An Evaluation of Speed and Sensitivity of Audiometry via the Auditory Steady State Response and the Auditory Brainstem Response

A Thesis Submitted in Partial Fulfilment of the

Requirements for the Degree

of Master of Audiology

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Abstract

Universal newborn hearing screening has been a mainstay of many developed countries since the early to mid-2000's, after evidence showed that the earlier hearing loss is detected, the better for the speech and language outcomes of the individual, as habilitation can commence quickly (Ching & Leigh, 2020; Ching et al., 2017; Ching et al., 2018; Cowan et al., 2018; Davis et al., 1997). The Auditory Brainstem Response (ABR) has long been used in newborn hearing screening programmes to determine hearing thresholds and diagnose infants with hearing loss, due to its objective diagnostic sensitivity in a population who otherwise could not provide information regarding their hearing levels. Whilst extremely accurate, the time needed to perform a full diagnostic ABR often exceeds the average infant sleep cycle (Janssen, 2010).

The desire to find an alternative electrophysiological measure that is as accurate as sensitive as the ABR but can be performed in a shorter test time has been the basis of much ongoing research. The Auditory Steady State Response (ASSR) is gaining traction as an alternative or supplementary method to the ABR (Sininger, 2018). Additionally, the interleaved ABR (Bencito, 2020) has been shown to maintain waveform morphology, whilst being substantially faster to obtain than the conventional ABR. The current study will compare both test time and the detection threshold provided by the ASSR and the interleaved ABR, to determine if either are a valid alternative to the conventional ABR.

Fifteen normally hearing participants (11 females and 4 males), aged 21 to 39 years (*M* = 28.1 *SD* = 4.6) underwent testing of both the ASSR and interleaved ABR in a counter balanced order. A chirp was utilised to elicit both responses, at the same three levels (20dB nHL, 30dB nHL and 40dB nHL). A fixed protocol for was used with each stimulus delivered for a set time of five minutes, before the next stimulus level or type began. The test time and sensitivity information were then extrapolated using offline analysis to determine if either method shows promise in replacing or supplementing the conventional ABR in newborn hearing screening protocols in Aotearoa and worldwide.

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List of Abbreviations

aABR	Automated Auditory Brainstem Response
ABR	Auditory Brainstem Response
AC	Air Conduction
AEP	Auditory Evoked Potentials
AM	Amplitude Modulated
ANSD	Auditory Neuropathy Spectrum Disorder
AoDC	Advisers on Deaf Children
ASSR	Auditory Steady State Response
BC	Bone Conduction
CF	Carrier Frequency
dB peETSPL	Decibel Peak-to-Peak Equivalent Threshold Sound Pressure Level
DND	Deafness Notification Database
EEG	Electroencephalogram
FFT	Fast Fourier Transform
FM	Frequency Modulated
Fmp	Multiple-Point F-ratio
Fsp	Single-Point F-ratio
JCIH	Joint Committee on Infant Hearing
MF	Modulation Frequency
MoH	Ministry of Health
NZSL	New Zealand Sign Language
OAE	Otoacoustic Emissions
PAMR	Post Auricular Muscle Response
PC	Phase Coherence
RETSPL	Reference Equivalent Threshold Sound Pressure Level
RN	Residual Noise
SNR	Signal to Noise Ratio
UNHS	Universal Newborn Hearing Screen
VRA	Visual Response Audiometry

1 Introduction

Congenital and early-onset hearing loss is considered a major public health issue that has driven the development of universal newborn hearing screening programmes (UNHS) worldwide. Extensive evidence has shown that the sooner the hearing loss is detected and habilitation commenced, the better the outcomes for the child's speech and language development (Apuzzo & Yoshinaga-Itano, 1995; Ching & Leigh, 2020; Ching et al., 2017; Ching et al., 2018; Cowan et al., 2018; Davis et al., 1997; Downs, 1995; Downs & Hemenway, 1969; Yoshinaga-Itano, 1999; Yoshinaga-Itano et al., 1998).

To determine an infant's hearing levels, an objective test using the Auditory Brainstem Response (ABR) is typically performed, as behavioural responses cannot be reliably obtained in this population. The ABR is an electrophysiological measurement of the brain's response to sound and needs to be performed on a patient that is asleep or extremely relaxed in order to obtain clear results, otherwise myogenic activity can easily overwhelm the electrical signal. The ABR is a highly accurate technique for estimating hearing levels, but the assessment can span multiple sessions to obtain conclusive results, and rarely fits into a single infant sleep cycle. Consequently, multiple appointments are often needed, which can place stress on the whānau whilst they wait for a diagnosis. This can potentially cause a greater chance of patient attrition, and requires extensive time to be spent on diagnostic assessments in an already busy audiology department.

A technique that could match the sensitivity of the ABR within one appointment would assist newborn hearing screening programmes in addressing the above-mentioned limitations, and allow more clinician time to be spent on counselling whānau and commencing habilitation where necessary. An alternative electrophysiological response known as the Auditory Steady State Response (ASSR) has been gaining traction in recent years as allows for more time-efficient testing, largely due to the ability to test using multiple stimuli at once. However, evidence regarding its sensitivity has been mixed, and it does

not provide all the diagnostic functions that the ABR can. Therefore, it is unlikely to provide a complete solution to the above-mentioned limitations.

Another proposed measurement is the interleaved ABR, which involves switching back and forth between left and right ears so that data from each ear is gathered simultaneously, instead of the classic monaural sequential stimulation approach. This should allow for a faster test time, whilst maintaining the diagnostic versatility the ABR is known for. However, it remains unclear whether the ASSR or the interleaved ABR represent the best solution in terms of balancing speed and sensitivity. The present study aims to address this gap in knowledge by comparing the ASSR and interleaved ABR for speed and sensitivity. This knowledge should help to inform newborn hearing diagnostic protocols in Aotearoa and worldwide.

The following review of the literature will explore the concepts underpinning both the ASSR and ABR in more detail, and will critically evaluate some of the existing evidence and underpinning research into both speed and diagnostic sensitivity of each technique before arriving at a specific research question. The ensuing chapters will then detail the methods used for addressing the question, the findings and will offer a discussion and conclusions.

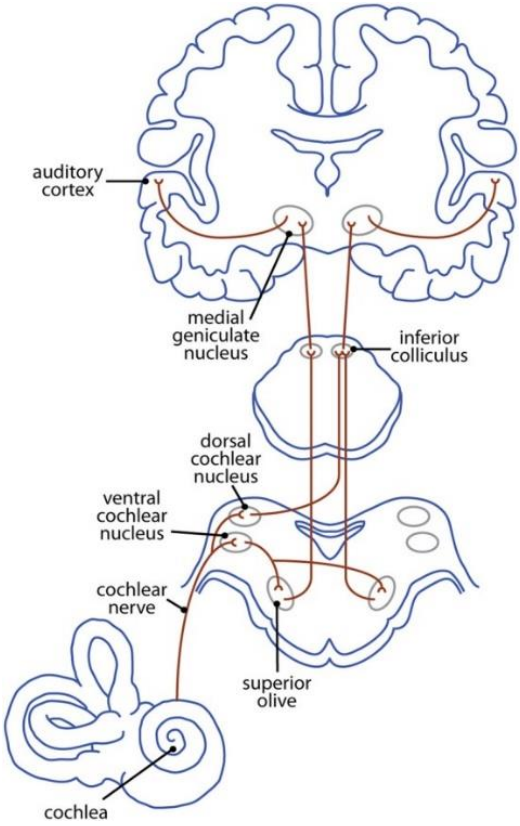
2 Review of Literature

2.1 The Use of Auditory Evoked Potentials in Clinical Audiology

The human auditory pathway begins in the periphery at the outer, middle, and inner parts of the ear. Once sound has reached the cochlea, it is transformed into electrical impulses, which travel up the ascending auditory pathway via the auditory nerve, to the central structures of the brainstem, mid brain and auditory cortex, the latter of which are involved in the perception and understanding of complex sound patterns such as speech (Picton, 2011). Using electrophysiological techniques, it is possible to objectively measure the response to sounds at various points of the ascending auditory pathway (Figure 2.1) (Butler & Lomber, 2013). Known as auditory evoked potentials (AEPs), acoustic stimuli are used to evoke electrical responses by the auditory nerve and other structures, which can be used to obtain information regarding a person's hearing levels (Krishnan, 2023; Picton, 2011). AEPs can be collected non-invasively, and their use is widespread among populations who are unable to provide behavioural responses to sounds used in hearing testing. The most common use of AEPs within clinical audiology is the use of the ABR for the screening and diagnosis of hearing loss in infants (Krishnan, 2023) in countries with newborn hearing screening programmes.

Figure 2.1

The Ascending Auditory Pathway from Cochlea to Cortex



Note. From "Functional and Structural Changes Throughout the Auditory System Following Congenital and Early-Onset Deafness: Implications for Hearing Restoration" by B. E. Butler and S. G. Lomber, 2013*, Frontiers in System Neuroscience 7(92)* (http://doi.org/10.3389/fnsys.2013.00092). CC BY 4.0.

2.2 History of the Newborn Hearing Screening Programme

Attempts to create a screening program to identify Deaf infants and infants with hearing loss began as early as the mid-1960's in the United States (Commission on Education of the Deaf, 1988, February 1; Downs & Sterritt, 1964; Hardy et al., 1959; Ruben, 2021). The behavioural methods in use were not considered sensitive nor specific enough to ensure sufficient capture on a population-based scale (Downs & Hemenway, 1969), nor was equipment available to perform testing easily and quickly on

large numbers of infants (Downs & Hemenway, 1969; Downs & Sterritt, 1964). Whilst effective newborn screening for all infants was not yet able to be implemented, risk factors for hearing loss in neonates were identified (Richard & Roberts, 1967), allowing for some monitoring of those children deemed at 'high risk' of developing hearing loss. In response to the early attempts at infant testing, the Joint Committee on Infant Hearing (JCIH) was formed in 1969, gathering professionals from the fields of audiology, otolaryngology, paediatrics and nursing with the mission of creating best practice recommendations regarding identification of children with hearing loss, and to promote the need for newborn hearing screening (Joint Committee on Infant Hearing, n.d). Their first statement in 1971 acknowledged programmes currently underway across the country, but stated strongly that the data available showed that universal screening could not, at that time, be justified due to lack of appropriate test procedures; and encouraged ongoing research towards the aim of detection hearing loss as early as possible (Joint Committee on Infant Hearing, 1971).

