a predetermined set of benchmark measures loaded in the testing software. When one or all of these measures are met, the software stops averaging for the selected stimulus parameter. Stop criteria can be set to a particular number of averages, as discussed above. It can also encompass residual noise, set to stop when the residual noise is less than the specified value (Marcoux & Kurtz, 2012). Another criterion is when a set Fsp value is reached, indicating good quality traces and SNR.

Artifact rejection also improves SNR by allowing a wave response to contribute to the average only if the peak amplitude is below a set noise limit, measured in nanovolts (nV) from peak to trough (also known as peak to peak – pp). Traces with amplitudes greater than the rejection level are regarded as having too much noise and are therefore excluded from the averaging process (Abou-Al-Shaar et al., 2019). While rejection criteria reduce the amount of noise in the response, having a rejection level that is too conservative can prolong test time unnecessarily, as more data would need to be collected for a sufficient number of averages due to a large number of rejected sweeps (Marcoux & Kurtz, 2012). Balance must therefore be achieved when setting the artifact rejection limit.

Utilising a combination of all three measures when determining a stop criterion is most ideal, as it capitalises on all three measures and objectively determines when to stop averaging. Traces which meet the above measures are accepted, while traces which fall outside the set criteria are rejected. Implementing a stop criterion ensures the most optimal SNR while maintaining time efficiency during clinical testing.

1.5.3 Electrode Placement and Interference

To obtain clear recordings, good SNR and wave morphology, measurement and test conditions should be optimised prior to commencing AEP recordings. Placement of surface electrodes is an important pre-test factor to optimise the signals recorded. The 10-20 electrode configuration system (Figure 5), initially proposed by the International Federation of Societies for Electroencephalography and Clinical Neurophysiology in 1958, is most commonly used to describe the electrode montage utilised during testing (Acharya et al., 2006; Atcherson et al., 2012; Jasper, 1958).

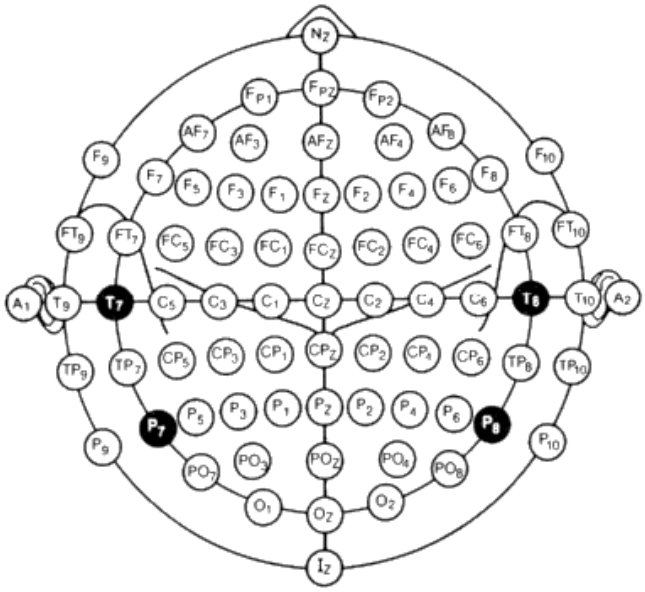


Figure 5

The 10-20 Electrode Configuration System (Acharya et al., 2006).

The two primary electrode montages used in AEP recordings are vertical (forehead to nape of neck) and mastoid (forehead to ipsilateral mastoid) placements (Dzulkarnain et al., 2014). An early study by Sininger and Don (1989) found smaller ABR responses with a vertical electrode montage compared to a horizontal/mastoid placement. King and Sininger (1992) later refuted this with a study which explored four different electrode placements to determine the relationship between electrode placement and wave responses in adults. The four electrode montages used were vertical, mastoid/horizontal, and two placements with the mastoid as a reference. They found significantly larger wave V responses and better morphology with the vertical electrode montage. Their findings are supported by multiple

consequent studies (Dzulkarnain et al., 2014; Dzulkarnain et al., 2008), making the recommended electrode montage for the ABR a vertical one. As for CAEPs, research shows a mastoid electrical montage is conventionally used (Billings et al., 2007; Punch et al., 2016). To date, no studies have been found which use a vertical montage for recording CAEP.

In addition to placement, interelectrode impedance is crucial to ensuring best signal recordings and to check for electrical interference. This is measured by applying a small electrical current to one electrode, while the current reaching the second electrode is measured. The desired impedance is between one and five kilohms (kΩ), with particular attention given to ensuring the impedances of all electrodes are balanced (Hall, 2006). Imbalance between the electrodes can lead to excessive interference, poorer common mode rejection and a lower overall SNR (Marcoux & Kurtz, 2012). It is a recommended common practice to gently scrub and exfoliate the skin prior to applying electrodes, as this serves to reduce impedance. While high impedances do not affect the recordings, they result in noise being picked up from electromagnetic interference, leading to a poor SNR (Marcoux & Kurtz, 2012).

1.6 Waveform Analysis

AEP wave responses can be analysed both subjectively and objectively. Subjective analysis relies on the proficiency and skill of the assessor/clinician to manually observe the averaged traces and visually detect diagnostic indicators, estimate hearing thresholds and make judgements on if and when adjustments to testing parameters need to be made (Albera et al., 1991; Campbell & Leandri, 2021). AEPs are considered objective auditory assessments as they do not rely on a behavioural response from participants, so are consequently less susceptible to subjective and/or prejudiced influence.

With this definition, the individual interpretation involved in the waveform analyses of AEP responses is often overlooked. It can therefore be argued that AEPs are not entirely objective, as identifying and labelling wave responses is largely done by the examiner/clinician. As such, subjective analysis of responses is susceptible to human error and variability within and between tests (Albera et al., 1991). Objective analysis is therefore preferrable as it minimises the occurrence of inconsistencies. Various methods seeking to empirically identify and label wave responses have been explored, however these are not widely used in existing clinical commercial software (Achimowicz, 1995; Campbell & Leandri, 2021; Hu et al., 2011; Limpiti et al., 2009; Suthakar & Liberman, 2019). Statistical

measures of ascertaining response quality, such as the Fsp, along with visual analysis by the clinician are currently the most widespread and conventional way to analyse AEPs.

1.6.1 Synchronous Firing

Synchronous neural firing is a key determinant of the quality of recorded responses for analysis. Both the ABR and CAEP rely on synchronous neuron firing to produce a measurable far field response. With the presentation of acoustic stimuli, a neural action potential takes place, causing synchronous activation of neurons (Eggermont, 2019; Sadeq et al., 2015). Following this response, another action potential must be generated before achieving the next synchronous response. As such, a period of rest must be had between successive neural responses. This is believed due to the neural neurotransmitter reserve pool being spent and needing to be replenished, or due the neurons having a subsequent higher activation threshold, or a combination of both (Briley & Krumbholz, 2013; Hall, 2006; Henson & Rugg, 2003; Wiggs & Martin, 1998). In other words, the stimulus repetition rate (SRR) must be optimal in order to achieve a synchronous neural response (Thornton & Coleman, 1975).

CAEPs can be evoked with both speech and pure tone stimuli (Almeqbel, 2013; Alvarenga et al., 2013; Bardy et al., 2016; Barlow et al., 2016; Kalaiah, 2018). Only broadband acoustic stimuli are used in ABR as they activate the largest area of the cochlear basilar membrane, which generates a synchronous firing of action potentials in the auditory neurons (Carricondo & Romero-Gómez, 2019). The tonotopic nature of the basilar membrane guides the high frequency components of click stimuli to the basilar end of the cochlea first, followed by a several millisecond delay of the low frequencies, a phenomenon referred to as the cochlear travelling wave delay (McNaughton & Papert, 1971). As the basal end of the cochlea is stimulated first, a consensus within the literature states responses of click-ABR mostly reflect regions at 2000 Hz and above, even though clicks are classified as broadband (Gorga et al., 2006; Gorga et al., 1985; Hyde & Blair, 1981; Jerger & Mauldin, 1978; Van Der Drift et al., 1987). While the whole cochlear region is activated when presented with a click, contribution from the apical end is represented to a lesser extent due to phase cancellation of activity from the high frequency basal end (Don et al., 2005).

With the advent of rising frequency chirps, the cochlear travelling wave delay can be overcome by presenting lower frequencies first, followed by higher frequencies (Chertoff et al., 2010; Fobel & Daub, 2004). This stimulates both the apical and basal ends of the basilar

membrane simultaneously, thus achieving maximum neural synchronicity (Riedel & Kollmeier, 2002). The resultant increase in neural synchrony has been shown to produce higher wave I and wave V amplitudes (Dau et al., 2000; Elberling & Don, 2008; Fobel & Daub, 2004; Morimoto et al., 2019). Shore and Nuttall (1985) applied this concept to tone-burst stimuli, with the same cochlear delay compensation observed.

1.6.2 Latency and Amplitude

Peak latency is the time, in milliseconds (ms), from the onset of the stimulus to the appearance of the peak voltage, which is wave V for ABR and the P1-N1-P2 complex for CAEPs (Baydan et al., 2019; Don, 2007). The amplitude of a wave response is measured in microvolts (μV) from peak to peak (i.e., the distance in μV from peak to trough). Latency represents the speed of transmission of the acoustic stimulus, whilst amplitude represents the number of neurons firing and the scale of the response (Hall, 2006; Kochanek et al., 2015). The interaural difference is also a significant interpretative measure for the ABR (Aihara et al., 2013; Hsu & Lin, 1998). The interaural difference, also known as IT5, is the difference in wave V latency between the ears. A key indicator during neurological ABR testing, the IT5 as it is a significant marker to diagnose unilateral retrocochlear pathologies (Cueva, 2004; Don, 2007; Don et al., 1997).

Measures of amplitude can have large inter-subject variability, meaning they are not as strong diagnostic indicators as latency (Hall, 2006; Sand & Saunte, 1994). Particularly with CAEP testing, the amplitudes of the P1-N1-P2 complex are highly correlated, whereby one peak affects the next. Therefore, the three amplitudes in the P1-N1-P2 complex are labelled and examined as follows: P1 amplitude, P1-N1 amplitude and N1-P2 amplitude. Factors influencing amplitude of responses also include, intensity of stimuli, state of arousal and electrode placement (Bidelman, 2015). For example, drowsiness during CAEP testing leads to a reduced P1-N1 amplitude but an increased N1-P2 amplitude. By contrast, having an alert status has been evidenced to produce a larger P1-N1 and smaller N1-P2 amplitudes (Crowley & Colrain, 2004). For ABR, a sleep-like or sedated state produces clearer responses and larger amplitudes (Aoyagi, 2010).

1.6.2.1 **ABR Latency**

Wave V is the main diagnostic indicator for ABR as it is generally the largest of the ABR wave responses and is the last of the wave responses to disappear (Kochanek et al.,

2015). Burkard (1991) found wave V to be the only consistent peak to identify with both click and tone-burst stimuli. The expected latency of the wave V ABR response occurs at approximately five to six milliseconds following the presentation of the stimulus for adults with normal hearing (Starr, 1976).

For individuals with cochlear pathologies, specifically sensorineural hearing loss, the expected latency and amplitude is expected to increase progressively regardless of whether the stimulus rate is fast or slow (Alhussaini et al., 2018; Almadori et al., 1988; Arslan et al., 1988; McCreery et al., 2015). However, for those with retrocochlear pathologies, the rate of response and latency of wave V has been shown to increase more rapidly with faster stimulus rates (Bauch et al., 1981; Kochanek et al., 2015; Pratt et al., 1981). This has diagnostic implications when recording ABRs from these individuals, as the latency of wave V is a significant diagnostic indicator, particularly when establishing hearing thresholds (Campbell & Abbas, 1987).

1.6.2.2 CAEP Latency

CAEPs typically occur approximately 100ms after the onset of a stimulus in adults (Agung et al., 2006). In the order of evoked potentials, CAEP is a sequence of peak responses which are categorised by their polarity and order of occurrence. The P1-N1-P2 complex is most commonly used for CAEP interpretation in the literature (Campbell et al., 2011; Sharma et al., 2005).

The P1 represents a small positive wave occurring approximately 100ms after stimulus onset for adults with normal hearing (Abraham et al., 2017; Sharma et al., 2005). This is followed by the wave's negative component, labelled N1, with the subsequent positive and negative peaks labelled P2 and N2 (respectively) occurring up to 250ms after stimulus onset (Gilley et al., 2005; Hall, 2006). In the paediatric population, the wave response is largely dominated by the positive P1 peak (occurring at approximately 100 to 250ms) followed by a late negativity response between 250ms and 400ms (De Oliveira et al., 2017; Gilley et al., 2005). As CAEPs mature, the prominence of the response shifts from P1 and N2 to be predominately dominated by the N1 and P2 peak responses in adults (Lightfoot, 2016).

1.6.3 Morphology

Wave morphology refers to the shape of the wave response. In addition to the quantitative measures of latency and amplitude, the shape of the waveforms and ease of identification of diagnostic markers is a significant analytic element (McKnight et al., 2018). The type and intensity of the stimulus, stimulus rate and SNR all have an effect on the resulting waveforms (Ballachanda et al., 1992; Valderrama et al., 2013). For example, Figures 6 and 7 show the difference in morphology between the slow and fast stimulus rates from a previous project by Bencito (2020) and the study by Pratt et al. (1981). In particular, the difference in morphology between the slow and fast rates is noticeable, with the waveform evoked by a fast stimulus rate showing less defined peaks and overall clarity of shape. Although morphology is not a quantitative measure, it is a valuable interpretation and analysis tool for the observant and experienced examiner/clinician (Hood, 2015).

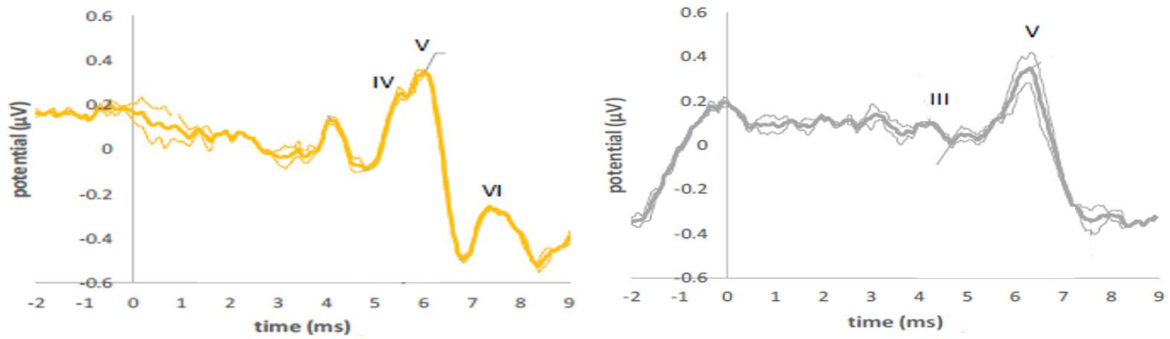


Figure 6

Comparison of ABR Stimulus Slow Rate at 45.5 Clicks per Second (left, yellow) and Fast Rate at 90.9 Clicks per Second (right, grey) (Bencito, 2020)

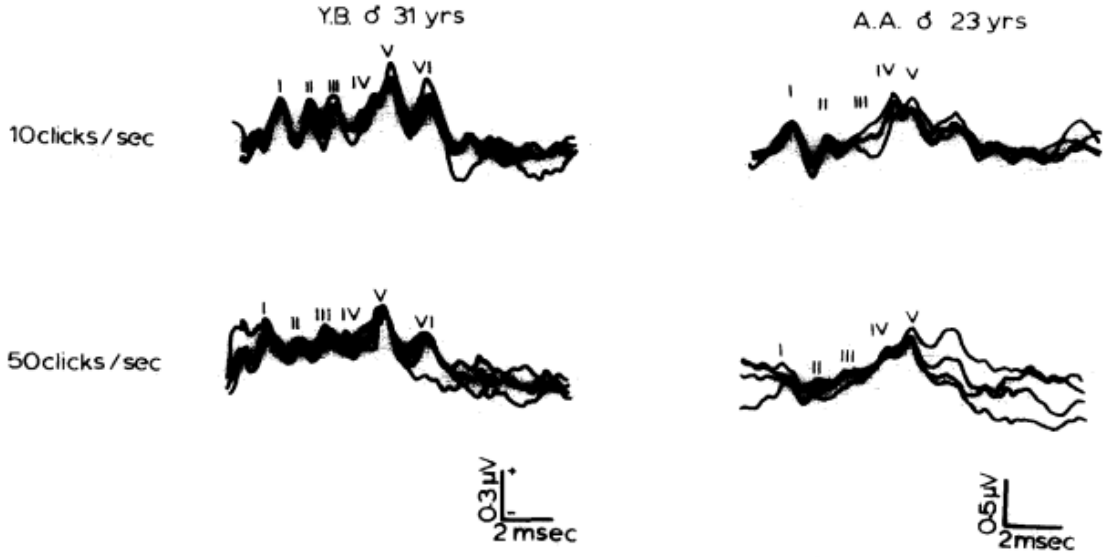


Figure 7

ABR of two Normal Hearing Participants at a Slow Rate of 10 Clicks per Second (top) and Fast Rate of 50 Clicks per Second (bottom)(Pratt et al., 1981).

1.7 Stimulus and Acquisition Parameters

The ABR is an obligatory exogenous response as it is highly dependent on the external factors of stimulus parameters (Aoyagi, 2010). CAEPs are also exogenous responses but are additionally considered endogenous non-obligatory responses as they also rely heavily on the state and attention of the individual (Bach et al., 2014; Pike et al., 2020). Therefore, specific stimuli parameters are required to achieve best results for each. Many stimulus parameters contribute to effective AEP recordings. Parameters for consideration include stimulus presentation rate (e.g.: fast or slow), frequency and intensity of stimulus, minimal noise level and rejection criteria.

1.7.1 Stimulus Type

In ABR testing, broadband stimuli is used as it activates the widest range of the basilar membrane, leading to synchronous firing of neurons at the onset of the acoustic stimulus (Sininger & Don, 1989). Clicks, chirps and tone-bursts are most commonly used in ABR hearing threshold seeking and estimation (Burkard & Sims, 2001; Sininger, 1993). While chirps and clicks are unable to be used for frequency specific threshold estimation,

frequency of the stimulus can be specified using tone-bursts. This is currently the protocol used for estimating hearing thresholds using ABR during the diagnostic assessment of newborn infants and the younger paediatric population in several countries including New Zealand, Australia, Canada and the United Kingdom, among others (Healthy Hearing Programme, 2016; King, 2010; National Screening Unit, 2016; Rennert et al., 2012; Stevens et al., 2007). Clicks are typically used for those with retrocochlear pathologies (Hoth, 1991), with tone-bursts also showing to have more sensitivity in detecting smaller tumours (Antonelli & Grandori, 1984).