Research did continue, both towards the advancement of techniques for objective hearing screening, and regarding the experiences of those with hearing loss. By the late 1980's, multiples studies showed that Deaf children and children with hearing loss did not develop expressive and language skills at the same rate as their peers, and in many cases were years below their age level (Geffner, 1987; Meadow, 1980; Moog & Geers, 1985; White & White, 1987). The seminal 1988 *Towards Equality: Education of the Deaf* report described the flow on effects of language deprivation, such as reduced educational achievement, employment options, earning capacity and quality of life (Commission on Education of the Deaf, 1988, February 1). By 1982, the JCIH position statement recommended screening and audiological follow up for infants deemed at high risk of hearing loss.[1] Whilst recommending the use

[1] Risk factors identified were: family history of childhood hearing loss, congenital perinatal infection (cytomegalovirus, rubella, herpes, toxoplasmosis, syphilis), craniofacial abnormalities of the head and neck, birth weight less than 1.5kgs, hyperbilirubinemia at levels requiring transfusion, bacterial meningitis, and severe asphyxia (Joint Committee on Infant Hearing, 1982).

of behavioural audiometry or electrophysiological measurements to determine hearing thresholds, they did not specify any particular methods, equipment or procedures, but did state that "acoustic testing of all newborn infants has a high incidence of false positive and false-negative results and is not universally recommended" (Joint Committee on Infant Hearing, 1982, p. 1). In 1990, they modified their statement to expand the list of risk factors[2] and to recommend the use of the ABR, going so far as to define stimulus parameters and passing levels for screening. However, the approach to screening only high-risk infants meant only around 50% of children with hearing loss were being identified (Pappas, 1983; Stein et al., 1983), and the average age of identification was 11 to 19 months of age for those with risk factors (Harrison & Roush, 1996; Mauk et al., 1991), and 15 to 19 months for those without (Harrison & Roush, 1996; Stein, 1995). Parents generally do not suspect a hearing loss in their child until they begin to miss speech and language milestones at 12 to 24 months of age, so those without any risk factors for hearing loss can go undiagnosed for some time (Yoshinaga-Itano et al., 1998).

During the 1970's and 1980's a committed group of medical professionals continued research in the field and advocated for the introduction of universal hearing screening. By 1994, JCIH released an updated position statement that promoted the universal screening of all newborns, as "failure to diagnose the remaining 50% of children with hearing loss results in diagnosis and intervention at an unacceptably late age" (Joint Committee on Infant Hearing, 1994, p. 1). As stated by (Downs, 1993, p. 1) "The sense of jubilation among professionals was tangible and intense… Finally, we thought, the long campaign to secure the right of newborns to be screened for hearing was over." Not only did the 1994 position statement justify the need for screening of all infants, it set out guidelines that infants should have their hearing loss identified by three months of age, and ideally soon after birth, based upon a

[2] Risk factors added were: ototoxic medications, mechanical ventilation for >10 days and syndromic diagnoses known to be associated with hearing loss (Joint Committee on Infant Hearing, 1990).

growing body of evidence that showed the sooner intervention began, the better the outcomes for speech and language development at a rate comparable to their normally hearing peers (Geffner, 1987; National Institutes of Health, 1993; Stewart & Downs, 1993; White & White, 1987). A similar consensus statement was reached in other parts of the world - Europe in 1994 (Lutman & Grandori, 1999), Australia in 2002 (Australian Newborn Hearing Screening Committee, 2001, November), and New Zealand in 2010 (New Zealand Government, 2010, August 11).

2.3 The Need for Early Detection of Hearing Loss

Whilst today there is a large body of evidence supporting the need for early detection, early on the need for universal infant hearing screening was not supported by all audiologists. Bess and Paradise (1994) published an article that objected to the JCIH position statement, suggesting that intervention before 6 months did not have a better impact than that started before 18 months, the stage that most infants with hearing loss would be detected (even those not in the high-risk category). Apuzzo and Yoshinaga-Itano (1995) were quick to refute this idea. They studied the outcomes of 69 children who had been diagnosed at differing times in their infancy, but received the same interventions once identified. Of the four groups, those identified to have hearing loss before three months of age (thus receiving intervention correspondingly earlier) showed significantly higher language scores than the other groups who were screened at older ages, regardless of other disabilities or severity of hearing loss. This study was conducted before the implementation of universal screening recommended by the JCIH. All the infants that were in the 'early identified' group (less than three months) were identified purely because they were in the high-risk category. The authors concluded that these results should help provide impetus for universal screening of infants.

Further studies on the efficacy of early intervention continued, alongside the rolling out of universal newborn hearing screening programs in the US, the UK and Europe, all of which supported the approach of early detection and intervention (Davis et al., 1997; Downs & Yoshinaga-Itano, 1999;

Yoshinaga-Itano, 1999; Yoshinaga-Itano & Apuzzo, 1998; Yoshinaga-Itano et al., 1998). By identifying hearing loss as quickly as possible, amplification and associated habilitative interventions can begin, and these interventions reduce the chance of receptive and expressive language delays.

2.4 Effectiveness of Newborn Hearing Screening Protocols

The introduction of universal hearing screening is admirable, but all interventions must have their benefits assessed. Research to quantify the effectiveness of newborn hearing screening programmes continued. Downs (1995) conducted a review of the Colorado UNHS programme three years after implementation, and found that it was extremely cost-effective, compared to other universal infant tests that are routinely performed in the United States. This was helped in part, by the ability to use non-professional personnel to perform the screening (Downs, 1995; Schmuziger et al., 2008), as well as the increasing access to automated electrophysiological equipment. A critical review Davis et al. (1997) in the UK supported these findings, and found that a newborn hearing screening programme had much higher sensitivity and specificity than the previous programme in place for 7–8-month-olds. Yoshinaga-Itano et al. (1998) studied children divided into two groups – those that were identified before six months of age, and those identified after, all of whom received amplification within two months of identification. The researchers controlled for other demographic subgroups that could impact expressive and receptive language abilities such as cognitive ability, communication mode, ethnicity, socioeconomic status, and presence of additional disabilities. Regardless of the degree of hearing loss, children who were identified before 6 months and therefore received intervention earlier, demonstrated significantly better receptive and expressive language skills, despite other demographic factors.

Similarly, the Australian Longitudinal Outcomes of Children with Hearing Impairments (LOCHI) study aims to determine the effectiveness of the UNHS and early intervention on improving outcomes for Deaf infants and infants with hearing loss on a population level (Cowan et al., 2018). The study

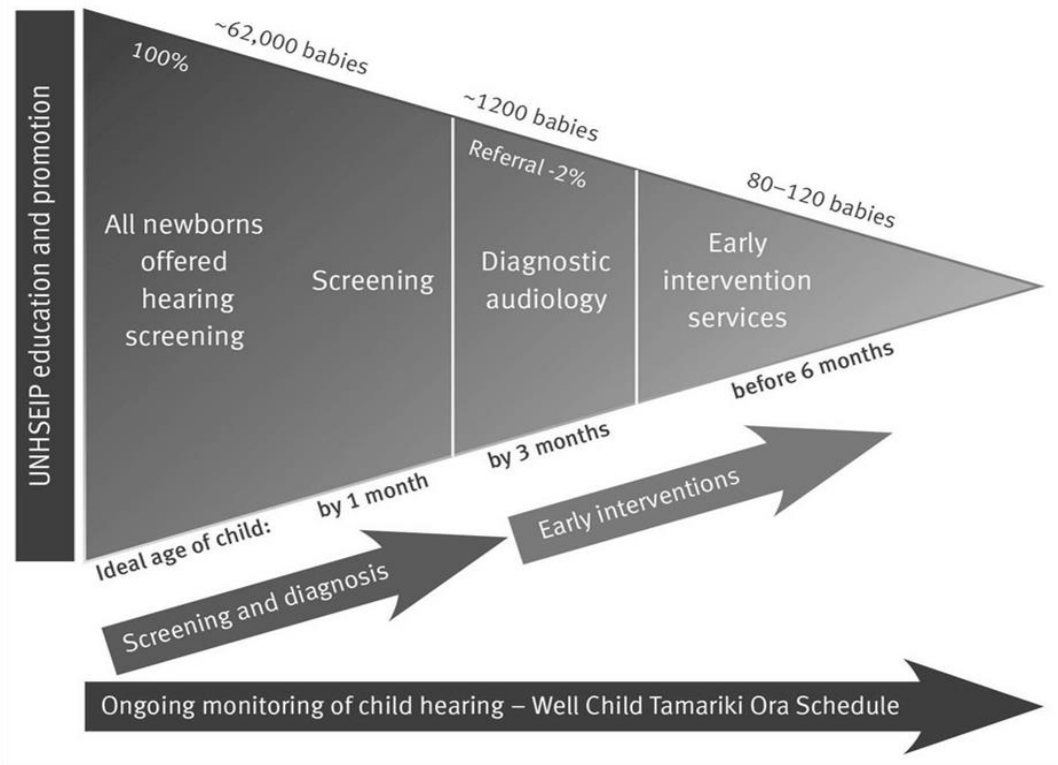
involved 470 children, all of whom had their hearing loss detected by three years of age. As the roll out of the UNHS in Australia took time, the opportunity arose for the researchers to ethically determine the impact of early detection and intervention on one cohort of infants born in a state where UNHS was already in place, compared to those in other states where screening was still being introduced. The median age of intervention for children that received screening at or shortly after birth was 3.9 months, compared to 17.3 months for group who did not receive newborn hearing screening (Ching & Leigh, 2020). All infants were eligible to access the same hearing healthcare and interventions once their hearing loss was identified. The study has assessed the participants at six months, 12 months, 3 years and 5 years post fitting/implantation, and their extensive research has found that diagnosis and intervention prior to 12 months is crucial for maximising speech and language outcomes and quality of life scores (Ching & Leigh, 2020; Ching et al., 2017; Ching et al., 2018; Dillon et al., 2013).

2.5 Universal Newborn Hearing Screening in Aotearoa

As this study focuses on the diagnostic portion of the universal newborn hearing screening protocol, the outline of the programme here in Aotearoa will be brief, simply to familiarize the reader with the procedures and timelines in place. Figure 2.2 provides an overview of the newborn hearing screening pathway.

Figure 2.2

The Newborn Hearing Screening Pathway in Aotearoa



Note. From *Universal Newborn Hearing Screening and Early Intervention Programme (UNHSEIP): National Policy and Quality Standards (2nd edn.)* (p. 3), by Ministry of Health, 2016, (https://www.nsu.govt.nz/system/files/page/unhseip-national-policy-and-qualitystandards-2nded-2016.pdf). Copyright 2016 by Ministry of Health. Reprinted with permission.

The Aotearoa New Zealand Universal Newborn Hearing Screening and Early Intervention Protocol (UNHSEIP) was established nationwide in 2010 after piloting in in the Waikato DHB in 2004[3] (New Zealand Government, 2010, August 11). The UNHSEIP was established with the aim of "early

[3] See (New Zealand Government, 2010, August 11) for a timeline of the UNHSEIP rollout in Aotearoa New Zealand.

identification of newborns with hearing loss so that they can access timely and appropriate interventions, inequalities are reduced and the outcomes for these children, their families and whānau, communities and society are improved" (Ministry of Health, 2016a). The targets of the UNHSEIP are described as '1-3-6' goals, which are based on the recommendations of the Joint Committee on Infant Hearing (2007):

1 = babies should be screened by one month of age

3 = Audiology assessment completed by 3 months of age (if appropriate)

6= Initiation of appropriate medical and audiological services, and early intervention education services, by 6 months of age (National Screening Unit, 2014, November 21).

2.5.1 Screening

The screening is undertaken at hospital in the days after birth, or at an outpatient's appointment within the first few weeks if the infant is not born in hospital. To meet the programmes goals, 95% of infants need to be screened by one month of age (Ministry of Health, 2016a). Automated ABR (aABR) testing is performed at 35 dB nHL, a level which will identify permanent congenital hearing loss of a severity that is likely to impact on the development of speech and language (Ministry of Health, 2016a). A clear response in both ears needs to be obtained for the infant to be discharged. If clear response/s are not obtained in one or both ears, the test is repeated in the next few days. If clear response/s are not detected at the second screening, the child will be referred to the local audiology department for a full diagnostic test. If the infant passes the screening but has identified risk factors for hearing loss (Figure 2.3), they will continue to be monitored by the audiology department for the timeframe specified in the protocol guidelines (Ministry of Health, 2016b).

Figure 2.3

Risk Factors Requiring Ongoing Surveillance by Audiology Departments

Risk factors for hearing loss requiring surveillance

Babies with one or more of following risk factors require hearing surveillance as part of the Universal Newborn Hearing Screening and Early Intervention Programme. This form is to be completed by medical, nursing or midwifery staff to enable newborn hearing screeners to make audiology referrals, or in the case of jaundice, to be re-screened.

Baby's name.....

Baby's NHI. ..... DOB.....

	YES
1. Does the baby have cranio-facial anomalies, including those involving the pinna, ear canal, cleft palate? (excluding ear pits and tags or cleft lip in isolation) *Note: if the baby has atresia or significant facial malformation they will not be screened automatically*	☐
2. Does the baby have a confirmed or suspected syndrome related to hearing loss?	☐
3. Does the baby have a proven congenital infection due to toxoplasmosis, rubella or CMV?	☐
4. Has the baby been ventilated using IPPV or HFV for more than 5 days, or Nitric or ECMO for any length of time? (CPAP excluded)	☐
5. Has the baby had severe asphyxia (Sarnat stage 2/3, cooled)?	☐
6. Has the baby had a brain haemorrhage (Grade 4+ post haemorrhagic hydrocephalus)?	☐
7. Has the baby been exposed to ototoxic medications at above therapeutic levels? (Paediatrician discretion – levels monitored after third course, refer only if outside of therapeutic range).	☐
8. Has the baby had severe neonatal jaundice at or above exchange transfusion level? (once resolved, notify UNHSEIP screening staff in your DHB for re-screening)	☐
9. Does the baby have confirmed or strongly suspected meningitis /meningoencephalitis?	☐
10. Has the baby received head/brain trauma (especially basal skull/temporal bone fracture)?	☐

Note. From *Risk factors for hearing loss requiring surveillance form,* by National Screening Unit, 2016 (https://www.nsu.govt.nz/resources/risk-factors-hearing-loss-requiring-surveillance-form). In the public domain.

2.5.2 Diagnostic Testing

Full diagnostic testing is performed by an audiologist at the local hospital or clinic. Within the three-month timeframe, they must perform a bilateral diagnostic ABR on the infant to determine hearing thresholds, regardless of whether the screening lacked clear responses bilaterally or unilaterally (Ministry of Health, 2016a). Order of testing depends on whether the referral was bilateral or unilateral, but is a full diagnostic test, covering at least six phases by air conduction (AC) (gathering thresholds at 0.5 kHz, 2 kHz, and 4 kHz in each ear, i.e., the 'core' audiometric frequencies that are considered to have the greatest relevance for speech perception), as well as bone conduction (BC) and masking if necessary. If the infant does not produce a recognizable wave V to tonebursts at the highest level of stimuli, then an AC click is delivered. This broadband sound is delivered at 95 dB HL (or the highest level of the audiometer)[4] as part of the procedure to determine if the infant may have Auditory Neuropathy Spectrum Disorder (ANSD). First described by Starr et al. (1996) ANSD indicates functional outer hair cell presence, but a dysfunctional eighth nerve. When an ABR is absent, it is of vital importance to determine if this is due to profound hearing loss or ANSD, as the management, treatment options and outcomes of the two diagnoses are vastly different. The ABR is a key electrophysiological test in the newborn hearing protocol for diagnosing ANSD. Related procedures like the ASSR are unable to offer the necessary information for an ANSD diagnosis, and this is perhaps one of the main reasons for continued reliance on the more-versatile ABR, despite possible speed advantage associated with the ASSR (see section 2.7.7 for details). Otoscopy, immittance testing and otoacoustic emissions (OAE's) are also performed during these appointments. Often it takes more than one appointment to determine the hearing thresholds of the infant, and implications of this are discussed later in this literature review.

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[4] Reference levels for the ABR stimulus used in Aotearoa New Zealand are non-standardized and the RETSPL of the stimulus are significantly higher than the ISO 389-6 standard. For an overview of the impacts of this see (Maslin et al., 2021; Maslin & O'Beirne, 2022)

Audiologists are also required to notify The Ministry of Health (MoH) Deafness Notification Database (DND) when diagnosing an infant or child with hearing loss, for the purposes of research, nationwide audit, and reporting.[5]

2.5.3 Amplification

If the infant is diagnosed with hearing loss, treatment options will be discussed with the whānau, including amplification, implantation, and use of New Zealand Sign Language (NZSL). Many whānau will use a combination of tools. Often an Advocate of Deaf Children (AoDC) is assigned to the whānau to assist them with navigating life with hearing loss, liaise with third parties such as treatment providers and education facilities, and to advocate on behalf of the child.[6] All infants diagnosed with hearing loss under the UNHSEIP are eligible for fully funded amplification until age 18, or 21 if in full time study. After this point they are discharged to private adult services and must access care and funding through these pathways.[7]

Newborn hearing screening and early intervention protocols rely on the ABR to provide critical information about an infant's hearing status that cannot could not otherwise be obtained at such a young age. This allows for amplification to be provided to those diagnosed with hearing loss, far earlier than it would be if we could only rely on behavioural audiometry, and in the critical period for age-appropriate speech and language development. The next section of this literature review will discuss the history of the ABR, specifics for its effective application, sensitivity and specificity, and one major drawback – test time. The following section will discuss attempts to modify the ABR to decrease the test

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[5] Annual reports collated from the data collected from the DND can be found here: https://audiology.org.nz/for-the-public/new-zealand-deafness-notification-database/nz-dnd-reports/

[6] For more information about the role of the AoDC, see https://www.education.govt.nz/school/student-support/special-education/supporting-children-who-are-deaf-and-hard-of-hearing/

[7] More information regarding the funding streams for adults in Aotearoa New Zealand can be viewed at https://audiology.org.nz/for-the-public/hearing-aid-funding/

time for infant diagnostic sessions, as well as examine an alternative method gaining popularity – the Auditory Steady State Response.