Despite the increase in the synchronisation of neural firing achieved by chirp stimuli, traditional ABR uses click stimuli and this is still the suggested protocol when testing for retrocochlear pathologies (Don, 2007). This could be due to the fact that most commercial ABR software does not have chirp stimuli readily available for clinical use. Additionally, while evidence has shown the benefits of using chirps, click stimuli still has clinical and diagnostic value, providing an overview of hearing, possible pathologies and a general estimation of hearing thresholds in a matter of minutes (Lu et al., 2017). Furthermore, the validation of chirp ABR as a diagnostic tool has not been explored or researched thoroughly, and certainly not to the extent of click and tone-burst ABR (Cobb & Stuart, 2016). Therefore, the majority of protocols do not incorporate chirp stimuli. This lack of inclusion of chirp stimuli in ABR protocols is perhaps the most significant factor, as ABR protocols for both adult and paediatric populations focus on click and tone-burst stimuli (Bagatto et al., 2010; Healthy Hearing Programme, 2016; King, 2010; Rennert et al., 2012). For the purposes of this research, the focus is on the method of ABR testing, regardless of the type of acoustic stimulus used.

Contrary to the ABR, CAEPs can be evoked with speech stimuli, in addition to clicks and tone-bursts (Almeqbel, 2013; Alvarenga et al., 2013; Bardy et al., 2016; Barlow et al., 2016; Kalaiah, 2018). CAEPs have even been evoked visually using flash stimuli (Achimowicz, 1995). Different types of speech stimuli can be used to evoke CAEPs, including vowels, syllables and words (Billings & Grush, 2016; Carter et al., 2013; Doellinger et al., 2011; Roque et al., 2019). Speech-evoked CAEPs are particularly used in the validation of paediatric amplification (Bakhos, Delage, et al., 2014), as well as in cognitive research, as demonstrated in a study by Agung et al. (2006) looking at the processes of neural speech encoding in adults, among other uses (Alvarenga et al., 2012; Bakhos, Bonnet-Brilhault, et al., 2014).

Early investigations of CAEPs have used tonal stimuli, such as tone-bursts (Davis et al., 1968). As CAEPs are generated higher along the ascending auditory pathway, they are most effectively elicited with longer duration stimuli compared to the ABR (Billings & Grush, 2016). The duration of the stimulus can be determined with rise and fall times. Rise and fall times refer to the time taken for a stimulus to reach its highest and lowest values (or wave peaks, respectively (Ushio et al., 2001). Clicks used in ABR testing are transient and have shorter durations (Hall, 2006; Suzuki & Horiuchi, 1981). The recommended rise and fall times for tone-burst stimuli in ABR is less than two milliseconds (Hatliński et al., 2008; Suzuki & Horiuchi, 1981), with speech stimuli having a rise and fall time of up to 100 ms (Purdy et al., 2005). CAEP stimulus rise and fall times of over 10 ms and even over 20 ms yielding the most effective responses (Billings et al., 2007; Punch et al., 2016), with a maximum of 50 ms rise/fall time and 30 ms stimulus duration (Antonelli & Grandori, 1984). Frequency specific tone-bursts are therefore ideal to use with CAEPs as a longer rise and fall time can be determined, producing stimuli that produce synchronous firing with sufficient durations and length of presentation.

Larger stimuli intensities generate larger wave responses in AEPs (Kaf et al., 2017; Pedriali & Kozlowski, 2006). The amplitude of wave responses is typically larger with the use of speech stimuli, whereas the latency occurs earlier when using pure tones (May et al., 1999; Tiitinen et al., 1999). Several ABR protocols recommend starting with high intensity clicks to visualise the wave V response, then gradually decrease the intensity until the audibility threshold is found (Bagatto et al., 2010; Rennert et al., 2012).

1.7.2 Stimulus Repetition Rate and Inter-Stimulus Interval

The rate at which the stimulus is presented is a major parameter during ABR testing. This can be categorised/referred to as the stimulus repetition rate (SRR), referring to how often the stimulus is repeated per second. For transient stimuli, the interval between the successive presentation of stimuli can be determined by dividing a selected time period by the time it takes to present stimuli. This is the inter-stimulus interval (ISI), the time between the end of one stimulus and the presentation of the next, measured in milliseconds (Sharma, Johnson, et al., 2014; Valderrama et al., 2013). SRR presented at the level of the ear is referred to as the peripheral rate, with the total rate from binaural stimulation at the levels of the brainstem and cortex represent central rates. The total central rate at the auditory cortex may depend on whether the acoustic stimulus was presented monaurally or binaurally

(Polyakov & Pratt, 2003). For example, presenting an ABR click at a peripheral rate of 45.45 clicks per second (or an ISI of 22 ms) binaurally means the auditory cortex receives the sum of this information from both ears, which is at a rate of 90.91 clicks per second. Therefore, the central rate will be 90.91 clicks per second, with the peripheral rate being 45.45 clicks per second. When the same stimulus is presented monaurally, the central rate remains the same at 90.91 clicks per second, but the peripheral rate doubles to 90.91 clicks per second, as the stimulus is being presented to one ear only rather than being split and presented to both ears simultaneously (Bencito, 2020).

The time-consuming nature of conventional AEPs is a major drawback for their clinical use, with the shorter SRR (longer ISI) and monaural testing being significant contributors to this (Agung et al., 2006; Gorga et al., 2006). Currently, a relatively long ISI is utilised to ensure best wave morphology for diagnostic purposes, which leads to longer test times (McKnight et al., 2018; Sakai et al., 1989). A logical solution to this would be to adopt a faster SRR and shorter ISI, with the assumption that the target number of averages would be reached quicker with less time between consecutive stimulus presentations and more stimuli presentations per second (e.g., more clicks per second). Don et al. (1977) compared click-evoked ABR at increasing SRR and found an increase in latencies and poorer waveform morphology at rates over 60 clicks per second. Various studies have also found the implementation of a faster SRR and testing both ears simultaneously to significantly reduce the diagnostic properties of the wave response (Burkard & Sims, 2001; Čeponien et al., 1998; Kochanek et al., 2015; Petoe et al., 2009). As discussed earlier in section 1.4, this is due to neural adaption in the peripheral auditory system, leading to a depletion in neurotransmitter and reduced neural activity and synchronicity (Fowler & Noffsinger, 1983). The current project will explore the effect that binaural interleaving with shorter ISI and longer SRR will have on the latency and morphology of wave responses.

1.7.3 Polarity

The initial electrical deflection of AEP stimuli is referred to as the polarity of the stimulus and can consequently affect the polarity of the resultant wave response. A positive electrical signal pushes the diaphragm of the transducer towards the tympanic membrane, resulting in a positive pressure wave known as condensation (Hall, 2006). A negative electrical signal results in movement of the transducer diaphragm away from the tympanic

membrane and is referred to as rarefaction. Alternating is a third polarity category, switching between condensation and rarefaction stimuli presentations.

Early investigations into polarity for click stimuli revealed shorter ABR wave V latencies with condensation clicks (Borg & Löfqvist, 1982; Coats & Martin, 1977; Pijl, 1987). Subsequent studies have provided contradicting evidence, with some finding no difference in latency due to polarity (Beattie, 1988; Fowler et al., 2002; Sand, 1991) and others finding shorter latencies with rarefaction stimuli (Emerson et al., 1982; Kevanishvili & Aphonchenko, 1981; Ornitz & Walter, 1975). Current evidence suggests the latter to be most accurate, as neural firings are triggered by the negative rarefaction cycle of a stimulus, resulting in larger amplitudes and shorter latencies (Fowler et al., 2002).

1.8 Monaural Testing of Auditory Evoked Potentials: The Gold Standard

Monaural testing with a relatively slow SRR is the current gold standard for AEP testing, including ABR and CAEPs (Aoyagi, 2010; Billings, 2013; Lajtman et al., 2002). It yields wave responses with clearer morphologies, shorter latencies and larger amplitudes, allowing AEPs to be used as valuable clinical tools for diagnosis and validation of aural services. This is especially true when compared with faster presentation rates, which lead to neural adaptation, fatigue and overall poorer morphology of diagnostic indicators (Morimoto & Sakabe, 2006).

Despite its advantages and clinical functionality, test time remains a major drawback with the use of monaural AEP testing (Bance et al., 1994; King, 2010). As AEP testing, particularly the ABR, is mostly used with infants and the paediatric population, test time relies on how long the child can stay asleep and/or remain still and quiet (Rennert et al., 2012). As such, test time is frequently cut short due to the unpredictable duration of each child's sleep/quiet time, thereby requiring several sessions for testing to be complete. Additionally, clinicians typically must infer diagnostic decisions based on the limited data they managed to acquire. As a fallback option, sedation may be required if data is unable to be acquired or if the child is older and unlikely to sleep during testing (Polonenko & Maddox, 2019).

Therefore, decreasing the time taken to complete ABR and CAEP testing could not only lead to better patient outcomes, it will also likely reduce the clinical resources needed to complete testing. As discussed earlier, using fast stimulus rates as a means of reducing test time leads to poorer diagnostic results (Pedriali & Kozlowski, 2006). Another way of

reducing time is to utilise bilateral testing, whereby stimuli is presented to both ears simultaneously. However, this approach hinders the interpretation of results as separation between the left and right ear wave responses becomes challenging and leads to inaccuracies (Maruthy et al., 2018). Therefore, a technique is needed which simultaneously reduces test time whilst maintaining a quality of wave responses and waveform morphology.

1.9 Interleaved Testing of Auditory Evoked Potentials

A solution for the time-consuming nature of AEP testing was proposed by Bidelman (2015), who explored testing both ABR and CAEP simultaneously. While the findings of this study were promising in favour of this simultaneous testing technique, it is rare to need both of these tests simultaneously in clinical settings. Research into the interleaved method of recording AEPs is very scarce thus far, with the focus of studies being on interleaving different stimuli characteristics and frequencies in the same ear rather than between the ears. An example of this is the Polonenko and Maddox (2019) study, which explored the interleaving of 50 dB tone-bursts at five frequencies, by utilising parallel presentation to each ear. Their findings indicate the efficacy of this technique as a means of saving time during ABR testing and are supported by studies such as Buran et al. (2020).

As monaural testing has been validated as a gold standard, the exploration into binaural testing has been overlooked (Aoyagi, 2010; Billings, 2013; Lajtman et al., 2002). While having monaural protocols for the recording of AEPs allows these tests to be utilised, the time taken to complete these tests remains a drawback. Simultaneous bilateral testing would result in a single binaural AEP response and thus differentiation between the two ears would become difficult (Maruthy et al., 2018). Additionally, binaural ABR testing to improve time efficiency is a significantly under researched area, with most ABR research focusing on stimulus type and rate to reduce test time (Burkard et al., 1990; McKnight et al., 2018; Pratt et al., 1981; Riedel & Kollmeier, 2002).

Thus far, no research has delved into the prospect of binaural CAEP testing with the use of interleaved or similar techniques, while binaural ABR testing has been recently explored in the past few years. To date, only one peer reviewed study has looked at a similar concept. Recently, Maruthy et al. (2018) introduced an ABR testing method which involves simultaneous binaural testing by rapidly alternating stimuli between the ears, a technique they termed ‘bilateral simultaneous ABR’ (BiSi-ABR). They used a repeated measures design with 25 young adults with normal hearing who underwent ABR testing using the

conventional method and their proposed BiSi ABR technique, with promising results. Using a click rate of 30.1 clicks per second (central rate of 60.2 clicks per second, Maruthy et al. (2018) found the wave III and wave V latencies and morphologies recorded with the BiSi-ABR method were comparable to that of conventional ABR testing, while being recorded in almost half the time as conventional ABR. These findings were observed down to intensities of 10 dB nHL (Figure 8).

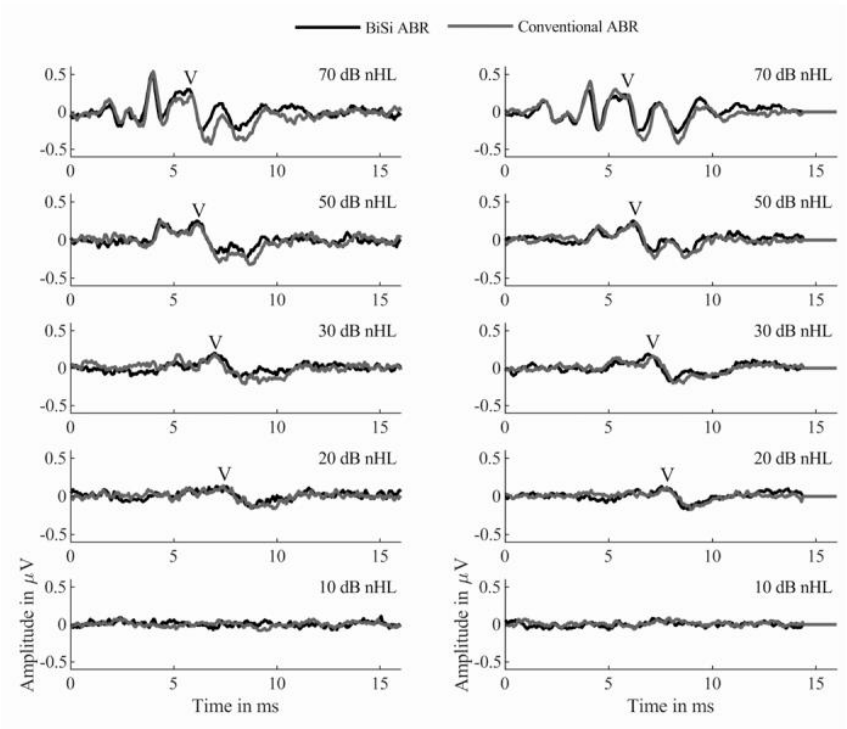


Figure 8

ABR Waveforms using BiSi Technique (Maruthy et al., 2018)

Another recent project by Bencito (2020) looked at the same interleaved ABR method that is proposed for this project. Using the 'Te Pihareinga' software developed by O'Beirne ((2015) at the University of Canterbury, Bencito (2020) tested 20 normal hearing adults under three conditions: monaural slow (central rate the same as conventional ABR), monaural fast (central rate equivalent to that of interleaved recordings) and the interleaved condition. He also examined the effects of using three stimulus repetition rates under each condition: 90.91, 76.92 and 45.45 clicks per second. Analysis of the latency of wave V with all three rates revealed no significant effect of rate on the latency results. That is, longer latencies were found in the fast condition when compared to the slow and interleaved conditions, for each of

the three SRR used. Additionally, no significant difference in wave V latency was found between the slow and interleaved conditions, for all three stimulus rates used.

Similar to Maruthy et al.'s results, the wave V latency in the interleaved condition was comparable to that of the monaural slow, with signifcant time savings with interleaved ABR. Wave V latencies were significantly shorter, and morphology significantly clearer, in the interleaved condition compared to the monaural fast ABR. Subsequently, he also found that using the fastest rate of 90.91 clicks per second would be the most clinically time efficient rate to use during ABR, without comprising the diagnostic analysis of wave V. This is thought to be because rapidly interleaving the test stimulus is assumed to activate the neural pathways separately. Hence, stimuli presented to each ear stimulate separate neural populations, reducing the effects of neural adaptation (Burkard et al., 1990; Thornton & Coleman, 1975).

Overall, research around the concept of the interleaved technique, albeit limited, shows favourable latency and morphology results of ABR wave responses with the same quality as the gold standard of conventional ABR. Additionally, interleaved testing has promising potential at improving test time efficiency. This project follows on from Bencito's (2020) research by extending it to CAEP, using the 'Te Pihareinga' software to compare the latency and morphology of wave responses between conventional and interleaved ABR and CAEP. It aims to investigate whether the benefits of interleaved ABR found by Bencito (2020) and Maruthy et al. (2018) carry over to interleaved CAEP.

1.10 Statement of Purpose

The primary objective of this study was to explore whether utilizing rapidly interleaved binaural stimuli in adults can increase ABR and CAEP testing efficiency and time when compared to typical monaural testing procedures. The primary research question is: in the ears of adults with normal hearing, are the latencies and waveform morphology of ABR and CAEP significantly affected by the "interleaved" condition? The secondary research question is: in the ears of participants with normal hearing, is there a significant difference in latencies of ABR and CAEP peak wave responses between the "monaural slow" and "interleaved" conditions? The final research question is: does the peripheral neural adaptation seen at the level of the brainstem during ABR testing extend to the cortex in CAEP? As the fastest rate used by Bencito (2020) of 45.45 per second in each ear was shown to be as

effective as the slower rates trialled, this was chosen to be used as the peripheral rate for the monaural slow and interleaved conditions.

The comparisons in the above research questions will involve evaluating the morphology, latencies and amplitudes of wave V for ABR and the P1-N1-P2 complex for CAEPs, for all three conditions. ABR and CAEP testing will occur under three conditions:

- The "interleaved" condition: stimuli are presented in the right then the left ear at an overall rate of 90.9 per second (45.45/s in each ear) for ABR and 2.009/s (1.0045/s in each ear) for CAEP (note: for simplicity, these two rates will be referred to hereafter as 2/s and 1/s).
- The "monaural slow" condition: stimuli are presented in the right ear at the slow stimulus overall rate of 45.45/s for ABR and 1/s for CAEP.
- The "monaural fast" condition: stimuli is presented in the right ear at an overall rate of 90.9/s for ABR and 2/s for CAEP.

1.10.1 Null Hypotheses

The null hypotheses for the research questions above are as follows:

1. Wave V amplitudes and latencies are not significantly affected by the "interleaved" conditions.
2. There is no significant difference in wave V latencies between the ears with the "monaural slow" versus the "interleaved" conditions.
3. There is no significant difference in wave V latencies between the ears with the "monaural slow" versus the "monaural fast" conditions.
4. There is no significant difference in wave V latencies between the ears with the "monaural fast" versus the "interleaved" conditions.
5. The P1-N1-P2 amplitudes and latencies are not significantly affected by the "interleaved" condition.
6. There is no significant difference in the P1-N1-P2 latencies between the ears with the "monaural slow" versus the "interleaved" conditions.
7. There is no significant difference in the P1-N1-P2 latencies between the ears with the "monaural slow" versus the "monaural fast" conditions.
8. There is no significant difference in the P1-N1-P2 latencies between the ears with the "monaural fast" versus the "interleaved" conditions.