2.6 The ABR

Alongside the movement to implement universal newborn hearing screening and extensive research highlighting the importance of early intervention, studies were being undertaken from the mid 1960's to determine the validity of scalp recorded electrical evoked potentials for use in estimating hearing thresholds in audiology. Early studies of electrical potentials were measured from the external ear (Sohmer & Feinmesser, 1967) and the scalp, with researchers hypothesizing that these short latency responses were generated by brain stem structures (Hecox et al., 1976; Jewett et al., 1970; Jewett & Williston, 1971; Starr & Achor, 1975). The ABR is far field potential,[8] arising from multiple generators in the brainstem nuclei, in response to transient sounds. It is an early, or short-latency AEP, occurring within 10-15ms of the presentation of the stimulus (Starr, 1976). It produces a characteristic peaked waveform (Figure 2.4), that is easily interpreted visually and the measurement of latencies, inter-peak latencies, and amplitude of the ABR waveform have several diagnostic applications, not limited to the field of audiology (Krishnan, 2023).[9] We label these peaks/waves with roman numerals I to VII as per the naming convention of Jewett and Williston (1971). Other uses of the ABR in an audiological context include determining the integrity of the VIIIth nerve and auditory brainstem pathway, and for use intraoperative monitoring of the auditory system during otologic surgery (O'Beirne, 2015; Starr, 1976).

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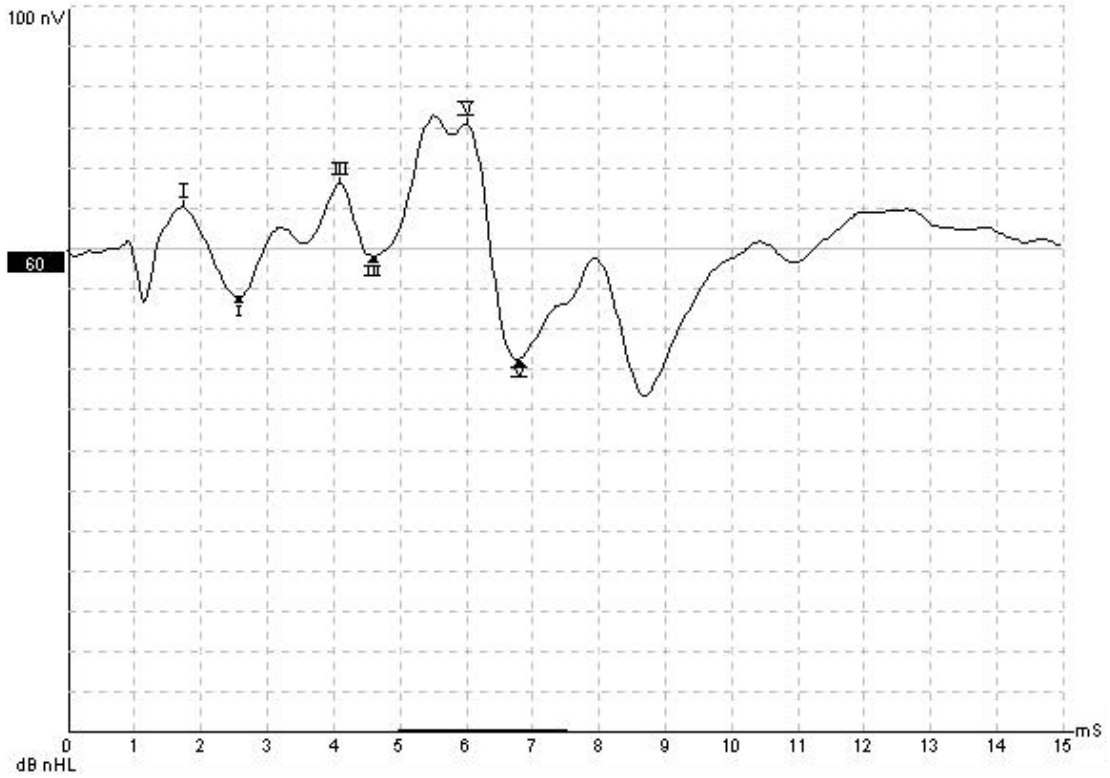
[8] Far field potentials refer to those that we measure at a distance from their origin. The ABR is typically measured from the vertex or forehead and mastoid positions, some distance from its origin at the brainstem.

[9] Newborn hearing screening is not mentioned in Jewett et al. (1970) paper on the ABR, instead they suggest its use for determining levels of brain damage and the presence of legion surrounding the nuclei and brainstem. The ABR has also been used a neurological assessment tool to diagnose Multiple Sclerosis.

Figure 2.4

An ABR Waveform, with Labelled Peaks



Note. Wave I, III and V are labelled. SN10 is the labelled negative peak around 7 ms. Stimulus used to elicit this ABR was a click at 60 nHL via an insert phone, with the electrode montage on the vertex-to-nape of neck.

2.6.1 Recording Parameters

The most commonly used electrode montage for the ABR is the 'ipsilateral extrude montage' in which the active electrode is placed on the forehead or vertex, the reference electrode on the mastoid of the ipsilateral ear to stimulation and a ground electrode placed further away on the neck, clavicle, or sternum (Hill, 2018, October 1). As the ABR has a small amplitude that is easily swamped by noise, it is important to reduce noise as much as possible during recording. Myogenic activity from the participant can overwhelm the signal, so the patient must be as relaxed as possible, and ideally sleeping. Working in a sound proof room is preferred to prevent acoustical noise from disturbing the patient. Electrical

interference from external sources also needs to be minimized. A common source of electrical interference is mains activity which can be minimized by room set up, but generally filtering of the response is utilised in order to attenuate the frequency (50 Hz in Aotearoa New Zealand) of main interference (Lightfoot & Stevens, 2014). It is common to filter the response with a bandpass from 30-80 Hz (high pass cut-off) and 1500–3000 Hz (low pass cut-off). Recording parameters for this study can be seen in Methods sections 3.2 and 3.4.

2.6.2 Effects of Stimulus Type, Intensity and Repetition Rate

The ABR is typically elicited using short duration sounds, with repeated presentations in the thousands, which allow for averaging of the response waveform to reduce noise power. Stimuli vary but in the context of newborn hearing screening, are likely to be tone bursts with a 2-1-2 envelope,[10] broadband clicks, or chirps (see Methods section 3.3 for more information regarding chirp stimuli). Toneburst stimuli are used to determine frequency specific hearing thresholds as the energy of the signal is targeted around the specific frequency (Picton, 2011). Broadband sounds like clicks and chirps are used to gauge the overall functioning of the auditory nerve, to find a starting level for threshold testing, and to test for ANSD (Starr et al., 1996).

Selecting an appropriate repetition rate for the stimuli is of utmost importance. As the ABR is a neurally generated onset response, the nerves require a refractory period before another action potential can occur (Hecox et al., 1976; Lanting et al., 2013). If the sounds are presented too close together, neural fatigue can occur and the waveform will degrade (Burkard et al., 1990; Don et al., 1977; Plourde et al., 1988). Don et al. (1977) demonstrated that this neural fatigue occurs primarily peripherally (i.e., in auditory nerve structures), rather than centrally (brainstem structures), by

[10]A stimulus with rise and fall times of 2 periods and plateau of 1 period. For more information see (Davis et al., 1984)

performing a study that played a sequence of 20 clicks to the participant at a rate of 100 clicks/second. The first click was played in to their right ear, the next 18 into the left, and the final click in to the right. The ear specific stimulation paradigm meant that while the brainstem structures were stimulated at 20 clicks per second, the right peripheral structures were stimulated with much longer gaps between each sound than the left structures. Waveform morphology for the right ear was unaffected, whilst the left ear showed an increase in Wave V latency and decrease in amplitude. The high stimulus rate of the left side did not impact on the right ear's ABR, proving the neural fatigue is caused in the peripheral section of the auditory system, rather than centrally. The refractory period of an auditory neuron is one to a few milliseconds (van den Honert & Stypulkowski, 1984), meaning the time between stimuli can be relatively short.

In combination with repetition rate, the duration of the stimulus used must also be appropriate to allow capture of the entire ABR waveform. As the ABR gets closer to threshold, the latency of wave V increases, so the epoch duration of the stimulus must be long enough to elicit the response. If using a low frequency toneburst, we must allow extra time due for the cochlear travelling wave to reach the apex. It is common to use a 20ms epoch for a higher frequency stimulus or a click, it extends to a 25ms epoch for a lower frequency stimulus or a broadband chirp. In addition, latency is typically extended in the cases of hearing loss. Epochs of these duration limit the rate to as much as 50/sec for a 20ms epoch, or 40/sec for a 25ms epoch (Hood, 1998; Lanting et al., 2013).

2.6.3 Detection of the ABR

The ABR waveform is viewed in the time domain. Wave V is followed by a negative drop in the potential, often below the baseline, referred to as SN10. As the epochs are delivered and the averaging takes place, a waveform will appear in which peaks can be visually identified by the audiologist. This is generally the primary method of identification, although objective methods are available and have been shown to be far more accurate at recording responses since the scope for misinterpretation is reduced

(Sininger et al., 2018; Sininger et al., 2020). These are explained in the following sections. Generally, a large number of epochs are delivered and averaged together. After the presentation (or towards the end) the audiologist should be able to identify and label the different waves. A range of measures can be undertaken on their amplitude, latency and interpeak latency to determine the integrity of the VIII nerve, but the threshold is estimated based on the lowest intensity level in which an ABR was identified.