9. The mean Fsp will not be significantly different with the “monaural slow” versus the “monaural fast” conditions for both ABR and CAEP recordings.
10. The Fsp will not be significantly different with the “monaural slow” versus the “interleaved” conditions for both ABR and CAEP recordings.
11. The Fsp will not be significantly different with the “interleaved” versus the “monaural fast” conditions for both ABR and CAEP recordings.

1.10.2 Expected Findings

The expected findings and directional hypotheses for this study are as follows:

1. Wave V amplitudes and latencies will not be significantly affected by the “interleaved” conditions.
2. There will be no significant difference in wave V latencies between the ears with the “monaural slow” versus the “interleaved” conditions.
3. Wave V latencies will be significantly shorter with “monaural slow” versus the “monaural fast” condition.
4. Wave V latencies will be significantly longer with the “monaural fast” versus the “interleaved” condition.
5. The P1-N1-P2 amplitudes and latencies will not be significantly affected by the “interleaved” condition.
6. There will be no significant difference in the P1-N1-P2 latencies between the ears with the “monaural slow” versus the “interleaved” conditions.
7. The P1-N1-P2 latencies will be significantly shorter with the “monaural slow” versus the “monaural fast” condition.
8. The P1-N1-P2 latencies will be significantly longer with the “monaural fast” versus the “interleaved” condition.
9. The mean Fsp will be significantly higher with the “monaural slow” versus the “monaural fast” conditions for both ABR and CAEP recordings.
10. The Fsp will not be significantly different with the “monaural slow” versus the “interleaved” conditions for both ABR and CAEP recordings.
11. The Fsp will be significantly higher with the “interleaved” versus the “monaural fast” conditions for both ABR and CAEP recordings.

Chapter 2: Methods

This research was approved by the Human Ethics Committee of the University of Canterbury, New Zealand (Reference: HEC 2021/34; see Appendix A). An application was also accepted by the Ngāi Tahu Consultation and Engagement Group for consultation around accommodating the cultural needs of potential Māori participants (see Appendix B).

2.1 Measures

The dependent variables for this project were the peak latencies, measured in milliseconds (ms), of wave V, P1 peak, N1 trough, and P2 peak. This includes the wave V, P1, P1-N1 and N1-P2 amplitudes, measured in nanovolts from peak to peak (μV pp). an additional dependent measure of quality of recordings is the Fsp.These continuous variables at the ratio levels of measurements. Therefore, parametric statistical testing will be used. The independent variables for this project were the three test conditions, which were “monaural slow”, “monaural fast” and “interleaved”, participants’ age and gender, and hearing thresholds.

2.2 Research Design

A quantitative within-subject, repeated measures design was used for this study. certain parts of this study required visual and subjective analysis. So while it is rare for a study to be wholly quantitative, this project is characterised as such as it relies on empirical data to support findings (Verma, 2015). Participants served as their own control with the “monaural slow” condition, in addition to undergoing the remaining two test conditions of “monaural fast” and “interleaved”, and all participants repeated testing under the three conditions (Verma, 2015). Furthermore, not only did this design require fewer participants, but it also reduced the chances of significant differences across test conditions going undetected, unreported or being obscured by 'random noise' in the data (Hegde & Salvatore, 2019). The order of testing conditions has been divided into six sequences, which were used in randomised order to account for any possible order effects (see Table 1).

Table 1

Sequences of the Randomised Order of Presentation of Test Condition Sequences

Sequence Number	Order of Presentation of Test Condition
Sequence One	Interleaved → monaural slow → monaural fast
Sequence Two	Interleaved → monaural fast → monaural slow
Sequence Three	Monaural slow → monaural fast → interleaved
Sequence Four	Monaural slow → interleaved → monaural fast
Sequence Five	Monaural fast → monaural slow → interleaved
Sequence Six	Monaural fast → interleaved → monaural slow

2.3 Recruitment and Eligibility

The target smaple size was calculated using the G*Power 3.1.9.7 calculator (Faul et al., 2009). An assumed alpha level of 0.05 was used, with a power of 0.80 and a medium effect size of 0.5 (Haynes & Johnson, 2009; Verma, 2015). The minimum sample size was determined to be six for both ABR and CAEPs (calculations shown in Figure 9 and Figure 10, respectively).

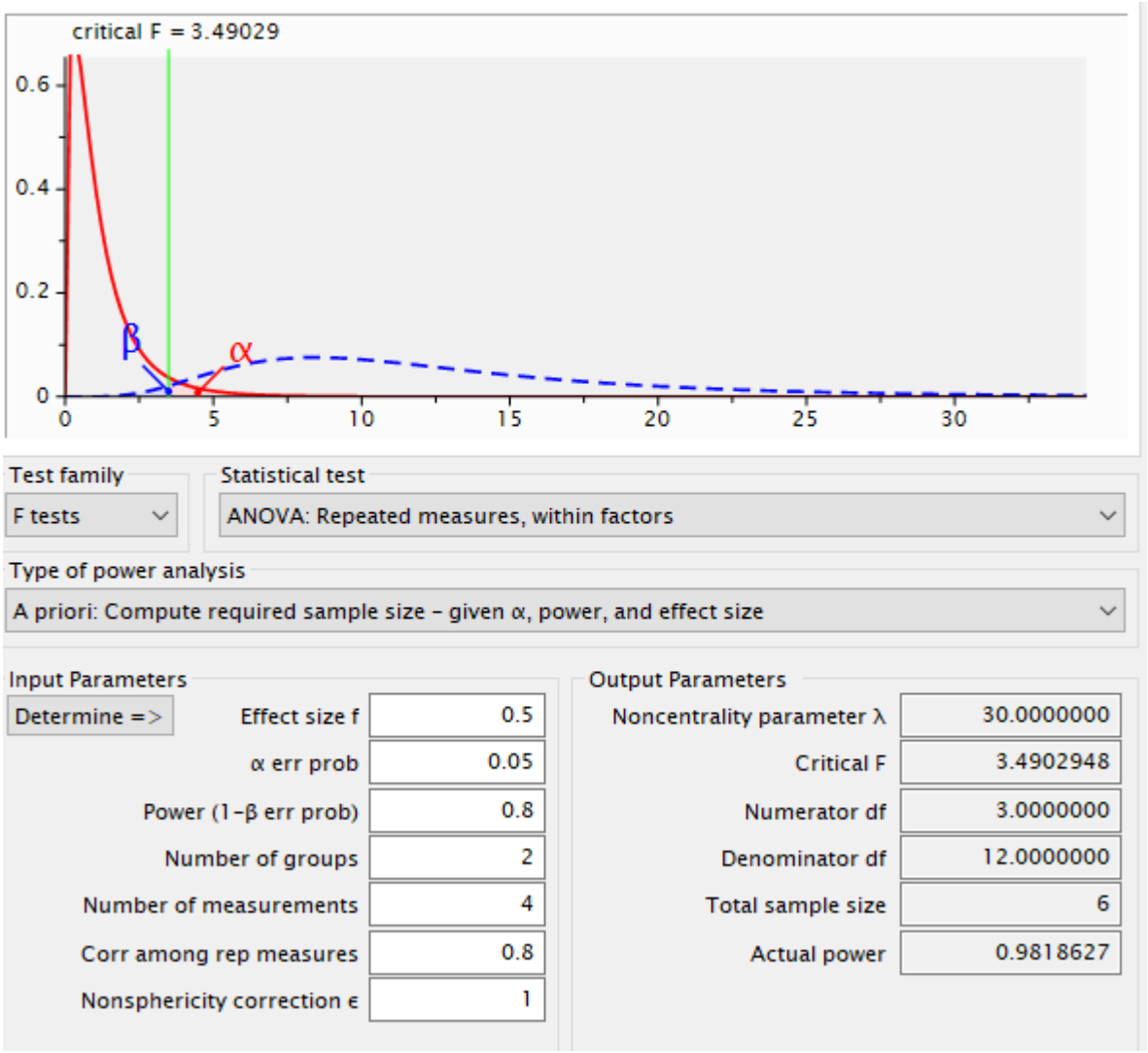


Figure 9

*Screenshot of G*Power Calculation of Minimum Sample Size for ABR*

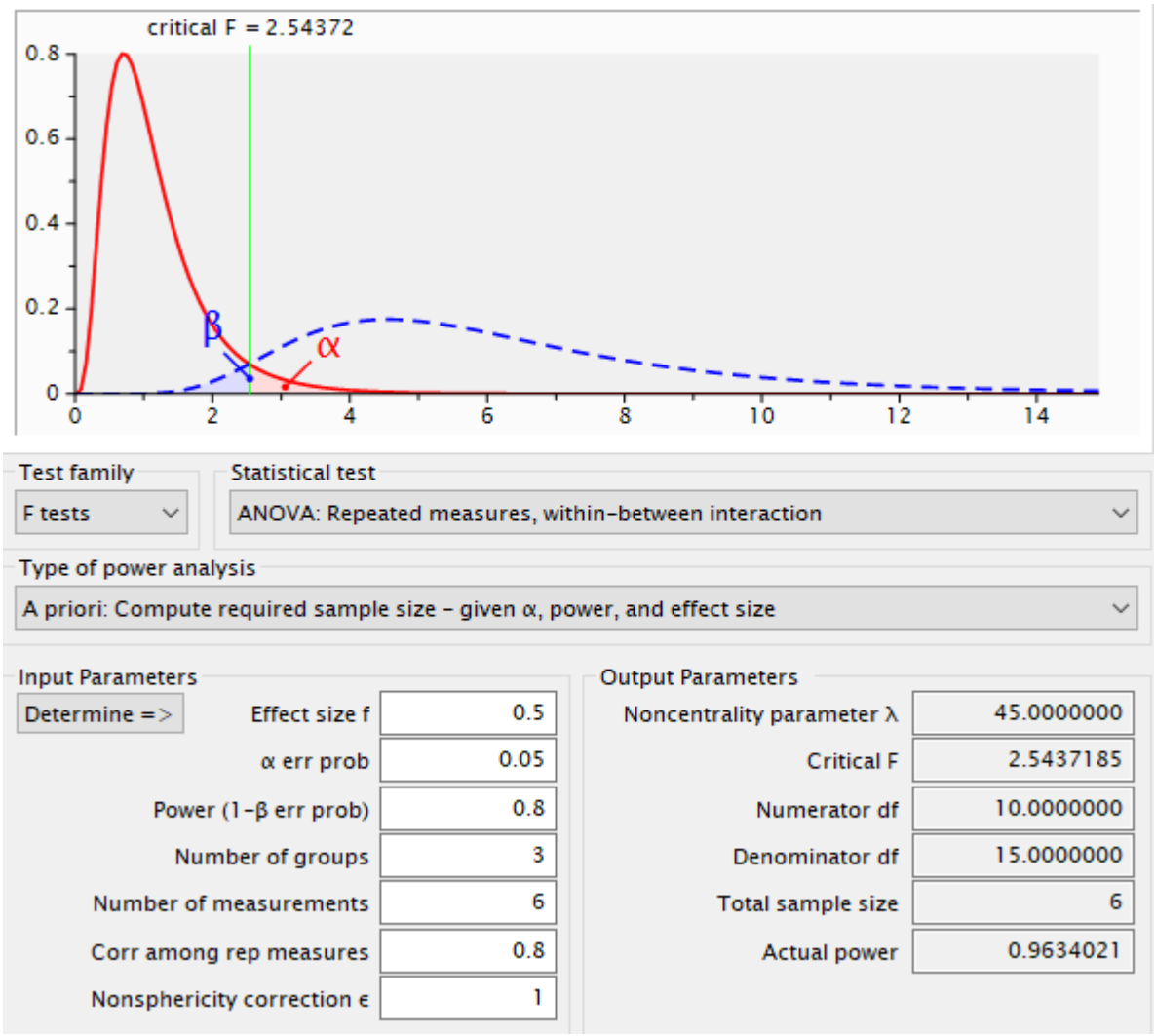


Figure 10

*Screenshot G*Power Calculation of Minimum Sample Size for CAEPs*

Participants were recruited via word of mouth and print advertising around the University of Canterbury Campus and local community boards, etc. (see Appendix C). The inclusion criteria were adults over the age of 18 years old were recruited, with normal hearing or a sloping, sensorineural hearing loss no worse than mild severity. This was to ensure the intensity of acoustic stimuli would be supra-threshold in order to achieve noticeable results for comparison. Therefore, hearing thresholds which were moderately-severe or higher were excluded. Prior to participation in the study, participants were given an information sheet outlining the details of the study (see Appendix D) and were given the opportunity to raise any questions or concerns. Next, written informed consent was given by participants (see Appendix E). Audiological assessment at the University of Canterbury Audiology Clinic was

performed to determine hearing thresholds. This consisted of a brief case history to rule out significant medical, surgical and noise-exposure history, followed by otoscopy, tympanometry and pure-tone audiometry. Participants who had audiograms less than 6 months old did not need to undergo another hearing assessment. Participants were thanked for their time with a $20 MTA voucher.

2.4 Equipment Setup

Recordings were obtained, measured and processed using the custom software ‘Te Pihareinga’ (O'Beirne & Bird, 2015), which was run on an HP laptop. This software was capable of implementing pre-programmed sequences using different settings. Additionally, settings such as test type, stimulus type, frequencies, intensities, durations, rise/fall time, interstimulus interval and polarity could be changed between recordings. Acoustic stimuli were produced by the system’s NI 9269 module. Stimuli were then amplified by a Rolls Stereo Mini-mix VI sound amplifier and passed to the E-A-RTONE insert earphones, while the NI 9222 module recorded the output from the CED1902 Mk III biological amplifier, to which the participants were connected (Figure 11). Figures 12 and 13 show screenshots of the configuration and parameters in the ‘Te Pihareinga’ software. The recoding windows included two milliseconds pre-stimulus onset for ABR and 100ms pre-stimulus for CAEP.

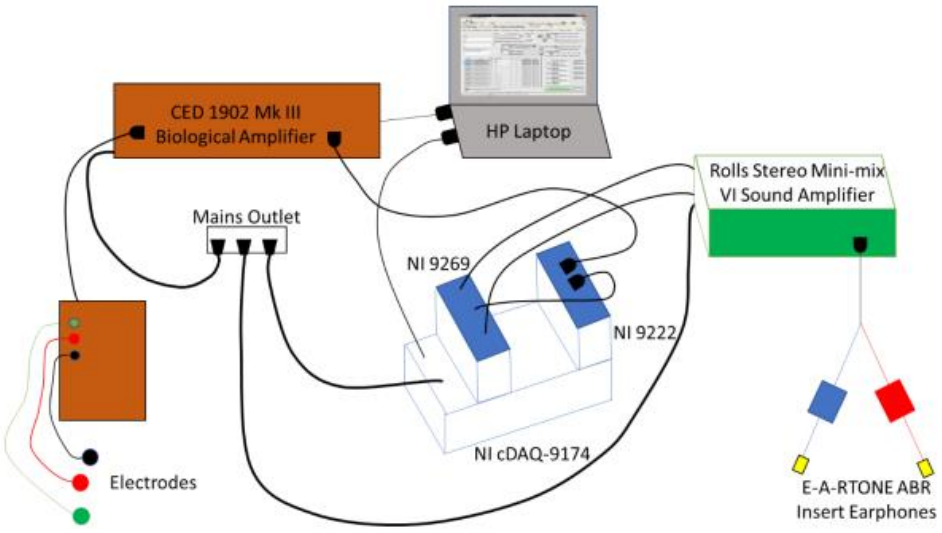


Figure 11

Schematic Diagram of Equipment Setup

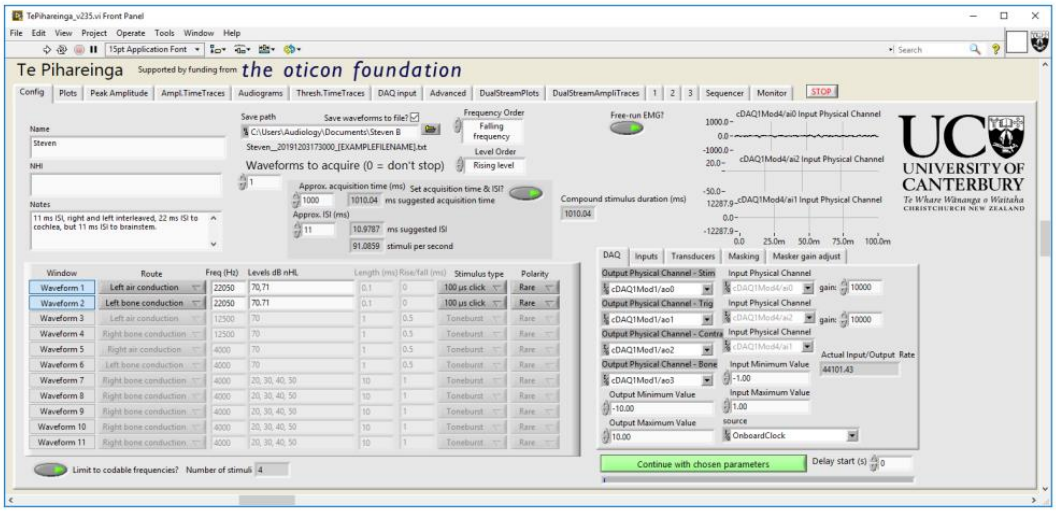


Figure 12

Screenshot of the 'Te Pihareinga' Software Showing the Main Configuration Page

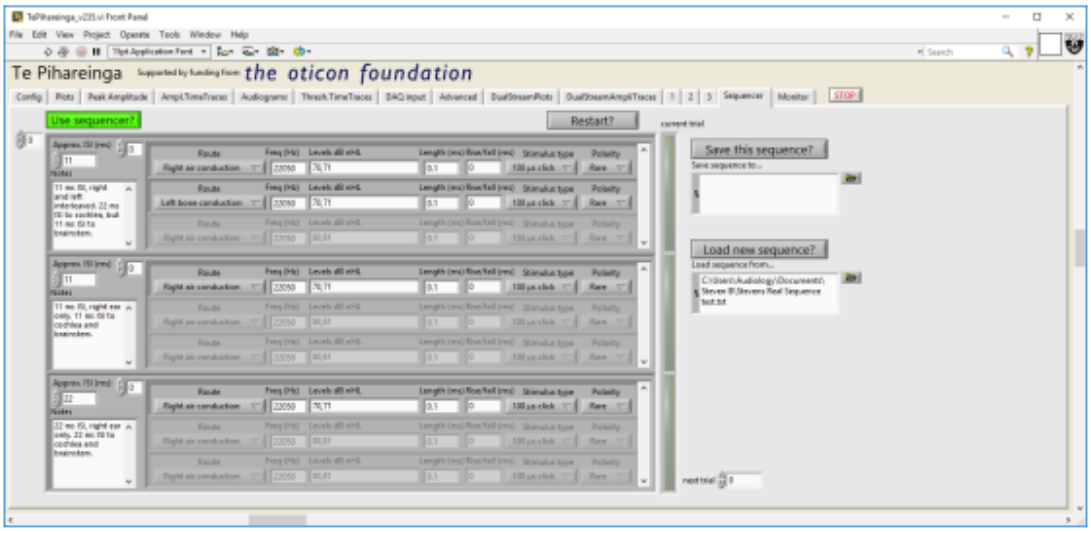


Figure 13

Screenshot of the' Te Pihareinga' Software Showing the Sequencer Feature

2.5 Participants

A total of 44 eligible volunteers aged 18 to 63 years participated in the study (M = 33, SD = 9.2), with 27 females and 17 males. Due to global circumstances throughout the duration of this study and some changes made to this thesis, only 10 participants were able to

participate in both ABR and CAEP testing at the time of recruitment. These participants are marked by an asterisk in Table 2 for ABR and Table 3 for CAEP. All participants had hearing thresholds at 40dB HL or better, Type A tympanograms indicating normal middle ear pressure and compliance, unremarkable otologic history and normal outer ear health as determined by otoscopic examination. Once eligibility was established, testing commenced.