2.6.4 Signal to Noise Ratio

At near threshold levels, the ABR has a peak to peak[11] amplitude of 0.05 – 0.5 µV, whilst electrical noise can range from 2 – 20 µV in an infant (Lightfoot & Stevens, 2014). This 'noise' is largely internal and usually of two categories – myogenic (muscular) and electroencephalogram (EEG). The strength of this noise activity can swamp the electrical response of the ABR. To be confident in the measurement of the ABR waveform, a range of strategies are employed in order to separate the signal from the surrounding noise. These strategies are employed in order to improve the signal to noise ratio (SNR) to some criterion value (typically 3:1), to make correct identification of Wave V more likely and to give the clinician or researcher more confidence in their results. Artifact rejection is one commonly used strategy. Any responses above the pre-set level will be rejected. This means any particularly noisy epochs – generally caused by movement of the participant – can be removed and do not contribute to the averaged trace (Lightfoot & Stevens, 2014; Sanchez & Gans, 2006). Most UNHS protocols outline a minimum number of epochs that must be performed before the ABR can be confirmed to be present or absent. This relies on the principle that the ABR is synchronous and time locked to the stimulus, whilst noise is random and asynchronous to the stimulus (Picton, 2011). By repeating the stimulus over and over and averaging the responses, the noise is reduced. Classical averaging weights all epochs equally, so long as they are below the artifact rejection level (Picton, 2011) Today, Bayesian or Kalman weighted

[11] The peak-to-peak amplitude refers to the amplitude of Wave V to the SN10.

averaging is more commonly to used address the anticipated fluctuation in noise over the course of the recording session due to movements and other transient artefacts that accompany changes in sleep state. Epochs with low noise are weighted statistically higher in the average than those with high noise (Elberling & Don, 1984; Elberling & Wahlgreen, 1985), with the final averaged waveform being more representative of the periods in which the noise was lower (Atcherson & Stoody, 2012; Norrix et al., 2019). The amount of noise left in the averaged trace is referred to as residual noise (RN). Bringing the RN below 0.02 µV is especially crucial for resolving responses at the lower end of the amplitude range described above, which typically occurs when the sound is relatively close to threshold. When the ABR is present and of a small amplitude, it can be difficult to tell (based on visual analysis alone) if it is absent, or just obscured by the residual noise (Lightfoot & Stevens, 2014).

2.6.5 Statistical Techniques for Objective ABR Detection

For the most part, visual identification of a waveform is the main method of ABR interpretation. This is a subjective feature of what could otherwise be a fully objective process. Research has shown that inter- and intra-subject interpretation of the ABR waveform is variable (Dzulkarnain & Che Azid, 2014; Rossman & Cashman, 1985; Zaitoun et al., 2014). Whilst this this variability decreases with experience (Zaitoun et al., 2014), there is a need for ongoing continual education of audiologists performing ABR waveform analysis, and the use of objective measures to supplement or replace subject analysis as the first measure of response detection (Dzulkarnain & Che Azid, 2014).

One such measure that is commonly in use today is the Fsp measure developed by Elberling and Don (1984). Fsp determines the variance of amplitude values across (non-rejected) epochs, and this is expressed as a ratio of the variance of amplitude values within the averaged epoch. Either a single point F-ratio (Fsp) or multiple point F-ratio (Fmp) are calculated across blocks of epochs. Amplitude variance within the averaged epoch should be high when there is a response present and residual noise is low.

The variance at a latency point(s) across blocks of 250 epochs is compared with the variance within the cumulative averaged response via the following equation:

$$Fsp = \frac{Variance(averaged\ epoch)}{Variance\ (single\ point)}$$

The Fsp value is updated every 250 epochs (the block size), and if a response is present, the value will grow as the residual noise reduces during averaging. Higher numbers indicate a better SNR, and eventually the number may exceed some critical value corresponding to the response confidence. Elberling and Don (1984) offered a conservatively derived critical value of 3.1, which corresponds to an estimate of the 99th percentile from a null distribution, albeit with data filtered with a high-pass cut-off of 100 Hz and a corresponding 10ms latency range for measuring variance in the averaged epoch. In a clinical setting, the Fsp allows audiologists to dynamically determine the lowest number of epochs needed to determine a 'response present' – or alternatively, a true 'response absent' – saving time when compared to fixed epoch numbers more commonly used in current protocols (Sininger et al., 2020). Sininger et al. (2018) point out that for suprathreshold responses, the number of epochs needed could be as low as 800 as the response is generally well above the noise. They argue that a fixed epoch number for testing means time is wasted, effectively over-testing at suprathreshold levels, rather than at/near threshold where the response can take longer to be detected objectively and visually (and a fixed number of epochs would risk under-testing).

2.6.6 Use of the ABR in the Aotearoa New Zealand UNHSEIP

The ABR has long been considered the gold standard[12] method for determining hearing levels in infants (Polonenko & Maddox, 2022; Sininger et al., 2018; Stapells et al., 1995). The presence or

[12] A common phrase used to define the best option for testing, the 'gold standard' in this context refers to the ABR's low cost per infant, excellent specificity and sensitivity, and the ability to detect ANSD, when compared to other methods available for objective hearing testing and screening (National Screening Unit, 2014).

absence of wave V is the used to determine hearing thresholds because it is generally the component with the largest amplitude and the last one to disappear as the response gets closer to hearing threshold, therefore the easiest to identify (Picton, 2011). Amplitude of the waves show intersubject variability, however the latency of the fairly consistent between participants. As stimulus levels increase, the ABR amplitude increases and the latency of the response decreases. A brief overview of the ABR protocol in Aotearoa New Zealand follows.

The process for determining a threshold in infants requires a bracketing procedure, in which stimuli are played at a range of levels to produce an intensity series. The intensity series begins at the minimum level required (or 'passing' criteria). In Aotearoa New Zealand that is 30 or 35 dB nHL (depending on the toneburst frequency). If an ABR at this level is obtained bilaterally at 0.5 kHz, 2 kHz and 4 kHz, the audiologist must increase the level of stimuli, to show growth in amplitude of wave V, as well as decrease in latency. Although each ABR is independent of others, this pattern of growth and latency shift will increase the overall confidence in interpretation. Audiologist's must also measure at 10dB below the provisional threshold to demonstrate an absent ABR.[13] If the responses are deemed satisfactory, the child can be discharged. For infants that do not show a response to the starting levels, the audiologist must ascend in 20-30dB steps until a response is found, then reduce the stimulus level and follow the same bracketing procedure above to determine threshold at each frequency. Testing via BC must also be performed to determine the nature of the hearing loss, and masking if necessary. For infants that do not show a response to the highest tone-specific stimuli, a broadband click is used to determine if ANSD is present (see section 2.6.2).

Figure 2.5 shows an example of an intensity series performed on a participant's right ear. The ABR threshold is defined as the lowest stimulus level that results in a clear response.

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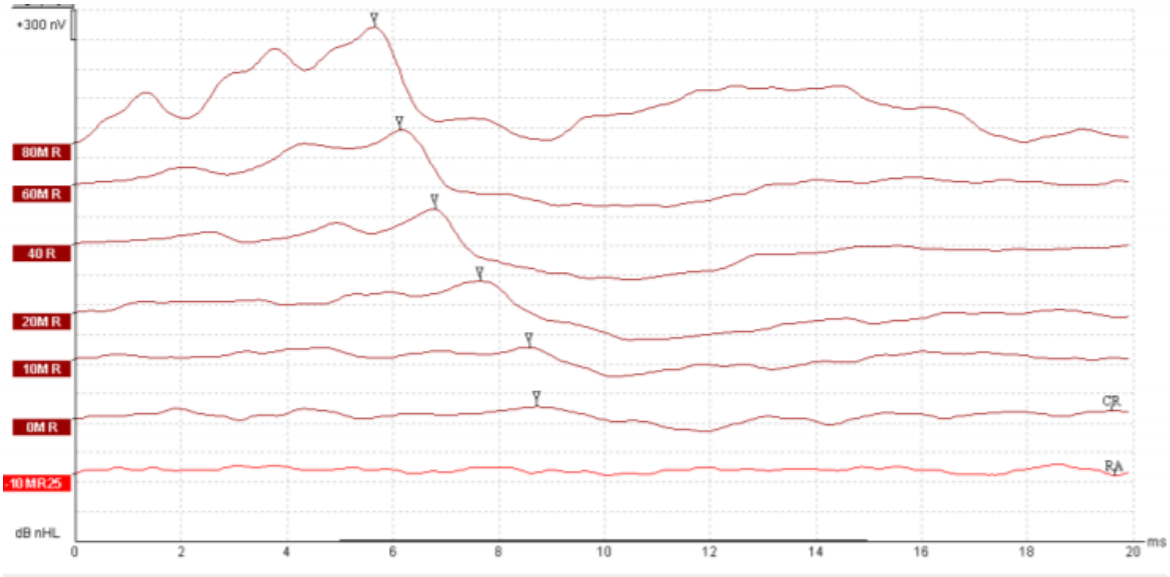
[13] The UNBHSEIP protocol does not set criteria for an inconclusive response. For more detail see

Figure 2.5

An ABR Intensity Series



Note. Wave V amplitude decreases and latency increases as the stimulus level decreases. Wave V is labelled by the tester until it is no longer visible. Threshold is defined as the last clear response (CR) and the absence of Wave V can be seen in the level below (RA).

2.6.7 ABR Test Time

Completing a full ABR assessment of eight frequencies (0.5 kHz, 1 kHz, 2 kHz, and 4 kHz in each ear, i.e., the 'core' audiometric frequencies that are considered to have the greatest relevance for speech perception) takes a significant amount of time, as each frequency must be measured individually, and the ears are stimulated sequentially as outlined in 2.6.6. If masking or bone conduction assessment need to be added, testing can take even longer. UNHS protocols often specify a set number of epochs that must be performed before a response can be determined at present (Ministry of Health, 2016b) Often the time to complete an ABR to the protocol guidelines exceeds the natural infant sleep cycle (Krishnan, 2023). Janssen et al. (2010) found that the average non-sedated infant sleep time at 4

months of corrected age[14] was 48.8 minutes, but 20% slept for less than 33.1 minutes. They tested both normally hearing infants and infants with hearing loss to determine how many responses could be obtained in the within the average sleep time. For normally hearing infants, an average of six thresholds could be obtained in one session, and four thresholds were obtained in 80% of these infants. However, the researchers found that in the hearing loss group, the minimum target of six frequencies (0.5 and 2 kHz by AC in each ear and 2 kHz by BC) prior to prescribing amplification were not met. An average of 5.2 thresholds was obtained in this group, meaning a second session would be needed to determine thresholds at all the audiometric frequencies necessary. In practice, the mismatch between the time taken for the ABR and the infant sleep cycle means the test is often aborted part way through when the infant wakes, leaving the clinician with incomplete information with which to make a diagnosis (Janssen et al., 2010). It is not uncommon for diagnostic ABR testing to take two or more sessions to get enough information for the audiologist to diagnose the child, or fully characterise a hearing loss. Alongside a delay in diagnosis, this approach leads to added stress and worry for the whānau, higher likelihood of attrition, extra clinical time and a delay in interventions being started (Polonenko & Maddox, 2019). Put simply, the current protocols work well for children that have been referred for a full diagnostic test but are indeed, normally hearing. The ABR can generally obtain enough information in the average infant sleep cycle to determine the infant is at low risk for hearing loss, and discharge them. However, for those that do have hearing loss, the process can take more than one session, delaying interventions beginning (Sininger et al., 2018; Sininger et al., 2020). As discussed earlier – the quicker interventions are in place for hearing impaired infants, the better the outcomes (Ching & Leigh, 2020; Downs & Yoshinaga-Itano, 1999; Yoshinaga-Itano, 1999). By this logic, having a sensitive, yet quick test to

[14] Corrected age is used for infants born at <37 weeks gestation, especially when determining progress towards developmental milestones. healthychildren.org (2018).

determine hearing thresholds is of vital importance to allow the habilitation process to commence. There has been significant research on AEP's other than the classic ABR in the last three decades, in the hope of achieving this goal, some of which will be examined in the following section.