Table 2

ABR Participants' Demographic Data, Audiometric Thresholds and Sequence of Test Conditions Used

Participants				Audiometric Air Conduction Thresholds in dB HL														
# ID	Sex	Age	Sequence	Right Frequencies (kHz)								Left Frequencies (kHz)						
				0.25	0.5	1	2	3	4	6	8	0.25	0.5	1	2	3	4	6	8
1	F	31	1	5	5	5	5	5	0	5	0	5	10	5	5	0	0	15	0
2*	F	36	2	5	5	5	10	10	10	20	10	0	0	5	10	10	5	15	15
3*	F	29	3	10	5	5	10	5	5	5	0	10	5	5	5	5	5	0	5
4	M	43	4	10	15	10	15	10	10	10	15	10	15	10	10	10	10	5	0
5	F	29	5	0	0	0	5	10	15	10	0	5	0	0	5	15	10	10	0
6	M	38	6	5	10	10	10	15	15	10	-5	15	10	10	15	15	15	15	5
7	F	32	1	5	10	10	10	10	5	10	0	15	10	10	5	15	15	25	15
8	F	33	2	5	10	10	5	15	5	0	0	5	10	5	10	5	5	0	-5
9	F	25	3	10	5	0	0	5	5	5	-5	10	10	15	15	15	15	10	-5
10	F	35	4	0	5	5	5	5	0	0	-5	0	0	10	5	5	0	0	0
11*	M	37	5	5	5	5	0	10	10	10	15	5	10	5	5	0	5	15	15
12	M	31	6	5	10	5	5	0	10	10	0	0	0	5	10	5	5	5	-5
13	F	27	1	0	0	0	10	15	15	10	-5	5	0	0	5	15	10	5	5
14	M	26	2	0	0	5	5	5	0	0	-5	0	5	5	0	5	0	0	-5
15*	F	26	3	5	5	5	10	0	10	10	5	10	10	10	10	5	0	0	5
16	F	19	4	10	10	10	20	15	15	10	5	5	5	10	20	10	15	15	-5
17	F	30	5	10	5	10	10	10	0	0	5	0	-5	5	0	10	0	0	-5
18*	F	37	6	15	15	10	0	5	5	15	15	10	10	5	5	0	15	15	25
19	F	25	1	-5	10	-5	0	0	-5	0	0	0	10	0	5	0	-5	15	0
20*	F	26	2	5	5	5	10	0	10	10	5	10	10	10	10	5	0	0	5
21*	M	19	3	10	0	5	10	15	15	15	0	5	0	0	5	5	0	0	0
22*	F	37	4	0	5	10	10	10	5	5	5	0	0	5	0	5	5	5	5
23*	M	23	5	-5	0	5	10	15	5	5	0	0	0	5	5	5	5	5	0
24*	M	30	6	5	5	5	5	5	5	10	10	5	5	5	10	5	10	10	10

* Denotes participants who took part in both ABR and CAEP testing.

Table 3

CAEP Participants' Demographic Data, Audiometric Thresholds and Sequence of Test Conditions Used

Participants				Audiometric Air Conduction Thresholds in dB HL														
# ID	Sex	Age	Sequence	Right Frequencies (kHz)								Left Frequencies (kHz)						
				0.25	0.5	1	2	3	4	6	8	0.25	0.5	1	2	3	4	6	8
1	F	45	1	5	10	20	20	25	15	25	30	5	10	20	20	20	25	20	30
2	F	63	2	10	15	20	15	20	20	15	15	20	20	20	20	25	20	30	30
3	M	46	3	15	15	15	20	15	20	15	15	15	15	15	20	20	15	10	10
4	M	30	4	5	10	10	5	5	10	5	5	10	10	10	5	5	15	0	0
5	F	33	5	10	10	10	10	0	0	0	0	10	10	5	10	10	10	0	10
6	F	21	6	0	5	15	0	5	5	5	5	5	5	10	10	5	5	5	5
7*	M	19	1	10	0	5	10	15	15	15	0	5	0	0	5	5	0	0	0
8*	F	37	2	0	5	10	10	10	5	5	5	0	0	5	0	5	5	5	5
9*	F	37	3	15	15	10	0	5	5	15	15	10	10	5	5	0	15	15	25
10*	M	23	4	-5	0	5	10	15	5	5	0	0	0	5	5	5	5	5	0
11*	M	38	5	10	10	5	0	-5	0	0	5	10	10	5	10	5	10	0	5
12	F	33	6	5	10	5	10	5	5	5	0	5	10	5	5	5	5	5	0
13*	F	29	1	0	0	0	5	10	15	10	0	5	0	0	5	15	10	10	0
14	F	21	2	5	5	5	5	5	0	0	5	5	10	0	0	0	0	0	0
15	M	43	3	5	5	10	5	10	5	5	10	5	5	5	10	0	0	-5	0
16	F	48	4	5	5	5	5	10	10	10	15	20	15	15	15	25	35	25	35
17*	M	30	5	5	5	5	5	5	5	10	10	5	5	5	10	5	10	10	10
18*	M	37	6	5	5	5	0	10	10	10	15	5	10	5	5	0	5	15	15
19*	F	26	1	5	5	5	10	0	10	10	5	10	10	10	10	5	0	0	5
20	M	22	2	10	15	15	5	0	0	5	-5	10	15	20	5	5	5	5	0
21	M	23	3	10	15	5	10	5	5	5	5	15	15	10	5	20	20	10	5
22	F	24	4	5	5	5	10	5	5	10	10	5	5	5	0	5	5	5	5
23	M	47	5	10	10	10	15	20	20	20	15	25	25	20	25	25	35	20	30
24	F	40	6	20	20	25	20	15	5	5	0	20	20	25	25	20	15	10	-5
25	F	24	1	10	0	5	10	10	10	5	0	5	5	5	10	10	5	5	5
26	F	29	2	10	5	5	10	5	5	5	0	10	5	5	5	5	5	0	5
27	M	36	3	15	20	15	5	5	15	10	5	20	20	20	10	5	10	10	25
28	M	46	4	15	15	10	5	25	35	35	40	10	10	10	5	10	30	30	40
29	F	39	5	15	20	20	20	15	20	30	30	10	10	10	15	15	20	30	30
30*	F	36	6	5	5	5	10	10	10	20	10	0	0	5	10	10	5	15	15

*Denotes participants who took part in both ABR and CAEP testing

2.6 Data Collection Procedures

Testing took place in the electrophysiology room at the University of Canterbury Speech and Hearing Clinic. This room is located at the end of a quiet hallway, ensuring minimal ambient noise. The Ambu BlueSensor brand ECG silver silver-chloride disposable electrodes were used. For ABR testing, electrodes were attached at four locations in a vertical montage, with the active electrode at the vertex/forehead, the indifferent electrode at the nape of the neck and the ground electrode on the clavicle (Figure 14). This montage was utilised as it has been evidenced to be most ideal for recording wave V (Atcherson et al., 2012). For CAEP testing, they were attached to five locations in a mastoid montage configuration: two at the vertex/forehead, one behind each ear at the mastoid, and one ground electrode placed on the clavicle. Impedances were calculated to ensure they were all matching and below 3 kΩ.

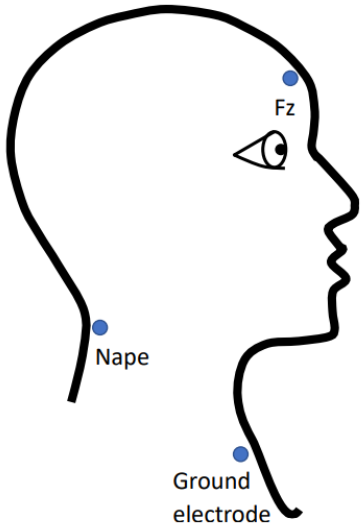


Figure 14

Locations of Electrodes for Vertical Electrode Placement During ABR Testing

Participants were instructed to lie as still and relaxed as possible in the reclining chair. For CAEP, they were asked to keep their eyes open and avoid falling asleep. Participants were then fitted with 3M E-A-RTONE ABR insert earphones, through which stimuli was played. Rarefaction click stimuli was used for ABR. A rarefaction 1000 Hz tone-burst was

used to elicit CAEP, with a rise, fall time and plateau time of 20 ms each, bringing the total duration to 60 ms.

Both clicks and tone-burst stimuli were presented at an intensity of 70 dB nHL. The noise rejection threshold was set to 40nV for both ABR and CAEP testing. While the Fsp was continuously measured throughout recording, the stop criteria were set to 2000 averages per ear for ABR and 150 averages for CAEPs (totalling 4000 averages for ABR and 300 averages for CAEPs in the "interleaved" condition). For all recordings, two replicate traces were measured. Conventional averaging was used so as to reduce the number of potential confounding variables. To make testing time for participants not too long, only the right ear was tested for the monaural slow and fast conditions, with the assumption that both the left and right ear would behave similarly given the symmetrical hearing thresholds of participants.

2.6.1 ABR Parameters

For the "interleaved" condition, clicks were interspersed between the right and left ears at an overall central rate of 90.9/s, which corresponded to 45.45/s for each ear. For the "monaural slow" and "monaural fast" conditions, clicks were presented to the right ears of participants at overall central and peripheral rates of 45.45/s and 90.9/s, respectively. Based on current best practice protocols, the frequency filter settings were set to 100 Hz for the high pass filet, and 2000 Hz for the low pass filter (Elberling & Don, 1984; Hall, 2006; King, 2010).

2.6.2 CAEP Parameters

A rarefaction 1000 Hz tone-burst in the "interleaved condition" was presented at a total central rate of 2/s (more precisely, 2.009/s), which corresponded to a peripheral rate of 1/s (more precisely, 1.0045/s). The "monaural slow" condition, the stimulus was presented at a central and peripheral rate of1/s. The "monaural fast" condition consisted of stimuli presented at 2/s as both a central and peripheral rate. Following CAEP testing protocols in the literature, the high pass filter was set to 0.2 Hz and the low pass filter to 30 Hz (Billings et al., 2007; Munro et al., 2020; Purdy et al., 2005).

Chapter 3: Results

Once recordings for all participants were completed, the raw data was transferred to a Microsoft Excel template. The ABR wave V, and the CAEP P1, N1 and P2 peaks were identified by visual inspection. Once wave peaks were manually identified and marked, the Excel template was devised to automatically calculate the Fsp, amplitudes and latencies of each of the waveforms. As statistical analyses were performed multiple times, a Bonferroni adjustment was applied to decrease the probability of committing a Type I error (Haynes & Johnson, 2009). The null hypothesis was answered by examining the *f*-value, the *p* value and Cohen's *d* effect size for post hoc testing. Results were considered significant if $p < .05$, and effect size was considered large if $d \geq 0.8$, medium if $d = 0.5$ and small if $d = 0.2$ (Girden, 1992; Hegde & Salvatore, 2019; Verma, 2015).

3.1 ABR

First, descriptive statistics were run for ABR, revealing no significant skewness or kurtosis. Table 4 shows each participant's latency and amplitude data, Table 5 shows the Fsp data for each replicate for all participants, while Table 6 contains the descriptive statistics. The assumptions of parametric testing were met for latency and amplitude as the data was normally distributed and no significant outliers were present. Therefore, parametric analyses were conducted. The assumptions of parametric testing were not met for Fsp as the Shapiro-Wilk test was significant ($p < .05$) for all conditions. The Central Limit Theorem states that as the sample size increases, the distribution of the sample means approaches a normal distribution (i.e., a "bell curve"), regardless of the population's actual distribution shape (Verma, 2015).

There is some discrepancy on the minimum sample size required to meet this theorem, however it is generally agreed the sample size should be equal to or greater than 25 (Fischer, 2010). The minimum sample size calculated for ABR was six participants (Figure 9), so with 24 participants the power of the study is increased (Serdar et al., 2021). Additionally, Krithikadatta (2014) states data with skewed distribution can still be representative of the population, particularly for measures which are naturally closer to zero, as is the case with Fsp. Fsp typically starts at zero and increases as myogenic noise is reduced and participants become more relaxed (Sininger, 1993). So, the While $N = 24$ narrowly misses this cut-off of 25, testing proceeded with parametric statistical analyses, as indicated above.

Table 4

ABR Participants' Wave V Latency (ms) and Amplitude (μV pp) Data for Each Condition

	Right Interleaved		Left Interleaved		Monaural Fast		Monaural Slow	
Participant	**Latency**	**Amplitude**	**Latency**	**Amplitude**	**Latency**	**Amplitude**	**Latency**	**Amplitude**
1	5.96	0.44	6.23	0.48	6.48	0.47	6.07	0.38
2	6.57	0.23	6.16	0.40	6.87	0.45	6.50	0.45
3	6.68	0.31	6.48	0.42	6.50	0.41	6.57	0.50
4	6.19	0.43	6.57	0.33	7.02	0.48	6.50	0.52
5	6.00	0.67	6.00	0.69	6.50	0.40	6.21	0.43
6	6.32	0.39	6.16	0.43	6.64	0.33	6.48	0.52
7	6.16	0.60	6.05	0.49	6.37	0.53	6.16	0.37
8	6.48	0.36	6.64	0.41	7.18	0.33	6.41	0.40
9	6.30	0.47	6.37	0.38	6.50	0.48	6.21	0.65
10	6.48	0.30	6.25	0.27	6.68	0.38	6.34	0.43
11	6.68	0.25	6.71	0.27	6.62	0.17	6.28	0.32
12	6.34	0.23	6.55	0.22	6.80	0.18	6.50	0.31
13	5.89	0.77	6.05	0.78	6.32	0.63	6.03	0.84
14	6.46	0.55	6.44	0.40	6.75	0.36	6.44	0.64
15	6.30	0.61	6.00	0.44	6.73	0.41	6.32	0.52
16	6.32	0.55	6.21	0.31	6.66	0.44	6.37	0.49
17	6.00	0.53	6.16	0.44	6.50	0.44	6.28	0.38
18	6.34	0.46	6.59	0.59	6.80	0.46	6.46	0.50
19	6.05	0.42	6.09	0.55	6.55	0.37	6.09	0.46
20	6.57	0.41	6.37	0.25	6.57	0.40	6.57	0.56
21	6.93	0.33	6.73	0.69	7.25	0.16	6.44	0.39
22	6.50	0.42	6.64	0.28	6.50	0.33	6.21	0.41
23	6.75	0.25	7.05	0.29	7.00	0.19	7.05	0.23
24	6.82	0.40	6.00	0.27	6.96	0.48	6.66	0.58

Note. Data points were rounded to two decimal places.

Table 5

ABR Participants' Mean Fsp Data for Each Condition

Participant	Right Interleaved	Left Interleaved	Monaural Fast	Monaural Slow
1	3.32	4.12	5.15	2.96
2	1.64	2.14	2.60	4.34
3	4.07	11.27	8.35	7.96
4	2.55	1.05	4.6	8.85
5	28.70	23.87	14.70	21.06
6	18.44	21.36	11.31	8.81
7	3.39	3.09	1.50	2.88
8	5.45	7.17	4.88	10.93
9	9.44	6.64	4.98	16.58
10	0.17	-0.26	0.34	0.87
11	0.15	0.85	0.08	0.95
12	1.56	0.90	-0.07	0.12
13	22.84	20.54	16.78	33.10
14	2.51	2.25	0.98	4.36
15	10.42	10.70	6.70	10.08
16	12.40	11.77	5.59	4.30
17	7.60	3.82	3.78	8.80
18	2.28	5.29	4.36	3.50
19	9.15	8.79	4.96	9.61
20	4.42	8.72	13.64	8.57
21	0.22	0.44	-0.31	0.03
22	1.69	1.67	2.76	2.92
23	0.57	0.72	-0.16	0.84
24	0.66	1.62	2.70	2.86

Note. Data points were rounded to two decimal places.

Table 6

ABR Descriptive Statistics for Wave V Latency (ms), Amplitude (μV pp) and Mean Fsp

				Skewness		Kurtosis		Shapiro-Wilk	
	Condition	**Mean**	**SD**	**Skewness**	**SE**	**Kurtosis**	**SE**	**W**	**p**
Latency	Right Interleaved	6.38	0.28	0.0512	0.472	-0.6955	0.918	0.974	0.762
	Left Interleaved	6.35	0.29	0.5705	0.472	-0.3201	0.918	0.932	0.109
	Monaural Fast	6.70	0.24	0.7791	0.472	-0.0652	0.918	0.923	0.067
	Monaural Slow	6.38	0.22	0.9544	0.472	2.4505	0.918	0.931	0.103
Amplitude	Right Interleaved	0.43	0.14	0.5585	0.472	0.1650	0.918	0.965	0.551
	Left Interleaved	0.39	0.15	0.7159	0.472	0.7380	0.918	0.955	0.341
	Monaural Fast	0.39	0.12	-0.3905	0.472	0.1846	0.918	0.938	0.150
	Monaural Slow	0.48	0.12	0.6848	0.472	1.5941	0.918	0.964	0.534
Mean Fsp	Right Interleaved	6.40	7.55	1.7552	0.472	2.6963	0.918	0.778	< .001
	Left Interleaved	6.60	6.97	1.3431	0.472	1.0092	0.918	0.825	< .001
	Monaural Fast	7.30	7.58	2.0286	0.472	5.0884	0.918	0.792	< .001
	Monaural Slow	5.01	4.82	1.1371	0.472	0.6415	0.918	0.873	0.006

Note. Mean and standard deviation (SD) were rounded to two decimal places.

Mauchly's test of sphericity was significant, $W(3) = 0.01$, $p < .001$, violating the assumptions of sphericity (Girden, 1992). Therefore, degrees of freedom were corrected using Greenhouse– Geisser estimates of sphericity ($\varepsilon = .502$). A Mixed Model, Repeated Measures Analysis of Variance (ANOVA) was preformed using the Jamovi 2.2.5.0 statistical software (2021), which showed a significant difference in wave V measures between the

three conditions ($F(3, 6) = 8.83$, $p < .001$, $\eta^2p = .224$). This was followed up with a series of separate univariate ANOVAs for latency and amplitude. Figure 15 demonstrates an example of ABR wave recordings, retrieved from the results of participant 7.

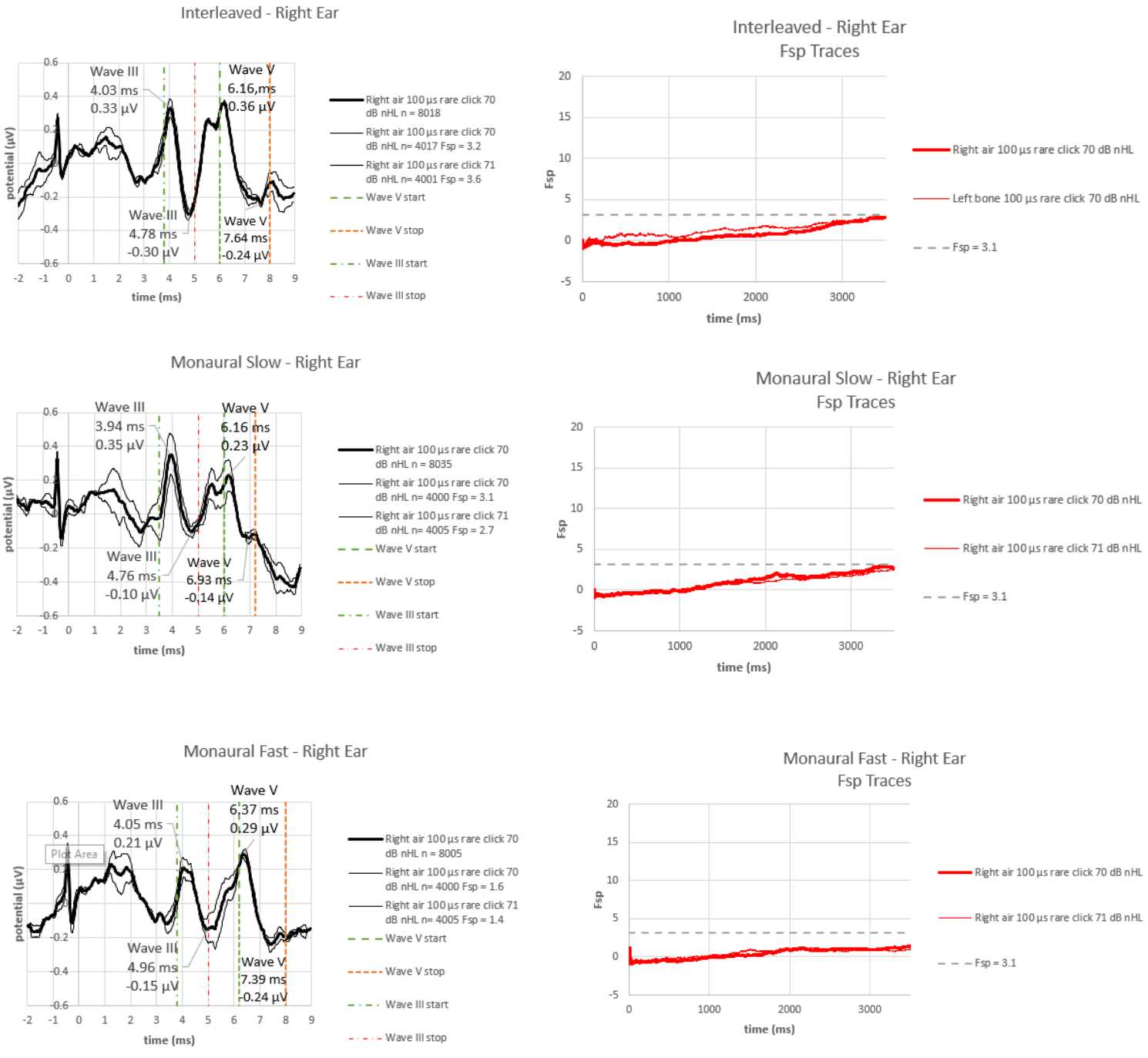


Figure 15

ABR Traces from the Recordings of Participant 7 for All Three Test Conditions

3.1.1 Wave V Latency

Figure 16 shows a series of box plots displaying the wave V latency, mean, median and range for each of the three conditions. The shaded boxes represent the interquartile range/middle 50% of each data set. The 'x' marks mean latency value. The line inside each box marks the median latency value. The yellow dot represents outliers.

There was a significant difference in the wave V latency between the conditions ($F(3, 50.8) = 9.89$, $p < .001$, $\eta^2p = .244$). Post hoc testing with a Bonferroni correction revealed significantly longer wave V latencies in the monaural fast condition relative to the monaural slow and right interleaved conditions ($p < .001$). This was further supported by the large effect sizes between the monaural fast condition when compared to the right interleaved ($d = 1.25$) and monaural slow ($d = 1.24$) conditions. Thus, the null hypothesis was rejected.

Additionally, no significant difference was found in the wave V latency between the monaural slow and right interleaved ($p = .951$, $d = .18$) conditions, confirming the null hypothesis. As expected, there was no significant difference found between the right and left ears in the interleaved condition ($p = .743$, $d = .10$).

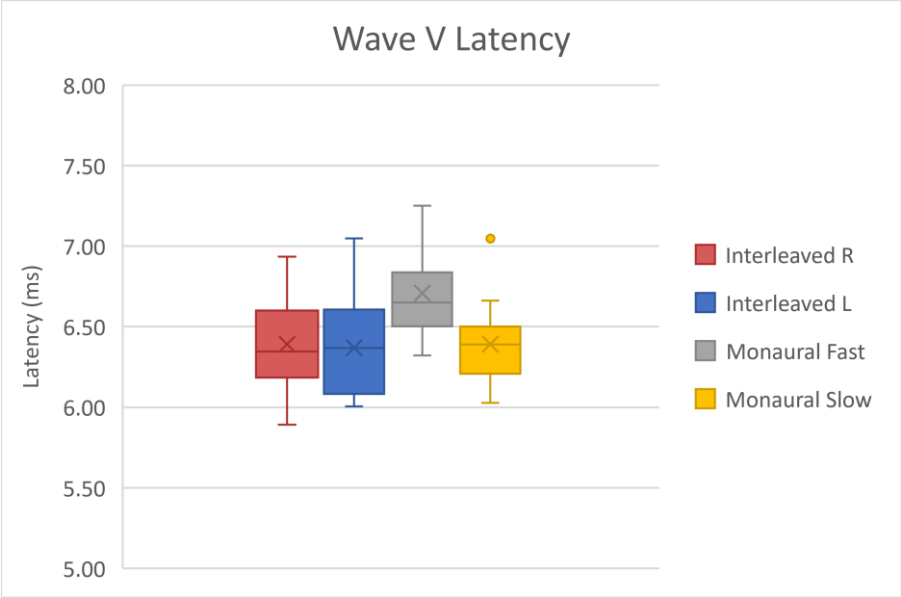


Figure 16

Box Plots of Wave V Latency for the Interleaved Left and Right, Monaural Slow and Monaural Fast Conditions

3.1.2 Wave V Amplitude

There was no significant difference found in the amplitude of wave V between the three conditions ($F(3, 50.9) = 1.89$, $p = .143$, $\eta^2p = .049$). Therefore, post hoc testing was not done. This supports the null hypotheses. As expected, no significant difference was found in the interleaved condition between the right and left ears. Figure 17 displays a series of wave V amplitude box plots with the interquartile range, mean, median, minimum and maximum wave V amplitudes for all conditions. The line inside each box marks the median amplitude value. The yellow dot represents outliers.

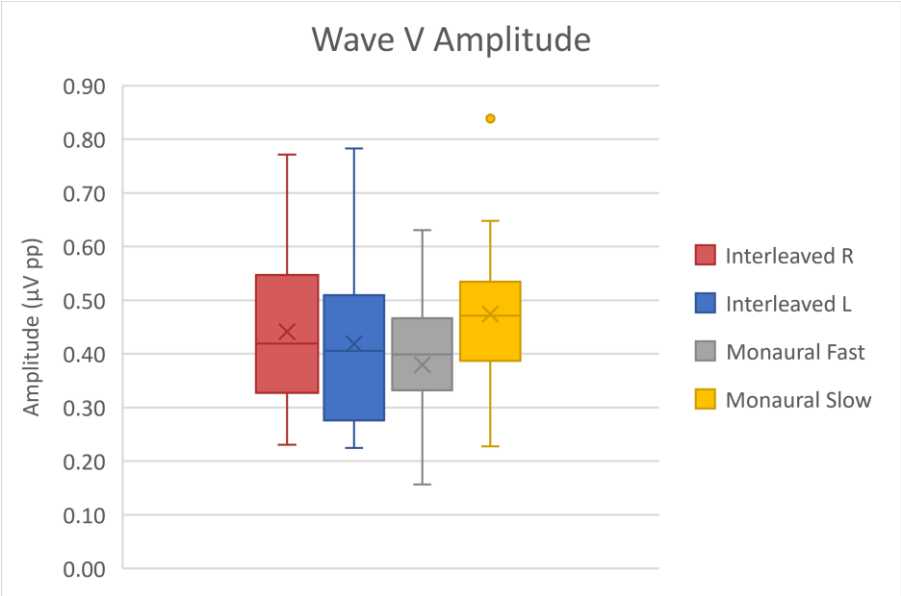


Figure 17

Box Plots of Wave V Amplitude for the Interleaved Left and Right, Monaural Slow and Monaural Fast Conditions

3.1.3 Mean Fsp

There was no significant difference found in the Fsp for wave V between the conditions ($F(3, 50.1) = 0.48$, $p = .699$, $\eta^2p = .015$). Therefore, post hoc testing was not done.

This supports the null hypotheses. As expected, no significant difference in Fsp was found in the interleaved condition between the right and left ears.

Figure 18 displays a box plot with the interquartile range, mean, median, minimum and maximum Fsp for all conditions. The dots represent outliers. The interquartile range and mean of the monaural fast Fsp sits visibly lower than that of the other conditions. Additionally, the monaural slow and interleaved conditions appear to have similar mean values. While no statistical significance was found, the Fsp for the monaural fast condition appears noticeably lower than the other two conditions.

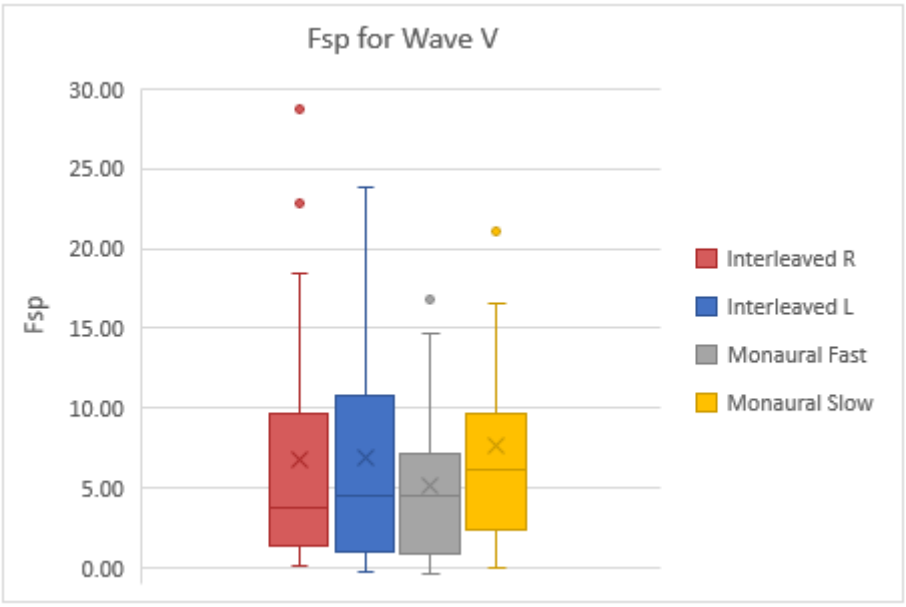


Figure 18

ABR Box Plot of the Fsp for the Interleaved Left and Right, Monaural Slow and Monaural Fast Conditions

3.2 CAEP

Descriptive statistics were first run with participant's P1-N1-P2 complex latency, amplitudes and mean Fsp (see Table 7 for latencies, Table 8 for amplitudes and Table 9 for Fsp) to check for bias and outliers. Normal distribution was found in all of the conditions with the exception of N1 in the left interleaved and monaural slow conditions, and the

assumptions for parametric testing were met for the latencies of P1, N1 and P2 and the N1-P2 amplitude. The Shapiro-Wilk test was significant ($p < .05$) for mean Fsp in the monaural fast and slow conditions, significant for all three amplitudes in the left interleaved conditions, in addition to the right interleaved condition for the P1-N1 and N1-P2 amplitudes the P1 amplitude in the monaural slow condition and N1-P1 amplitude in the right interleaved condition (see Table 10). This indicates these data were not normally distributed and did not meet the assumptions of parametric testing. As $N = 30$, the Central Limit Theorem applies in this instance, and statistical analyses was able to proceed with parametric testing.

Table 7

CAEP Participants' Latency (ms) Data for Each Condition

	Right Interleaved			Left Interleaved			Monaural Fast			Monaural Slow		
Participant	**P1**	**N1**	**P2**	**P1**	**N1**	**P2**	**P1**	**N1**	**P2**	**P1**	**N1**	**P2**
1	32.65	93.20	147.17	21.09	69.61	173.70	32.88	98.19	199.09	32.65	89.12	196.83
2	46.26	88.00	144.90	41.27	89.12	137.87	44.22	81.63	134.69	43.99	93.88	183.45
3	37.00	89.34	127.21	40.36	85.26	145.35	37.19	88.40	194.30	42.18	89.12	166.70
4	35.37	74.60	109.52	33.79	72.56	195.46	37.87	78.91	159.18	35.15	80.50	162.13
5	32.43	65.76	121.32	33.11	63.04	126.30	48.53	72.20	117.91	33.33	62.81	158.05
6	34.47	86.85	136.73	34.24	87.53	138.32	37.19	89.12	152.80	32.88	85.03	139.91
7	36.51	108.39	187.53	31.07	103.85	179.59	59.64	149.89	178.46	36.73	89.80	127.66
8	32.88	97.28	148.07	28.34	92.52	127.21	60.80	105.20	180.95	32.20	90.25	159.64
9	40.36	96.83	148.98	37.64	98.87	155.56	51.25	121.80	189.80	36.73	94.33	156.01
10	39.68	88.21	104.08	37.87	87.07	115.65	69.84	142.63	198.64	39.23	87.76	154.20
11	35.15	99.32	124.49	36.73	91.16	123.13	75.28	97.05	147.60	35.60	92.97	134.47
12	41.95	84.35	105.67	39.23	70.29	140.59	50.34	102.04	194.78	39.00	93.88	145.58
13	31.97	71.43	136.05	32.88	79.82	135.60	59.86	96.37	265.08	27.66	79.82	127.44
14	35.83	93.65	137.20	35.15	92.29	127.66	36.73	94.33	133.11	38.32	87.98	129.93
15	43.08	86.39	164.85	39.00	88.66	157.37	56.46	81.41	190.70	42.63	89.80	168.48
16	40.59	92.97	144.67	35.83	85.94	144.22	58.73	97.51	130.20	37.19	83.67	144.90
17	40.14	68.93	146.71	41.72	84.35	141.04	81.20	102.49	150.80	36.05	67.80	138.10
18	51.70	94.78	207.94	45.80	94.10	181.86	55.10	89.34	196.15	47.62	82.99	180.05
19	33.79	89.57	145.12	32.65	61.90	145.80	70.75	132.65	161.68	33.33	91.16	146.71
20	23.36	67.12	137.96	27.66	63.72	119.70	31.29	49.21	127.00	33.56	82.99	134.92
21	46.71	90.02	117.91	43.31	88.44	129.02	48.30	91.84	121.32	44.90	93.65	125.85
22	40.59	125.40	176.64	40.30	54.88	153.29	36.05	66.89	79.14	37.41	89.80	155.78
23	36.28	71.66	182.77	37.41	89.80	146.49	53.97	121.77	198.64	40.14	67.80	154.88
24	39.46	71.43	136.51	38.10	70.29	146.03	53.29	81.41	147.60	41.04	87.53	160.77
25	37.19	93.65	124.49	20.18	92.97	119.73	56.69	91.38	139.00	43.54	94.56	121.09
26	32.43	74.60	187.07	34.24	91.16	123.58	32.88	87.30	170.52	33.33	79.82	121.10
27	34.92	93.88	170.52	35.83	95.92	179.14	56.60	78.68	171.20	36.28	96.60	196.37
28	41.04	79.60	154.65	36.05	89.80	162.36	39.68	74.15	159.41	37.19	90.70	193.88
28	31.75	72.11	146.49	31.75	82.77	158.96	61.68	108.39	177.32	22.22	73.24	141.27
30	34.47	83.45	143.76	37.64	83.45	145.12	38.78	124.94	194.10	36.96	89.80	167.35

Note. Data points were rounded to two decimal places.