2.7 The Auditory Steady State Response

The ASSR is an electrical potential, which is evoked by a periodically varying acoustic stimuli to produce a continuous (steady state) response (Rance, 2008). The stimulus is varied through frequency modulation (FM), amplitude modulation (AM), or both (Krishnan, 2023; Picton, 2011). With respect to amplitude modulation, an alternative perspective is to consider the stimuli are presented at a high enough rate to cause overlapping of the transient responses to successive stimuli, and the response will be shown in the frequency domain only at the frequency of modulation/rate of presentation, and its harmonics. (Galambos et al., 1981; Picton et al., 2003; Rance, 2008; Van Maanen & Stapells, 2009). Steady state evoked potentials were initially recorded for visual and somatosensory research and applications, before their popularization in the audiological field (Hillyard et al., 1978; Namerow et al., 1974; Regan, 1977). Early studies mentioned the ASSR in their literature (Geisler 1960, Campbell et al 1977) but it was Galambos et al. (1981) who described in detail the parameters required to evoke a visible ASSR in adults. Using a range of different stimulation rates from 3.3 to 55/second, they determined the largest amplitude response in adults was at a 40 Hz modulation rate. Through an intensity series they showed that the response amplitude remained large at levels near the behavioural thresholds of the participants, and could be used for hearing threshold prediction. Further research showed that the 40 Hz rate could not be reliably obtained in infants or young children, and that it could only be recorded in awake participants (Kuwada et al., 1986; Linden et al., 1985; Stapells et al., 1988; Suzuki & Kobayashi, 1984). Interest in the ASSR waned for a few years, and the ABR became the more popular AEP for clinical testing, as it was not affected by low participant arousal state or age – making it the ideal objective test for sleeping neonates. Interest was renewed in the early 1990's when Cohen et

al. (1991) were able to show that the ASSR could reliably be recorded in adults at higher modulation rates (>70 Hz), and further studies showed these higher rates could also be used in sleeping participants and infants (Aoyagi et al., 1993; Rance et al., 1995; Rickards et al., 1994). In children under 13 years of age, the 80 Hz response has a statistically similar amplitude as the 40 Hz response (Pethe et al., 2004) however the EEG is significantly lower at 80 Hz (van der Reijden et al., 2005). Termed the 80 Hz ASSR[15], this period saw the introduction of the response as we know it, and these days the ASSR is largely elicited using 75-110 Hz modulation/repetition rates in sleeping individuals (Korczak et al., 2012).

2.7.1 Recording Parameters, Stimulus Type, Intensity and Number

The electrode montage for the ASSR is generally the same or similar to that of the ABR (see section 2.6.1) (Korczak et al., 2012). The ASSR can be used to determine hearing thresholds, using both frequency specific and broadband sounds. The Carrier Frequency (CF) is centred at the audiometric frequency of interest, and the modulation frequency (MF) or rate of presentation is the feature of the sound that drives the response at a particular steady state, thus is where the EEG activity occurs that is measured to determine a response. The CF's used when determining frequency-specific hearing thresholds are the same as the ABR- 0.5 kHz, 1 kHz, 2 kHz and 4 kHz. Alongside tone specific CF's, broadband sounds such as clicks and chirps can be used to elicit the ASSR (Korczak et al., 2012). Initially, the ASSR was stimulated using a single modulation frequency, in which one CF was modulated, and presented to one ear at a time, similar to a typical ABR presentation (Picton et al., 2003). A multiple frequency stimulation technique was soon developed, to allow for a lower test time (Lins & Picton, 1995). Up to eight carrier frequencies can be delivered at once (four per ear), each with their own modulation frequency. The CF must be separated by more than half an octave, and the analysis

[15] Today, what was originally termed the '80 Hz ASSR' is the most commonly used in clinical practise. There is range of different modulation rates >75 Hz that can be used to elicit this response. For the rest of this paper, the term ASSR will be used when referencing the '80 Hz ASSR'.

procedure must have frequency tuning fine enough to measure each response without contaminating the other frequencies (John et al., 1998), or in other words sufficiently narrow frequency bins when converting the time domain response to the frequency domain. In normally hearing listeners, it has been shown there is no significant difference in amplitude or threshold detection when using multiple frequency stimulation (Herdman & Stapells, 2001; John et al., 1998; Lins & Picton, 1995). Whilst there may be some reduction in amplitude of the responses, efficiency remains so long as the amplitudes do not decrease more than a factor of √K, when K is the number of simultaneous stimuli (Picton, 2011). Put simply, two stimuli presented together that have amplitude response greater than 70% of the amplitudes they would exhibit if elicited separately, it is more efficient to present them together (Picton et al., 2003). Naturally, this multi-stimulus approach can reduce the test time when determining hearing thresholds.

Initially, research suggested that masking effects on the basilar membrane may also take place in listeners with hearing loss when multiple stimuli are presented. Broader tuning curves are often exhibited by this population, and low frequency masking can occur, elevating the thresholds obtained (Dimitrijevic et al., 2002; Picton et al., 1998). Herdman and Stapells (2003) however, were able to obtain accurate results in patients with steeply sloping losses when using multiple stimuli, with no masking effects on the response.

Importantly, measuring up to eight CFs at once does not allow for threshold estimation to be eight times as fast, if the stimuli are at the same intensity. Patient thresholds occur at different levels across frequencies, and at least in historical setups, the recording process continued until all eight responses were obtained – so the multiple stimulus approach was only as fast as the slowest response. Overall, threshold estimation of up to eight CFs was shown to be two the three times faster than single frequency testing (John et al., 2002; Picton, 2011; Picton et al., 2003). Van Dun et al. (2008) suggested that ‘on the fly’ protocols be implemented in ASSR equipment. If a response is deemed present for one

stimulus, it can be reduced in intensity, whilst the other stimuli continue at the original intensity. This can assist with to speeding up the threshold estimation process. This approach became common in ASSR equipment and protocols across the 2010's and 2020's (British Society of Audiology, 2022; Cebulla & Stürzebecher, 2015; Luts et al., 2008) and has allowed for the multiple ASSR to improve its speed advantages. As shown by Sininger et al (2018), ASSR and classic ABR techniques performed on the same sleeping infants indicated testing times approximately 30% quicker with the ASSR.

2.7.2 Detection and Analysis of the ASSR

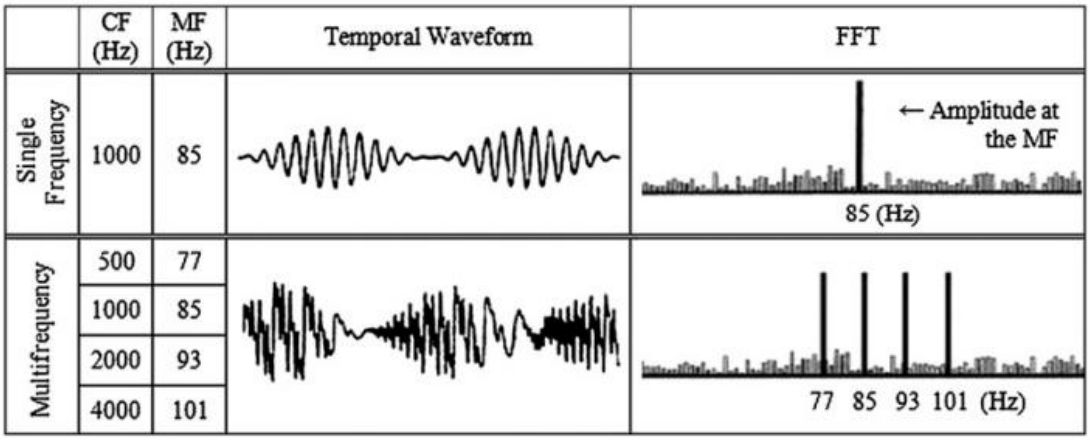
All AEP's produce waveforms, the latency and amplitude, and residual noise measurements can be interpreted by the audiologist to determine if a response is present, absent, or inconclusive. The ASSR however, is typically analysed in the frequency domain, and it is measured objectively, relying on statistical methods to calculate amplitude and phases of the frequency, rather than subjective visual interpretation to determine if a response is present or absent (Korczak et al., 2012).