Table 8

CAEP Participants' Amplitude (μV pp) Data for Each Condition

	Right Interleaved			Left Interleaved			Monaural Fast			Monaural Slow		
Participant	**P1**	**P1-N1**	**N1-P2**	**P1**	**P1-N1**	**N1-P2**	**P1**	**P1-N1**	**N1-P2**	**P1**	**P1-N1**	**N1-P2**
1	2.07	5.81	10.39	1.39	7.46	9.14	2.16	6.15	1.26	2.09	7.24	10.75
2	1.44	2.04	1.46	1.53	3.73	4.58	1.76	1.48	2.19	1.66	3.36	3.58
3	0.46	2.71	2.94	1.31	3.29	5.43	0.90	2.77	2.71	1.54	2.63	4.92
4	0.38	2.70	2.06	0.45	1.86	4.38	1.18	3.60	5.69	2.22	4.84	7.57
5	1.76	2.15	2.98	2.00	3.50	4.20	1.51	1.55	3.55	1.29	2.87	6.79
6	1.81	3.41	4.07	2.61	2.73	4.40	0.43	3.55	2.42	1.39	5.01	8.01
7	2.05	2.69	1.78	1.24	3.00	3.11	1.71	1.73	2.99	0.89	0.32	3.44
8	2.21	3.83	4.89	1.75	4.28	1.83	1.04	2.65	3.72	2.28	6.34	6.41
9	0.80	2.70	4.80	1.60	3.40	1.10	1.50	3.80	3.40	1.50	6.00	4.90
10	1.41	3.40	4.62	1.63	1.63	3.35	0.37	3.95	1.97	1.54	2.90	2.48
11	2.38	2.98	3.06	2.03	2.05	3.70	2.77	3.63	4.93	2.11	5.96	4.33
12	1.39	3.78	2.66	4.18	1.67	2.76	0.82	1.44	3.26	1.84	4.35	6.29
13	1.41	5.34	6.86	1.41	2.82	9.69	1.67	1.27	4.55	0.05	6.27	2.85
14	2.34	5.72	2.64	2.08	7.57	2.83	1.42	4.04	3.51	1.06	5.33	4.49
15	2.33	3.56	9.30	0.77	4.57	9.54	0.19	2.59	6.51	2.28	9.45	11.42
16	2.75	5.86	3.14	1.51	3.61	3.52	1.54	0.91	2.08	2.74	6.17	5.50
17	1.22	3.88	7.13	0.90	3.24	4.83	1.04	0.86	2.43	1.47	4.14	8.46
18	2.20	3.98	6.65	0.94	4.01	6.78	1.42	2.24	3.51	1.87	7.58	10.56
19	1.57	1.30	4.58	0.88	2.36	2.80	3.10	2.32	0.69	1.05	4.59	3.35
20	2.56	4.52	1.91	2.65	1.37	4.08	1.85	2.70	1.53	3.93	0.71	1.87
21	1.70	4.66	2.27	2.29	4.30	4.28	1.45	3.53	2.17	1.82	4.60	4.20
22	0.59	3.76	1.07	1.52	4.07	5.62	0.56	1.63	5.22	0.90	4.21	4.85
23	2.77	11.23	8.20	2.27	8.88	7.69	0.64	2.22	3.26	5.86	13.53	13.51
24	2.00	3.85	5.85	1.35	3.17	7.58	1.05	2.61	2.94	1.43	5.25	7.14
25	0.74	3.91	2.55	2.31	4.68	2.57	0.65	3.49	2.89	3.04	2.38	3.27
26	1.78	4.87	12.06	2.33	2.89	3.04	2.69	2.69	5.73	0.54	8.64	8.38
27	1.69	4.43	5.78	1.58	4.48	5.78	1.05	2.32	6.80	1.94	6.63	8.80
28	1.98	3.37	2.83	1.93	4.48	5.67	0.81	3.51	4.73	1.59	4.87	5.85
28	1.00	3.87	3.65	0.89	3.77	4.37	1.84	2.02	2.43	0.53	4.99	4.31
30	1.17	4.23	3.09	2.11	3.00	3.16	1.90	4.36	0.48	1.70	6.04	7.58

Note. Data points were rounded to two decimal places.

Table 9

CAEP Participants' Mean Fsp Data for Each Condition

Participant	Right Interleaved	Left Interleaved	Monaural Fast	Monaural Slow
1	1.44	1.69	-0.03	1.99
2	0.49	0.29	0.01	1.29
3	0.05	0.69	-0.72	0.82
4	0.32	0.18	-0.31	125.84
5	0.47	1.15	-0.14	0.95
6	-0.45	-0.35	0.29	1.43
7	0.41	0.62	1.44	0.64
8	1.01	1.28	-0.56	1.19
9	0.13	0.00	-0.01	0.34
10	-0.38	2.14	-0.10	-0.43
11	0.55	0.28	-0.34	0.35
12	-0.44	-0.20	-0.27	0.19
13	-0.13	0.71	-0.35	0.07
14	0.04	2.13	-0.39	0.93
15	0.68	0.99	0.78	1.46
16	0.88	-0.07	-0.23	1.03
17	-0.10	0.79	0.11	0.10
18	2.49	2.13	0.67	3.36
19	-0.28	-0.52	0.08	0.58
20	0.07	0.43	-0.44	0.45
21	3.21	1.59	2.39	0.82
22	1.00	0.65	0.35	5.47
23	1.50	0.48	-0.52	1.65
24	0.87	0.99	-0.47	1.86
25	0.10	-0.03	-0.51	0.11
26	0.78	0.72	-0.01	0.23
27	-0.13	1.91	-0.33	2.28
28	1.00	2.89	0.48	1.82
29	-0.59	0.32	-0.76	0.63
30	0.06	0.59	-0.64	0.64

Table 10

CAEP Descriptive Statistics for Latency (ms), Amplitude (μV pp) and Mean Fsp

				Skewness		Kurtosis		Shapiro-Wilk	
	Condition	**Mean**	**SD**	**Skewness**	**SE**	**Kurtosis**	**SE**	**W**	**p**
P1 Latency	**Right Interleaved**	37.33	5.518	0.301	0.427	1.2914	0.833	0.957	0.265
	Left Interleaved	35.34	5.736	-0.941	0.427	1.4172	0.833	0.939	0.085
	Monaural Fast	51.10	13.335	0.347	0.427	-0.5336	0.833	0.952	0.190
	Monaural Slow	36.97	5.207	-0.440	0.427	1.2763	0.833	0.965	0.411
P1 Amplitude	**Right Interleaved**	1.67	0.664	-0.292	0.427	-0.6695	0.833	0.970	0.532
	Left Interleaved	1.71	0.735	1.135	0.427	3.0870	0.833	0.925	0.036
	Monaural Fast	1.37	0.714	0.608	0.427	0.1813	0.833	0.961	0.326
	Monaural Slow	1.80	1.087	1.929	0.427	6.1057	0.833	0.844	< .001
N1 Latency	**Right Interleaved**	86.43	13.219	0.622	0.427	1.1891	0.833	0.935	0.066
	Left Interleaved	83.37	12.112	-0.779	0.427	-0.1694	0.833	0.918	0.024
	Monaural Fast	96.57	22.342	0.569	0.427	0.5014	0.833	0.959	0.294
	Monaural Slow	85.97	8.578	-1.309	0.427	1.1720	0.833	0.862	0.001
P1-N1 Amplitude	**Right Interleaved**	4.02	1.755	2.393	0.427	9.3451	0.833	0.796	< .001
	Left Interleaved	3.73	1.719	1.452	0.427	2.5553	0.833	0.863	0.001
	Monaural Fast	2.72	1.173	0.678	0.427	0.9619	0.833	0.951	0.181
	Monaural Slow	5.24	2.579	0.908	0.427	2.8173	0.833	0.937	0.076
P2 Latency	**Right Interleaved**	145.57	25.187	0.573	0.427	0.1662	0.833	0.953	0.208
	Left Interleaved	145.86	20.696	0.675	0.427	-0.1586	0.833	0.944	0.113
	Monaural Fast	165.37	35.588	0.175	0.427	1.3449	0.833	0.955	0.236
	Monaural Slow	153.12	21.942	0.480	0.427	-0.4881	0.833	0.949	0.158
N1-P2 Amplitude	**Right Interleaved**	4.51	2.757	1.172	0.427	0.8643	0.833	0.890	0.005
	Left Interleaved	4.73	2.218	0.873	0.427	0.2051	0.833	0.920	0.028
	Monaural Fast	3.32	1.611	0.465	0.427	-0.2284	0.833	0.964	0.392
	Monaural Slow	6.20	2.877	0.735	0.427	0.0550	0.833	0.950	0.174
Mean Fsp	**Right Interleaved**	0.50	0.85	1.482	0.427	2.8279	0.833	0.881	0.003
	Left Interleaved	0.82	0.84	0.670	0.427	-0.0818	0.833	0.951	0.184

			Skewness		Kurtosis		Shapiro-Wilk	
Monaural Fast	-0.01	0.67	2.055	0.427	5.3394	0.833	0.813	< .001
Monaural Slow	5.27	22.80	5.455	0.427	29.8338	0.833	0.214	< .001

Note. Mean and standard deviation (SD) were rounded to two decimal places.

Figure 19 demonstrates an example of CAEP traces, retrieved from the results of participant 18. The left column shows the wave responses for each condition and the right column shows the Fsp traces for each condition.

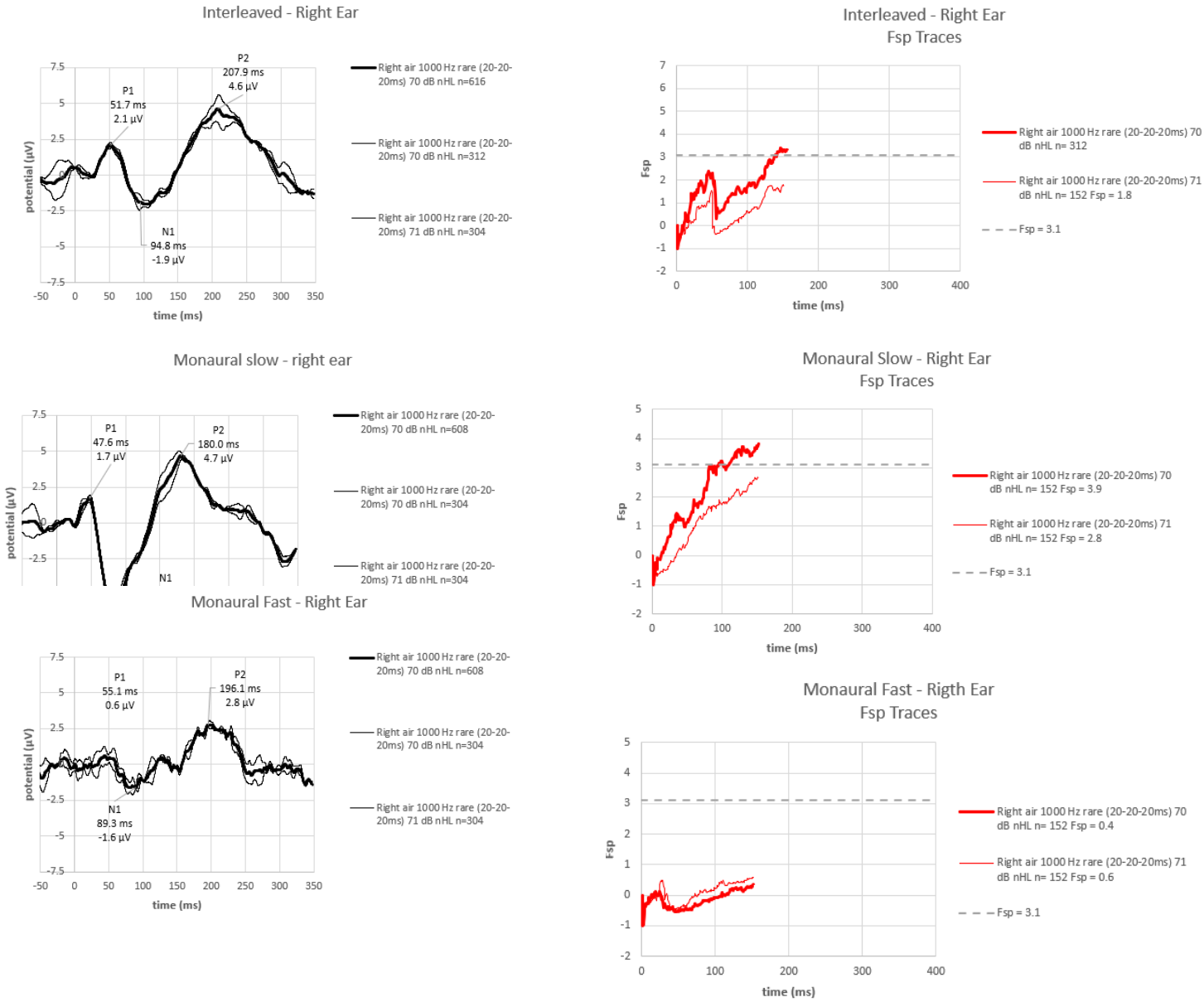


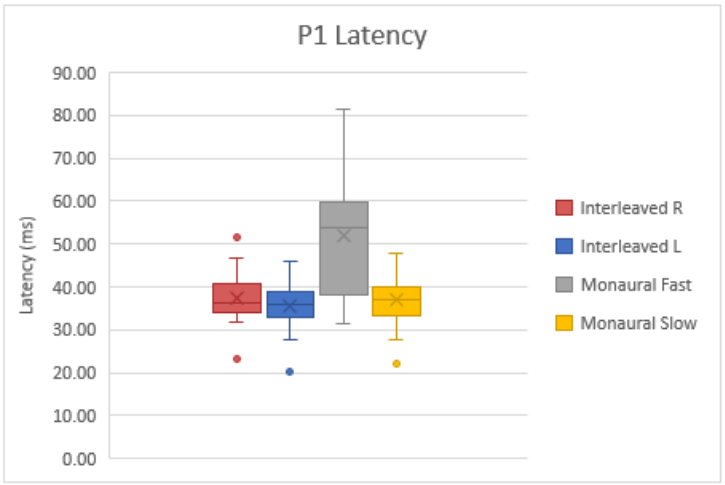
Figure 19

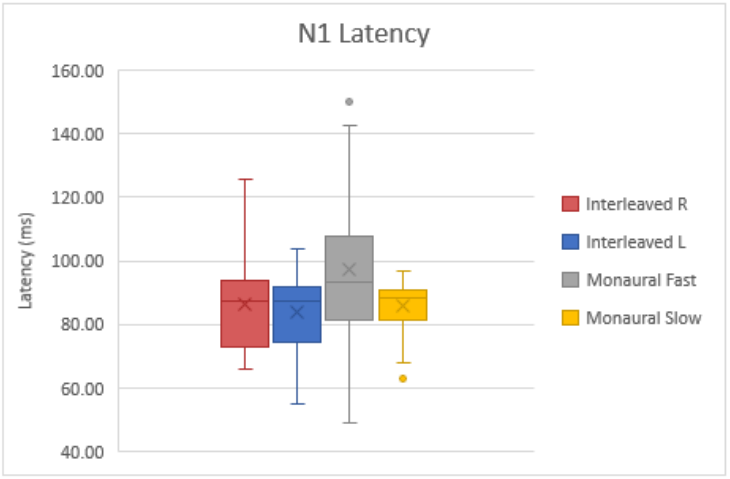
CAEP Traces from the Recordings of Participant 18 for All Three Test Conditions

Mauchly's test of sphericity was significant, $W(3) = 1.41$, $p < .001$, violating the assumptions of sphericity. Therefore, degrees of freedom were corrected using Greenhouse–Geisser estimates of sphericity ($\varepsilon = .367$). A Mixed Model, Repeated Measures Analysis of Variance (ANOVA) was preformed using the Jamovi 2.2.5.0 statistical software (2021), which showed a significant difference in the P1-N1-P2 complex measures between the three conditions, $F(3, 6.60) = 7.56$, $p < .001$, $\eta^2p = .164$.

3.2.1 Latency

Univariate ANOVAs were carried out for each of the peaks. There was a significant difference between the conditions for the latencies of P1 ($F(3, 62.9) = 11.67$, $p < .001$, $\eta^2p = .383$), N1 ($F(3, 62.0) = 2.654$, $p = .004$, $\eta^2p = .105$) and P2 ($F(3, 63.6) = 2.72$, $p = .014$, $\eta^2p = .087$). Figure 20 shows a series of box plots displaying the outliers, interquartile range, mean, median and range for the P1, N1 and P2 latencies for each of the three conditions. For all three measures, the box of the monaural slow, right interleaved and left interleaved conditions overlap with similar means and medians, while the interquartile range of monaural fast condition sits higher, indicating longer latencies in this condition.





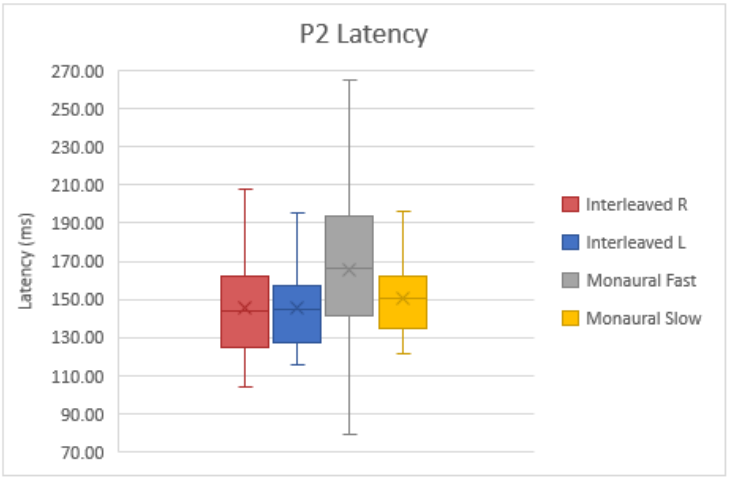


Figure 20

Box Plots of P1, N1 and P1 Latencies for the Interleaved Left and Right, Monaural Slow and Monaural Fast Conditions

For the P1 latency, post hoc testing with a Bonferroni correction revealed significantly longer latencies and large effect sizes in the monaural fast condition when compared to the monaural slow ($p < .001$, $d = 1.73$) and right interleaved conditions ($p < .001$, $d = 1.68$), thus disproving the null hypothesis. Conversely, no significant difference in P1 latency was found between the monaural slow and right interleaved conditions ($p = .83$, $d = .04$), supporting the null hypothesis.

For the N1 latency, post hoc testing revealed significantly longer latencies and large effect sizes in the monaural fast condition when compared to the monaural slow condition ($p = .042$, $d = .71$), rejecting the null hypothesis. However, no significant difference was found for the right interleaved condition when compared to the monaural slow ($p = .91$, $d = .03$) and monaural fast ($p = .05$, $d = .68$) conditions, supporting the null hypothesis.

Finally, testing for the P2 latency revealed significantly longer latencies in the monaural fast condition compared to the right interleaved condition ($p = .027$, $d = .75$), rejecting the null hypothesis. However, no significant difference was found in P2 latency was found in the slow condition as compared to the monaural fast ($p = .46$, $d = .46$) and right interleaved conditions ($p = .27$, $d = .28$), supporting the null hypothesis.

Table 11 summarises the *p* value and Cohen's *d* for the latencies of the P1-N1-P2 complex. As expected, there was no significant difference in latency between the left and

right ears in the interleaved condition for the latencies of all measures of P1 (p = .348, d = .24), N1 (p = .430, d = .20) and P2 (p = .966, d = .015). Additionally, small effect sized were found between the ears for all three latencies.

Table 11

Summary Matrix of Significance and Effect sizes for CAEP Latencies for the P1-N1-P2 Complex

	Condition	Right Interleaved	Monaural Slow
P1 Latency	Monaural Slow	p = .83 d = .04	——
	Monaural Fast	p < .001 * d = 1.68	p < .001 * d = 1.73
N1 Latency	Monaural Slow	p = .91 d = .03	——
	Monaural Fast	p = .05 d = .68	p = .042 * d = .71
P1 Latency	Monaural Slow	p = .27 d = .28	——
	Monaural Fast	p = .027 * d = .75	p = .46 d = .46

* Denotes if p < .05, indicating a significant difference
—— Not applicable

3.2.2 Amplitude

Univariate ANOVAs were carried out for each of the amplitude measures. No significant difference was found between the conditions for P1 amplitudes (F(3, 63.8) = 1.71, p = .173, η^2p = .040), thus proving the null hypothesis and eliminating the need for further post hoc testing. There was a significant difference between the conditions for the amplitudes of P1-N1 (F(3, 62.4) = 9.18, p < .001, η^2p = .192) and N1-P2 (F(3, 62.7) = 7.15, p < .001, η^2p = .156).

Figure 21 shows a series of box plots displaying the outliers, interquartile range, mean, median and range for the P1, N1 and P2 amplitudes for each of the three conditions.

As can be seen for the P1-N1 and N1-P2 amplitudes, the interquartile range, mean and median for the monaural slow condition is higher than the other two conditions, with minimal overlap of the shaded areas. This indicates larger amplitudes in the monaural conditions for these measures. Additionally, the interquartile range, mean and median of the monaural fast condition sits lower than that of the interleaved condition, indicating smaller amplitudes in the monaural fast condition. In contrast, the box plots for the P1 amplitudes appear to be similar, with no significant difference in the interquartile range, the median and the mean between the conditions.

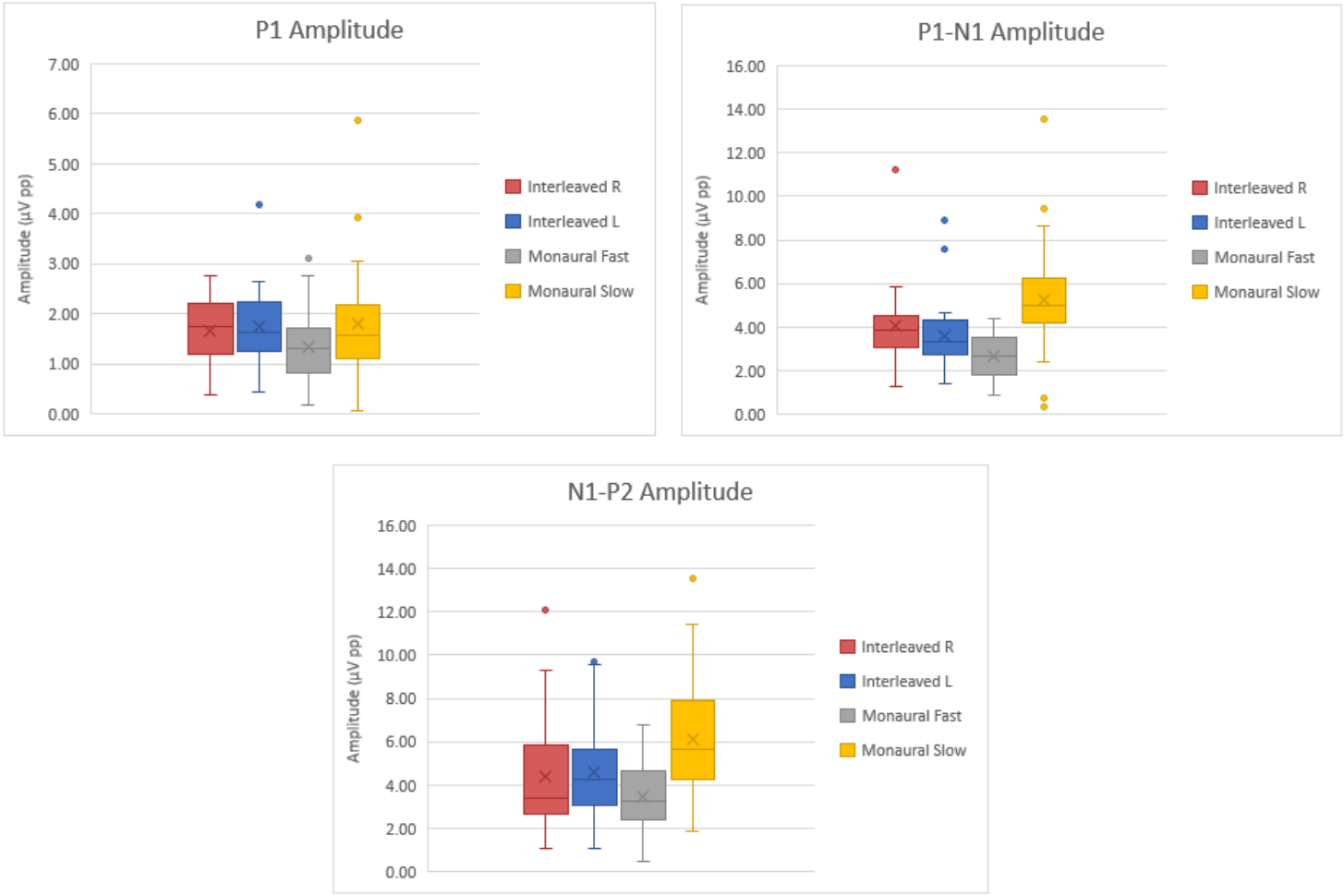


Figure 21

Box Plots of P1, P1-N1 and N1-P2 Amplitudes for the Interleaved Left and Right, Monaural Slow and Monaural Fast Conditions

Comparisons for the monaural fast condition was done with post hoc testing with a Bonferroni correction. This revealed significantly smaller amplitudes and large effect sizes between the monaural fast and monaural slow conditions for each of P1-N1 ($p < .001$, $d = 1.34$) and N1-P2 ($p < .001$, $d = 1.19$), thus rejecting the null hypothesis. However, no significant difference was found between the monaural fast and right interleaved conditions for P1-N1 ($p = .051$, $d = .69$) and N1-P2 ($p = .354$, $d = .49$), proving the null hypothesis. Testing for the right interleaved condition revealed no signifcant difference in amplitude when compared with the monaural slow for P1-N1 ($p = .078$, $d = .65$), confirming the null hypothesis. However, significantly smaller amplitudes were found in the right interleaved condition compared to the monaural slow condition for P1-N1 and N1-P2 ($p = .048$, $d = .70$), disproving the null hypothesis.

Table 12 summarises the *p* value and Cohen's *d* for the P1-N1 and N1-P2 amplitudes. As expected, no significant difference was found in the interleaved condition between the right and left ears for P1-N1 ($p = .552$, $d = .15$) and N1-P2 ($p = .728$, $d = .09$).

Table 12

Summary Matrix of Significance and Effect sizes for CAEP the P1-N1 and N1-P2 Amplitudes

	Condition	Right Interleaved	Monaural Slow
P1-N1 Amplitude	Monaural Slow	$p = .078$ $d = .65$	——
	Monaural Fast	$p = .051$ $d = .69$	$p < .001$ * $d = 1.34$
N1-P2 Amplitude	Monaural Slow	$p = .048$ * $d = .70$	——
	Monaural Fast	$p = .354$ $d = .49$	$p < .001$ * $d = 1.19$

* Denotes if $p < .05$, indicating a significant difference
—— Not applicable

3.2.3 Mean Fsp

There was no significant difference found in the Fsp of the P1-N1-P2 complex between the conditions ($F(3, 61.1) = 1.37$, $p = .255$, $\eta^2p = .034$). Therefore, post hoc testing

was not done. This supports the null hypotheses. As expected, no significant difference in Fsp was found in the interleaved condition between the right and left ears.

Figure 22 displays a box plot with the outliers, interquartile range, mean, median, minimum and maximum Fsp for all conditions. The interquartile range of the monaural fast Fsp sits visibly lower than that of the other conditions. Its mean and median are also lower. This indicates lower Fsp in the monaural fast condition as compared to the interleaved and monaural slow conditions. Additionally, the monaural slow and interleaved conditions appear to be similar in mean and median. While no statistical significance was found, the Fsp for the monaural fast condition appears noticeably lower than the other two conditions.

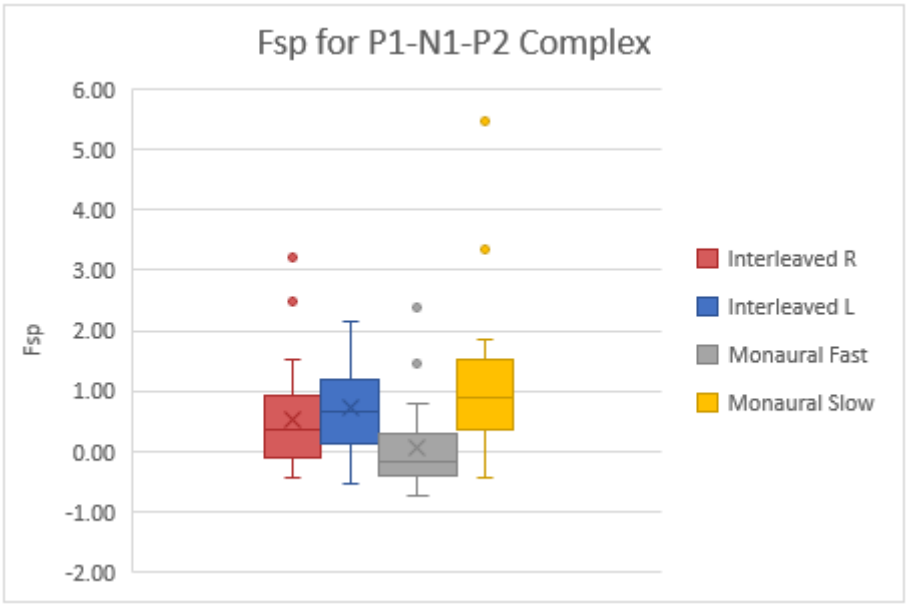


Figure 22

Box Plot of the P1-N1-P2 complex Fsp for the Interleaved Left and Right, Monaural Slow and Monaural Fast Conditions

Chapter 4: Discussion

This study sought to explore whether the interleaving of ABR and CAEP stimuli between the left and right ears yielded comparable traces to the gold standard of monaural testing, thus producing accurate diagnostic results on par with monaural testing but in less clinical time. Previous research found interleaved ABR produced quality traces relative to monaural ABR testing with significant time savings. These findings further support the concept of neural adaptation and fatigue occurring in the peripheral, rather than the central, auditory pathway, thereby allowing for bilateral and interleaved testing.

No previous research has explored the field of bilateral testing for CAEP. In fact, research into improving CAEP testing has been stagnant for the past 20 years, once it was established that a slow stimulus repetition rate produces comprehensible waveforms (Cone-Wesson et al., 1987; Jacobson et al., 1992). Consequently, exploring ways to improve the clinical efficacy of CAEP has not been a well researched area for some time. This study delved into the prospect of reducing CAEP test time by utilising bilateral testing in such a way so as to bypass the neural adaptation and fatigue effects observed when using fast stimulus repetition rates (Jacobson et al., 1992; Jewett & Williston, 1971).

The results yielded from this study involved examining wave latencies and amplitudes of interleaved ABR and CAEP traces. Waveform latencies and amplitudes were compared for all three conditions in the right ear. Results from both the right and the left ear were recorded for the interleaved condition. As the right ear was used for the monaural conditions, comparisons with the interleaved condition were made for the right ear only. As only participants with normal, symmetrical hearing thresholds were included, the presence of a significant difference between the ears was ruled out.

4.1 Discussion of Results

4.1.1 Latency

As hypothesized, statistical analyses showed no significant difference in the latency of wave V for ABR and the P1-N1-P2 complex for CAEP between the monaural slow and interleaved conditions, but significantly longer latencies and poorer morphology for the monaural fast condition. This is highlighted in Figure 15 for ABR and Figure 19 for CAEPs, which display participant traces showing poorer morphology in the fast condition and comparable, cleaner morphology in the slow and interleaved conditions. These findings

support the underlying theory of this research, which states that neural adaptation occurs peripherally and therefore does not hinder bilateral, interleaved ABR and CAEP testing.

While no study has previously been done on bilateral, interleaved CAEP testing, the ABR findings are supported by Maruthy et al. (2018), who compared their 'bilateral simultaneous ABR' (BiSi-ABR) method with conventional ABR and found no significant differences in the latencies of waves III and V at 70 dB nHL. While they only parametrically analysed data collected at 70 dB nHL, they also observed (via non-parametric testing) no significant difference in participants' ABR thresholds down to 10 dB nHL. Given the similarities in objective, testing technique and acquisition and stimulus parameters between this study and the current, this observation highlights positive implications for the clinical feasibility of bilateral ABR testing.

It should be noted Maruthy et al. (2018) used a peripheral rate of 30.1 clicks per second, totalling a central rate of 60.2 clicks per second in the interleaved condition. Despite the discrepancies in rate, the results from the faster rate used in this research are consistent with the literature. Also significant to note is the consideration of order effects. Maruthy et al. (2018) alternated the order in which the initial click of the 'BiSi' condition was presented to rule out possible order effects between which ear received the first signal. They found no evidence of an order effect based on which ear received the first presentation of the stimulus. The absence of an order effect reinforces the underlying theory behind this study, that the neural generators of the ABR are separate for each ear. Similarly, the current study also sought to exclude the possibility of order effects between the three conditions by arranging all six possible orders of presentation of each condition into sequences and randomly assigning them to participants (see Table 1). There was no order effect observed between the conditions for both ABR and CAEP testing.

Previous research by Bencito (2020) at the University of Canterbury also backs up the findings of the current study. However, Bencito (2020) did not account for any possible order effects, presenting the three conditions in the same order of interleaved first, monaural fast second and monaural slow last. As a result, it's possible that if the three test conditions were presented in a different order, his results might have been significantly different. For example, participants could have been more relaxed at the beginning of testing versus the end, resulting in better traces for the interleaved condition as compared to the fast or even slow traces. By using the same equipment and test procedures but varying the presentation order of the test conditions, the current study conclusively supports Bencito's promising results with the interleaved condition when comparing wave V latencies between the three

conditions, regardless of the order of presentation. The findings from this current study support the extension of these results to higher up the ascending auditory pathway for CAEP testing.

4.1.2 Amplitude

Interestingly, the amplitudes of wave V and P1 showed no significant difference between the three conditions, while P1-N1 and N1-P2 amplitudes were significantly larger for the monaural slow conditions compared to the other two conditions. The former effects observed with the wave V amplitude was also seen in Bencito's (2020) study. The latter findings support the null hypothesis stating test condition will have no significant effect of wave amplitudes.

It was hypothesised no significant difference would be found between the slow and interleaved amplitudes, which was proven by the results. Typically, a faster overall rate as presented in the fast condition would be expected to produce wave responses with smaller amplitudes (Alhussaini et al., 2018; McKnight et al., 2018). Therefore, it was expected the monaural fast condition would yield smaller amplitudes. However, this disproven by the results for ABR wave V and CAEP P1 amplitudes.

A key observation is the large range between the minimum and maximum amplitudes for the P1-N1-P2 complex in the fast condition as seen in the box plots in Figure 21. This is to be expected, as the morphology of the traces yielded with the monaural fast condition were poorer than those of the interleaved and slow conditions. Therefore, identifying the wave peaks and troughs proved very difficult in some cases, leading to large variability in amplitudes acquired via the monaural fast condition.

The unexpected amplitude results could also be due to the high intensity with which the clicks were presented. The amplitude is characteristically proportional to the intensity of the stimulus, whereby as the intensity is increased, a greater number of neurons response, leading to larger wave amplitudes (Beattie, 1988; Donaldson & Rubel, 1990). A level of 70 dB was chosen for this research as it would be audible to participants and elicit a clear and visible response. The intensity of 70 dB used in this study could have been suprathreshold to participants' audiometric threshold to the degree of producing larger amplitudes or similar size, regardless of stimulus rate (Keesling et al., 2017; Pedriali & Kozlowski, 2006). If so, using a lower intensity could exhibit the smaller amplitudes typically expected when using fast stimulus rates.

A second theory, based on Mason and Mellor (1984) findings, is that the decreased amplitudes could be due to the far-field recording effects caused by changes in tissue electrical conductivity and the distance between the generator and recording electrodes. An alternate theory is that the convergence of auditory information in the ascending auditory pathway could contribute to similar amplitudes, regardless of stimulus rate (Cope et al., 2015; Malmierca et al., 2002). However, convergence typically happens higher up the pathway at the level of the ventral cochlear nucleus, inferior colliculus and above (Rothman et al., 1993), so it is unlikely convergence contributed to the observed amplitude effect in wave V. It is worth noting, the *p* value of this measure was very near to meeting the criterion of being significant. The difference in determining the lack of significance for this measure was 0.15, suggesting a significant difference may be found between the three conditions with further testing, a larger smaple size and particular focus on wave V amplitude in diagnoses protocols (Abadi et al., 2016).