2.7.3 F-testing

The response to the stimulus is transformed in to the frequency domain using the Fast Fourier Transform (FFT). The power of the signal at the MF is then compared to the power of the neighbouring frequencies, which represents residual noise. If power at the MF is statistically significantly larger than the surrounding frequencies, an ASSR is deemed present. Visually, the response can be seen 'spiking' above the noise of the surrounding frequencies, and is used in both single frequency and multi-frequency analysis (Figure 2.6). In multi-frequency analysis, the complex signal (when viewed in the time domain) is separated into the discrete frequency components associated with each MF.

Figure 2.6

Analysis of the ASSR Response in the Frequency Domain



From "Auditory Steady State Responses" by P. Korczak, J. Smart, R, Delgado, T. M. Strobel and C. Bradford, 2012, *Journal of the American Academy of Audiology, 23(3),* p. 154 (https://doi.org/10.3766/jaaa.23.3.3). Copyright 2012 by Thieme Medical Publishers. Reprinted with permission.

2.7.4 Use of Multiple Harmonics for Response Detection

Cebulla et al. (2006) were responsible for the development of the q-sample test, which allowed for the detection of ASSRs using multiple harmonics, instead of just the fundamental MF. They found that the application of a q-sample test led to a higher detection rate, compared to that of the original one-sample F-test. Put simply, the more information about the response that is included, the higher the detection rate (Cebulla et al., 2006). As stimulus levels decrease, the ASSR amplitude also decreases, making it harder to detect responses in the frequency domain when close to/at threshold. Generally, the first six to 12 harmonics are considered, as the amplitude of latter harmonics is generally too small for detection (Cebulla et al., 2006).

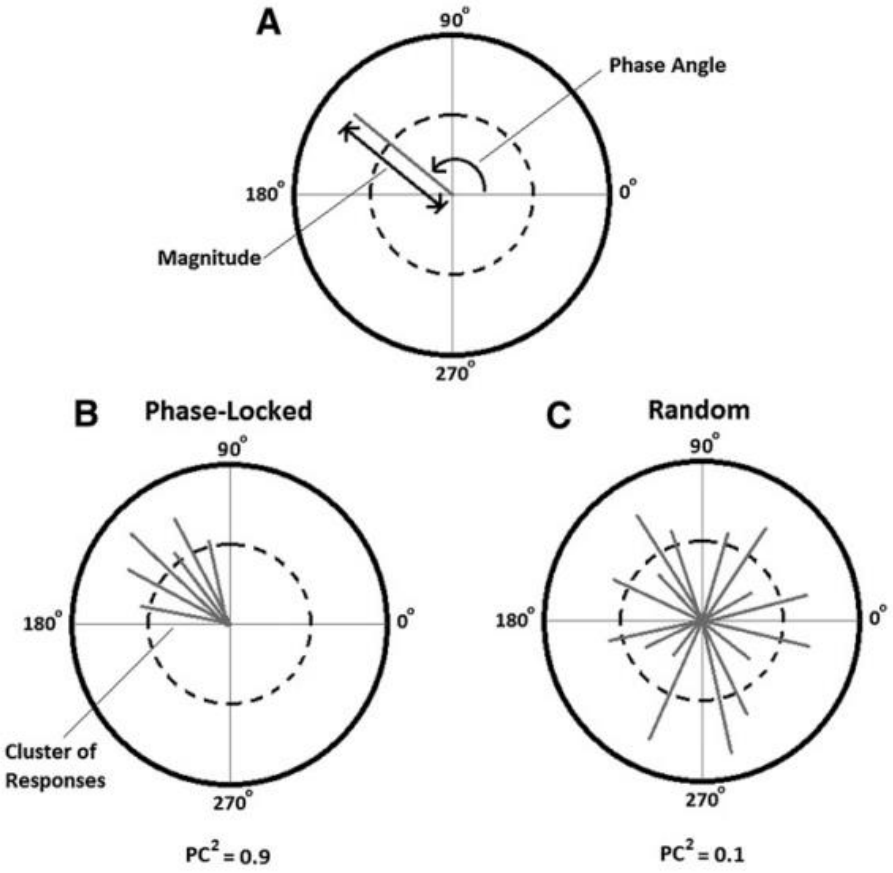
2.7.5 Phase Coherence

Phase coherence (PC) utilises the fixed timing relationship between a true response and stimulus modulation, to determine a response present or absent. The ASSR has a predictable phase delay in response to the stimulus. The PC value is squared (PC^2), and measured on a range of 0 to 1. Instead of a waveform, a 'polar plot' is displayed, showing whether the responses are phase locked to the stimuli, or random (Figure 2.7). The more phase coherence the responses have (the higher their value is), the more likely it is the sound was heard, and distinguishable from background noise. The phases are the timing information of one frequency, normally the fundamental MF (F0), while 0 degrees on the polar plot refers to the starting point of the stimulus modulation cycle.

For a confirmed response, the indicators (known as vectors) must be clustered in the same quadrant, showing the response is phase locked to the stimuli presentation. The length of the vector indicates the magnitude of the signal. Only those that reach above some criteria (the dotted line in Figure 2.7) are of high enough amplitude to be considered a response. If the vectors are randomly dispersed across quadrants and the PC^2 values are closer to 0.0, it indicates the response is 'random' and not a true, time locked ASSR. In a random plot, there is no consistent phase relationship between the energy at this frequency and the stimulus. These indicate two types of responses: response absent and inconclusive. If the residual noise is low, the magnitudes of each vector would be below a criterion (the dotted line), indicating a response absent. If the residual noise was high (the vectors were above the dotted line), it would signify an inconclusive response.

Figure 2.7

An ASSR Polar Plot



Note. Plot A shows phase angle and magnitude of vectors. Plot B shows a cluster of phase locked responses (a true response), and Plot C shows random or non-phase locked responses (no ASSR detected). From "Auditory Steady State Responses" by P. Korczak, J. Smart, R, Delgado, T. M. Strobel and C. Bradford, 2012, *Journal of the American Academy of Audiology, 23(3),* p. 153 (https://doi.org/10.3766/jaaa.23.3.3). Copyright 2012 by Thieme Medical Publishers. Reprinted with permission.

2.7.6 Repeated Testing

Using a standardized or fixed critical test value (such as the F-test, Q-sample test, or the Fmp) for determining a response present is problematic in instances where repeated statistical testing is being undertaken on dependent data (such as ASSR epochs from the same participant) (Korczak et al., 2012). In this context, repeated testing means, for instance, checking to see if a response is present after 1000 epochs (ABR) or 1 minute of testing (ASSR), and then checking again after 2000 epochs (ABR) or 2 minutes of testing (ASSR). Some of the data used in the subsequent check would already have been involved in earlier checks. This repeated testing increases the possibility of false rejection of the null hypothesis (in this context, a 'response' might be detected inappropriately, thus suggesting the ASSR has a faster detection time and/or superior sensitivity than is in fact the case) (Sturzebecher et al., 2005). Development of critical significance values that can accommodate for repeated testing on dependent data was first proposed by Sturzebecher et al. (2005), and expanded further in later studies by the same authors. A more pragmatic approach is to re-calculate critical test values for each step or 'check,' with a step width that progressively increases with test duration (Cebulla & Stürzebecher, 2015; Stürzebecher & Cebulla, 2013). As the probability of a falsely detected response increases in comparison to the preceding test step, the critical test value must also increase with every step, rather than remaining fixed (Cebulla & Stürzebecher, 2015; Stürzebecher & Cebulla, 2013). One method for determining the change in critical test value is known as the Bonferroni correction, which halves the critical significance point (or critical p-value) after each check. However, unfortunately while this reduces the type 1 error rate it also rapidly increases the type-2 error rate in the context of ABR or ASSR analyses when considering the frequent checks that occur during a test sequence. To bypass these difficulties, utilizing raw (noise-only) EEG data to determine type 1 and type 2 error rates, Stürzebecher et al. (2015) were instead able to implement a table of the critical test values for each step number that correctly corresponds to the given error probability of that step. This method is referred to as the 'table look up'

and is used currently utilised in many clinical devices when measuring and analysing the ASSR. Not only does this approach improve sensitivity of the test, it also shows promise for reducing test time (Stürzebecher & Cebulla, 2013).

The combination of the q-sample procedure, the 'table look up' values for ASSR detection, as well as the ability to perform multi-frequency testing, have helped to reduced test time and improve detection probability of the ASSR. These new improvements in ASSR detection (along with stimuli like chirps) have led to the development of what is known as the "Next Generation ASSR," which is most commonly in use today (Sininger et al., 2018).

2.7.7 Use of the ASSR in Infant Hearing Testing

Like the ABR, the ASSR can be used to determine hearing thresholds for infants. As the audiologist is not performing interpretation via visualising a waveform as with ABR, they are instead relying solely on statistical methods of detection to determine if a response is present or absent. Most diagnostic ASSR equipment offers either a 99% (sensitivity) or 95% (speed) response confidence setting, depending on the requirement for the test, which refers to the alpha level of the test. For example, a 99% response confidence setting would suggest a lower false positive/type 1 error rate than the 95% setting, but a correspondingly higher type 2 error rate. It is the discretion of the tester as to which setting is selected (British Society of Audiology, 2022), but Sininger et al. (2020) suggest 95% to decrease test time (see section 2.8 for a more detailed discussion of Sininger's manipulation of test variables to reduce test time). Once the confidence level is set, the tester can choose the starting level of the stimulus and the maximum test duration. Once the test is started, the automatic detection algorithms will undertake response detection checks at specified intervals (British Society of Audiology, 2022; Korczak et al., 2012). If the signal detected remains stable over concurrent checks, it will be determined present and the test will stop. Generally, there is a visual indication of the confidence level vs time available, and residual noise, on the screen for the test to view. The tester can extend the test time if

necessary, such as in cases of excessive residual noise. Like the ABR, a bracketing procedure can be undertaken to determine threshold, and residual noise values are used to determine if the response is absent or inconclusive. Currently, stopping criteria based on residual noise values vary significantly between manufacturers and are equipment specific (due to being measured in different ways), but some recent research has suggested a 10nV criteria (based on rms noise values at frequencies other than MF) allows for standardisation when determining an absent response (British Society of Audiology, 2022; Dimitrijevic et al., 2002; Michel & Jørgensen, 2017)