A final explanation could be due to a poor SNR during testing, which impacts the amplitude of waveforms. As mentioned earlier, the Fsp is an objective measure of the SNR and consequent quality of wave responses, with an Fsp of 3.1 or greater indicating relatively good quality recordings. In particular, the Fsp for the ABR wave V was above five for all conditions, which is consistent with the amplitudes of these recordings as no difference in amplitude was found between the conditions. Conversely, the Fsp for the monaural slow condition for CAEP was above five, thus better amplitudes. This is backed by the P1-N1 and N1-P2 amplitudes, which had significantly higher amplitudes in the monaural slow condition. This theory appears to best explain the observed amplitude effects and is backed by the Fsp findings.

The above theories could explain the similarities in amplitudes, which also links with Bencito's study where no difference in wave V amplitudes between the conditions was found. However, it is important to remember the P1-N1 and N1-P2 amplitudes displayed the expected pattern, with larger amplitudes yielded with the monaural slow condition. Overall, the current findings support the use of the interleaved technique for ABR testing, as latencies were improved, and amplitudes were unaffected in this condition. However, further research is required to evaluate the effect of the interleaved technique on the amplitudes of the P1-N1-P2 complex.

4.1.3 Mean Fsp

Two replicate traces were recorded for each wave response. For each response, the mean Fsp of both replicate traces were then averaged. The mean Fsp for each condition was then calculated from these averages. There was no significant difference found in the Fsp of both ABR and CAEP traces between all three conditions, indicating no difference in the quality of waveforms based on test condition. A key finding is the lack of significant difference in Fsp between the monaural slow and interleaved conditions for both ABR and CAEP, emphasising the interleaved technique's equivalence and compatibility with traditional monaural testing once more. This further supports the underpinning theory of this project that use of the interleaved technique bypasses the effects of peripheral neural fatigue on wave responses.

The Fsp is an objective measure of a waveform's SNR, with the amplitude being a key factor in determining the noise component of the SNR. The Fsp results support the null hypothesis and reject the alternative hypotheses, which is to be expected given the amplitude data. If a significant difference between the conditions were found for Fsp, this would be expected to carry-over to measures of amplitude. That is to say, the interleaved condition did not appear to affect the SNR, and by extension, Fsp and amplitude.

4.2 Study Limitations

While precautions were taken to design a sound and reliable research model, some limitations were nonetheless present in this study. The relatively small participant size and participant recruitment pool limit the generalisability of the results to the general population. This was largely due to the time constraints arising from the global COVID-19 pandemic throughout the recruitment phase and duration of this research. Although the number of participants exceeded the minimum power assumption calculation (see Figures 9 and 10), the assumptions of normal distribution were not met for the amplitudes and some of the latencies of the recorded parameters, leading to a threat in the validity of statistical conclusion (Hegde & Salvatore, 2019). Preferably, more participants would have been recruited until normal distribution was achieved in order to meet the assumptions of parametric testing and minimise the risk of research validity (Verma, 2015).

Limiting the inclusion criteria to persons with normal hearing also greatly affects the generalisability of the results. While this was done in an effort to eliminate confounding

variables during the initial testing phase for this technique, ideally participants with hearing impairment would have been included to assess the feasibility of interleaved testing with this population of interest. As such, the current findings can be directly generalised to adults with normal hearing, while inferring similar results for other populations has not yet been proven and therefore weakens the external validity of this study (Girden, 1992; Haynes & Johnson, 2009).

Also affecting generalisability to clinical settings is the test environment. This study was performed in a controlled research setting with minimal electrical and environmental noise present, however this is not indicative of clinical and hospital settings, where AEP testing is typically performed. This is mainly a concern with CAEP recording where the amplitudes of the P1-N1-P2 complex were significantly smaller in the interleaved condition when compared to monaural testing. Hence, there is a possibility of reduced amplitude or morphology for results yielded with the interleaved condition due to external noise factors found in clinical settings, consequently leading to diagnostic implications. This is unlikely to be an issue for ABR, as both the monaural and interleaved conditions yielded comparable results in all parameters.

Additionally, the quantification and labelling of wave responses is done subjectively both in clinical and research contexts, through manual and visual inspection. While every care was taken during manual inspection of the results by the primary and supervising researchers, the risk of bias cannot be eliminated completely. Alternatively, an independent trained professional could have been recruited to further examine and mark the wave responses.

4.3 Future Research Directions and Applications

The major underlying concept behind this thesis was to address the time-consuming nature of AEPs, with the ultimate goal of improving their clinical feasibility. Ideally, all aspects of interleaved ABR and CAEP testing are included in a research project. However, a single thesis can only address a limited number of these aspects of clinical AEP testing. The current study can be seen as part of the preliminary research around bilateral and interleaved AEP testing, which opens up multiple pathways and opportunities for further research in this topic. With the goal of increasing the clinical feasibility and reducing testing time in mind, further research could focus on the use of the interleaved technique with different types if stimuli, such as chirps and frequency-specific tone-bursts for ABR, the latter being relied

upon heavily in infant ABR testing. Subsequent research into bilateral and interleaved CAEP using click and chirp stimuli. Maruthy et al. (2018) included intensities down to 10 dB nHL in their study but did not analyse these parametrically. Therefore, further parametric investigation is essential with the interleaved techniques at descending intensities, as done in monaural testing for threshold estimation.

This study explored ABR and CAEP, which represent the lower and the upper ascending auditory pathway on the assumption that the pathway for each ear is independent from the other. Theoretically, this assumption could carry over to the other AEP along this pathway. This includes responses such as the ASSR and AMLR. It can also include the stacked ABR response used in the diagnosis of retrocochlear pathologies (Don et al., 2011; Don et al., 2005; Philibert et al., 2003).

Furthermore, the study populations for bilateral and interleaved hearing should be enlarged to include both adults and children with various types of hearing loss, including conductive hearing loss and sensorineural hearing loss, the former found in both adult and paediatric populations and the latter being perhaps the most commonly seen type of hearing loss in infants undergoing diagnostic ABR. Consequently, CAEP testing to verify the amplification of infants also commonly involves those with sensorineural hearing loss. In particular, sensorineural hearing loss above mild severity and with different configurations should be explored, as only mild, sloping sensorineural hearing losses were included in this study. Retrocochlear pathologies resulting in hearing loss are also common among adults. It was intended for this type of hearing loss to be explored as part of the current study, with the opportunity of re-introducing ABR with the interleaved method to be a time-saving and cost-effective preliminary diagnosis tool for retrocochlear pathologies such as vestibular schwannomas. Due to the global COVID-19 pandemic, recruitment of this population was difficult and was therefore not explored in the current study but presents an interesting research prospect.

Finally, extending the test population from adults to paediatrics is a crucial step for the use of AEPs in clinical diagnostics and rehabilitative settings. While studies into bilateral AEP testing have focused on adults so far, testing infants and older children is essential for the generalisability of findings to clinical contexts. Particularly infants' responses with bilateral and interleaved ABR and CAEP are important, as they most frequently undergo AEP testing for the diagnosis of hearing loss and verification of intervention (Bagatto et al., 2010; Hazzaa et al., 2016).

Chapter 5: Conclusion

This thesis sought to evaluate the use of the efficacy of interleaved technique for ABR and CAEP testing as compared to the gold standard of conventional monaural testing with a slow rate. The interleaving of stimuli has the potential to reduce the clinical test time for ABR and CAEP, provided it yields wave responses comparable to those of the conventional method. This is particularly important in paediatric clinical settings, where clinical test time is key. This study found that the peak wave latencies acquired with the interleaved technique were not significantly different from those collected with the monaural slow condition for both ABR and CAEP. These findings support the underlying theory that neural adaptation occur peripherally as opposed to centrally in the auditory pathway. This indicates the effectiveness of bilateral interleaved testing, as opposed to using a fast stimulus rate which leads to poor results.

The Fsp and amplitudes of wave V for ABR and P1 for CAEP were also not significantly different between the interleaved and monaural slow conditions. However, the CAEP Fsp and amplitudes of P1-N1 and N1-P2 were significantly smaller in the interleaved condition as compared to the conventional monaural slow condition. While amplitude does not hold the same diagnostic importance as latency, the observed CAEP amplitudes may still be a contra-indication for use with the interleaved condition.

Overall, the results generally support the underlying hypothesis of this study concerning the efficacy of the interleaved technique for ABR testing. While this technique proved effective for the latencies of the P1-N1-P2 complex, further investigation into its effects of CAEP amplitudes in needed to justify its use in lieu of the conventional monaural slow technique. Additionally, the interleaved technique followed similar processes and procedures as those in clinical settings. This minimises the need for clinical retraining, saving on clinical resources.

References

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Appendices

UNIVERSITY OF CANTERBURY
Te Whare Wānanga o Waitaha
CHRISTCHURCH NEW ZEALAND

HUMAN ETHICS COMMITTEE

Secretary, Rebecca Robinson
Telephone: +64 03 369 4588, Extn 94588
Email: human-ethics@canterbury.ac.nz

Ref: HEC 2021/34

2 June 2021

Hsin-Jui (Regina) Lien and Shatha Nofal
School of Psychology, Speech and Hearing
UNIVERSITY OF CANTERBURY

Dear Hsin-Jui (Regina) and Shatha

The Human Ethics Committee advises that your research proposal "Interleaved Recording of the Auditory Brainstem Response" has been considered and approved.

Please note that this approval is subject to the incorporation of the amendments you have provided in your email of 28th May 2021.

Best wishes for your project.

Yours sincerely

Dr Dean Sutherland
Chair
University of Canterbury Human Ethics Committee

Appendix A: Ethics Approval

Appendix B: Ngāi Tahu Consultation Acceptance Letter

Ngāi Tahu Consultation and Engagement Group

15 March 2021

Tēnā koe Greg

Re: Interleaved Recording of the Auditory Brainstem Response

This letter is on behalf of the Ngāi Tahu Consultation and Engagement Group (NTCEG). The NTCEG considered your proposal and acknowledge it is a worthwhile and interesting project and you are clear about how you ought to take participants' (cultural) needs into account if and when applicable.

Given the scope of your project, no issues have been identified and further consultation with Māori is not required.

Thank you for engaging with the Māori consultation process. This will strengthen your research proposal, support the University's Strategy for Māori Development, and increase the likelihood of success with external engagement. It will also increase the likelihood that the outcomes of your research will be of benefit to Māori communities. We wish you all the best with your current project and look forward to hearing about future research plans.

The Ngāi Tahu Consultation and Engagement Group would appreciate a summary of your findings on completion of the current project. Please feel free to contact me if you have any questions.

Ngā mihi
Research & Innovation (on behalf of the NTCEG)

Research & Innovation | Te Rōpū Rangahau
University of Canterbury | Te Whare Wānanga o Waitaha
Private Bag 4800, Christchurch | Ōtautahi
ethicsmaoriconsultation@canterbury.ac.nz

Appendix C: Print Advertisement for Recruitment

UNIVERSITY OF CANTERBURY
Te Whare Wānanga o Waitaha
CHRISTCHURCH NEW ZEALAND

Hi everyone,

VOLUNTEERS NEEDED!

We are developing a new way to monitor hearing. This test will use in-ear headphones. We will play sounds through these two speakers and measure tiny electrical signals from your skin. We will measure responses from two different types of signals: one ear at a time and both ears at the same time.

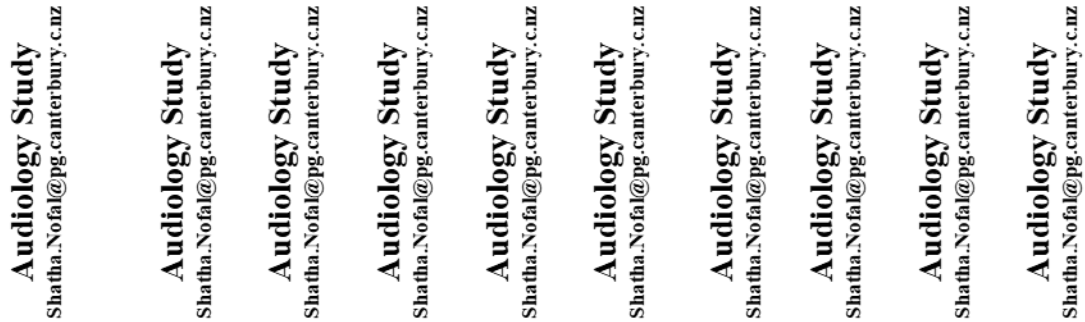
If you are:
1. 18 years of age or older, with or without hearing loss, then please get in touch with us!

This study will take place at the University of Canterbury Speech and Hearing Clinic throughout 2021.

You would be needed for one 2 hour session, during this time you will:
2. receive a free hearing test
3. help to develop a new hearing monitoring technique
4. receive a $20 fuel voucher as a token of our appreciation.

For more information, or to be involved in this project, please contact **Shatha Nofal (shatha.nofal@pg.canterbury.ac.nz)** or tear off the contact information below. Thank you for reading ☺

This project has been reviewed and approved by the University of Canterbury Human Ethics Committee.



Appendix D: Information Sheet for Participants

School of Psychology, Speech and Hearing
Telephone: +64 33694313
Email: shatha.nofal@pg.canterbury.ac.nz
2 March 2021
HEC Ref: 2021/34

Interleaved Recording of the Auditory Brainstem Response
Information Sheet for Persons Participating in Research Studies

My name is Shatha Nofal, and I am a 2nd year Master of Audiology students conducting research on the auditory brainstem response (ABR). The goal is to determine if using an interleaved (also known as alternating) method of presenting sounds in ABR recordings will offer advantages the quality of the response and reduce the time it takes to complete the test.

You have been approached to take part in this study because you are over 18 years old, have normal hearing, and are able to have the auditory brainstem response recorded. If you choose to take part in this study, we will ask about a history of your ear health and hearing and have a look at your ears. You will then have a hearing test. In-ear headphones will be used to play tones at different pitches to determine your hearing threshold. You will be asked to press a button when you hear the tones. This will take about 20 minutes. After the hearing test, we will begin the ABR test. You will be asked to sit in a comfortable armchair in a relaxed position. While you are sitting comfortably, we will measure tiny electrical signals from your scalp that are produced by the brain in response to sound (the "auditory brain-stem response"). Using a tissue and some cleaning alcohol, we will first lightly exfoliate the skin by rubbing firmly with an alcohol wipe in places where the adhesive sensors will be placed to make sure they can pick up the tiny signals. Sounds will be played through earphones placed on both ears while we record the signals. During tests, you don't have to do anything except sit and relax. After testing, the sensors will be carefully removed, and the session will be finished.

The procedures in this study are the same procedures a client would normally encounter in a hearing evaluation. When cleaning and preparing electrode sites the skin is lightly exfoliated (rubbed firmly with an alcohol wipe), which can occasionally cause these areas to be reddened. Alcohol hand cleaner will also be used, which can sometimes cause skin irritation, but if this occurs, a soothing cream will be provided. There is always a risk of emotional distress when undertaking hearing-related research. For most participants, this risk is no greater than the risk any adult would normally experience when consulting for hearing services, as most of the procedures in this study are the same procedures a client would normally encounter in a hearing evaluation (i.e., there is no deviation from the normal clinic protocol used by the University of Canterbury). There is the possibility that the placement of electrodes during ABR testing could trigger some sort of anxiety, but this would be an extremely rare occurrence - the procedure is generally low stress, and we encourage the clients to be relaxed or even asleep so the waveforms can be more robust and therefore easier to interpret.

Participation is voluntary and you have the right to withdraw at any stage without penalty. You may ask for your raw data to be returned to you or destroyed at any point. If you withdraw, I will remove information relating to you. However, once analysis of the raw data starts on 1 August, it will no longer be possible to remove your data as it will be integrated with other data. Participants will receive $20 petrol vouchers as a token of appreciation.

The results of the project may be published as part of a Master's thesis or in a journal article. But you may be assured of the complete confidentiality of data gathered in this investigation: your identity will not be made public. To ensure confidentiality, participants will be assigned an ID number. Data (hearing history sheet, hearing test results, speech perception test results) will contain only the participant ID. The data will be stored securely and may only be accessed by the primary researcher and thesis supervisors. Identifying information (consent forms, release of information forms, and requests for study results) will be stored securely and separately from the data. The stored data will be destroyed after 5 years. A thesis is a public document and will be available through the UC Library.
Please indicate to the researcher on the consent form if you would like to receive a copy of the summary of results of the project.

The project is being carried out as a requirement for a Master of Audiology thesis by Shatha Nofal under the supervision of Greg O'Beirne, who can be contacted at **gregory.obeirne@canterbury.ac.nz**. He will be pleased to discuss any concerns you may have about participation in the project.
This project has been reviewed and approved by the University of Canterbury Human Ethics Committee, and participants should address any complaints to The Chair, Human Ethics Committee, University of Canterbury, Private Bag 4800, Christchurch (human-ethics@canterbury.ac.nz).
If you agree to participate in the study, you are asked to complete the consent form and return to Shatha Nofal, contacted through email at **shatha.nofal@pg.canterbury.ac.nz**.

Appendix E: Consent Form

School of Psychology, Speech and Hearing
Telephone: +64 33694313
Email: shatha.nofal@pg.canterbury.ac.nz
2 March 2021

UNIVERSITY OF CANTERBURY
Te Whare Wānanga o Waitaha
CHRISTCHURCH NEW ZEALAND

Interleaved recording of the Auditory Brainstem Response
Consent Form for Persons Participating in Research Studies

1. I have been given a full explanation of this project and have had the opportunity to ask questions.
2. I understand what is required of me if I agree to take part in the research.
3. I understand that participation is voluntary and I may withdraw at any time without penalty. Withdrawal of participation before 1 August will also include the withdrawal of any information I have provided. It will not possible to remove the influence of your data on the results after 1 August.
4. I understand that any information or opinions I provide will be kept confidential to the researcher and their primary supervisor and that any published or reported results will not identify the participants. I understand that a thesis is a public document and will be available through the UC Library.
5. I understand that all data collected for the study will be kept in locked and secure facilities and/or in password protected electronic form and will be destroyed after five years.
6. I understand the risks associated with taking part and how they will be managed.
7. I understand that I can contact the researchers Shatha Nofal (**shatha.nofal@pg.canterbury.ac.nz**) or supervisor Greg O'Beirne (**gregory.obeirne@canterbury.ac.nz**) for further information. If I have any complaints, I can contact the Chair of the University of Canterbury Human Ethics Committee, Private Bag 4800, Christchurch (human-ethics@canterbury.ac.nz)
8. I would like a summary of the results of the project.
9. By signing below, I agree to participate in this research project.

Name:_____ Signed:_____ Date:_____

Email address *(for report of findings, if applicable)*:_