2.7.8 ASSR for Threshold Estimation

Multiple studies have been undertaken in adults and children to determine the correlation of ASSR to behavioural thresholds. In adults, thresholds obtained using the ASSR are compared to behavioural thresholds to determine correlation. Pearson co-efficients of 0.85 to 0.95 are reported, except for 0.5 kHz, where correlation is lower at 0.65 to 0.87 (Dimitrijevic et al., 2002; Herdman & Stapells, 2003; Van Maanen & Stapells, 2005). When compared to the behavioural audiogram, ASSR thresholds vary more widely in normally hearing listeners (Cone-Wesson et al., 2002). For those with hearing loss the correlation between ASSR and behavioural thresholds is closer (Dimitrijevic et al., 2002). Similar patterns are noticed in infants and children; however, methodology of the studies varies widely (Rance, 2008). Some studies compared the ASSR thresholds obtained by the ABR, and some compared to behavioural thresholds obtained when the child was old enough for such testing (Werff et al., 2008). Thresholds at 0.5 kHz continued to show the lowest correlation (Han et al., 2006; Luts et al., 2006). This research suggested that the ASSR was unable to distinguish between normal hearing and mild hearing loss, and as recently as 2007 it was not considered sensitive enough to be used in paediatric populations (JCIH, 2007).

More recent studies with larger participant pools have shown that the correlation of ASSR to behavioural thresholds in children may be as high as 0.96 to 0.98, for the four core frequencies (Michel

& Jørgensen, 2017; Rance & Rickards, 2002; Rance et al., 2005; Rance & Tomlin, 2006; Sininger et al., 2018). This has prompted further study in the area, including this paper. Recent comparison studies of the ABR and ASSR measures will be discussed later in section 2.8. The British Society of Audiology has recently released Practice Guidelines on its use in infant hearing threshold estimation, but did not go as far as recommending its widespread use, due to variability in the testing systems available, in both their verification and statistical detection methods (British Society of Audiology, 2022). Regardless, research on the ASSR increased in the 2010's and 2020's and there is a growing body of evidence to suggest its ability to replace or compliment the ABR in newborn hearing screening (Michel & Jørgensen, 2017; Sininger et al., 2018).

2.8 Comparison Studies

Given the clinical desire to speed up newborn hearing screening procedures involving hearing threshold estimations, there have been multiple studies comparing the performance of the ABR to the ASSR. Some of these are summarised in Table 2.2 and more recent studies are discussed below.

Table 2.1

Previous Comparison Studies of the ABR and ASSR

Study	Population	ASSR	ABR	Results	Notes
Rance et al. (2006)	N = 17. Term neonates up to 6 wk with normal hearing	500 and 4000 Hz AM and FM-modulated detection by phase coherence	500 and 4000 Hz tone bursts and visual detection	ASSR thresholds higher and more variable	Thresholds were high by both methods. Both tests same day
Van Maanen and Stapells (2010)	N = 53. Median age16.3 mos with hearing loss	Continuous AM (81–100 Hz) tones. Binaural multifrequency; detection at mod frequency by *F* test	Standard 4 tone bursts and visual detection	Mean threshold differences 10.7, 9.5, 9.2, and 6.3 dB (500–1000–2000–4000 Hz) with ASSR thresholds higher. High correlations	Not always same day: 2 to 6 sessions needed
Rodrigues and Lewis (2010)	N = 17, 2 mo–3 yr with hearing loss	Tone pips at rates of 77–103 Hz. Binaural multifrequency, phase, and amplitude detection *F* test	Standard 4 tone bursts and visual detection	ASSR slightly better (0–5 dB) good correlations. ASSR well correlated to behavioral	Both tests on the same day. ASSR often present at high levels when no response was found by ABR
Michel and Jørgensen (2017)	N = 67. 4 days to 21 mos, normal and hearing loss	NB CE-Chirps-Binaural Multiple Frequency. Next Generation Detection	Standard 4 tone pips and visual detection	Good correlations ASSR slightly lower thresholds	Testing on the same day

Note. From *"Evaluation of Speed and Accuracy of Next-Generation Auditory Steady State Response and Auditory Brainstem Response Audiometry in Children with Normal Hearing and Hearing Loss,"* by Y. S. Sininger, L. L. Hunter, D. Hayes. P. A. Roush, K. M. Uhler, 2018, *Ear and Hearing, 39(6)*, p. 3 (https://doi.org/10.1097/AUD.0000000000000580). Copyright 2018 by Wolters Kluwer Health, Inc. Reprinted with permission.

Van Maanen and Stapells (2010) were some of the first researchers to compare the multiple ASSR with the toneburst ABR in infants and young children. 98 infants with hearing loss and 34 infants with normal hearing underwent multiple frequency ASSR and tone burst ABR at the core audiometric frequencies. Most infants were tested in one session. Correlation analysis of the ASSR and ABR thresholds revealed correlation coefficients between 0.77 and 0.89, but the difference scores for 0.5 kHz were statistically significant, in line with previous studies of the ASSR in children (Cone-Wesson et al., 2002; Han et al., 2006; Lins et al., 1996). They also fund that the ASSR appropriately obtained pass results for infants with normal hearing levels, and elevated responses were flagged in children with hearing loss, suggesting the ASSR would not accidently miss a child with hearing loss and give them a

'pass' result. The researchers also found an average test time of 6.3 minutes per frequency, or 22.05 minutes for the full eight frequencies. Because of the lack of normative data for the ASSR in infants with hearing loss, the researchers did not recommend the ASSR as the primary measure for determining hearing thresholds. However, they did suggest its use at the beginning of testing, to quickly determine if the child has normal or elevated hearing levels before switching to tone-ABR to determine exact thresholds if needed (Van Maanen & Stapells, 2010).

Rodrigues and Lewis (2010) compared the multiple-ASSR to the ABR in 17 infants and young children (2 to 30 months, *M* = 11 months) with confirmed sensorineural hearing loss. Stimuli used were tone bursts for the ABR and multiple frequency modulated tones for the ASSR. It took 2-6 sessions per infant to obtain all the thresholds under natural sleep, which were then compared to behavioural thresholds obtained via Visual Response Audiometry (VRA) once the child was old enough for this testing. They found that both the ABR and ASSR correlated well to the behavioural thresholds, and to one another. They found the ASSR was present at high levels when the ABR was absent in children with profound hearing loss. They concluded that the ASSR data was promising, but that further research as needed to ensure robust published data on ASSR sensitivity before it is used as an assessment tool in infants.

Venail et al. (2015) used narrow band CE-chirps to elicit the ASSR and compared the thresholds to those of click evoked ABRs in in 32 (64 ears) infants from one to 17 months (*M* = 7.4 months) and compared them to results obtained through behavioural response audiometry. Correlation coefficients between 2 kHz and 4 kHz ASSR thresholds to click ABR thresholds were high (0.97) with a mean difference of 1.36 dB. Eight ears fell outside of the ±10 dB range between the two measures, due to overestimated ASSR's in those with profound hearing loss, and two cases of steeply sloping hearing loss, which the authors concluded could lead to misdiagnosis and potentially premature cochlear implantation, or hearing aid fitting that is over amplified. The duration of the ASSR testing of the four

frequencies was 22 minutes. Time for the ABR was 13.9 minutes, but as frequency specific stimulus were not used, a direct comparison is invalid.

Michel and Jørgensen (2017) evoked the ASSR using narrowband chirps and the ABR using tone pips. 67 infants from 4 days to 22 months old (*M* = 96 days) were tested with both measures on the same day, but most did not sleep long enough for all thresholds to be measured. 97 ears were tested, and 60 were found to have hearing loss for at least one frequency. Thresholds were measured at the core frequencies, and strong correlation was found in all thresholds for the hearing loss group (0.90 – 0.96) and those with normal hearing showed corrected[16] ASSR thresholds in line with the ABR. They did not report on test time for the two measures.

Sininger et al. (2018) describes a relatively recent study in which the multifrequency ABR and the ASSR were compared for speed and sensitivity in infants, both normally hearing and with hearing loss. Building on the sensitivity data previously collected, they also sought to determine the test time taken for each measure. Participants were 102 infants and toddlers from 0.7 to 80 months (*M* = 12.55 months) with the majority of participants (82) tested in one session, some under natural sleep and some under anaesthesia. They were the first researchers to use level specific narrowband CE-chirps for both the ASSR and ABR, and using the same stimuli tends to increase the validity of a direct performance comparison. The mean number of thresholds achieved for each measure was 7.43 (SD 1.51) for the ABR and 7.36 (SD 1.98) for the ASSR. They found the thresholds obtained by both techniques were highly correlated, with regression slopes from 0.79 to 0.97 and r^2 values from, 0.769 to 0.963. They also found that the ASSR thresholds were consistently lower than ABR thresholds (and therefore closer to behavioural thresholds). The difference was most pronounced at 0.5 kHz and became progressively

[16] Correction factors used were from the BSA NHSP Guidelines http://www.thebsa.org.uk/wp-content/uploads/2014/08/NHSP_ABRneonate_2014.pdf

lower with frequency. The mean test time for an eight-frequency audiogram (four in each ear) using chirps could be estimated in 19.71 (*SD* = 8.73) minutes using the ASSR and 32.38 (*SD* = 18.23) minutes using the ABR. This is a statistically and clinically significant result. Furthermore, the test time for ASSR did not increase under general anaesthesia, unlike ABR, although the reason for this is not known. Given the costs and health risks associated with general anaesthesia, this time saving is not to be underestimated.

Alongside the comparison of sensitivity and test time for the two measures, Sininger et al., (2018) extensively outlined their clinical testing protocol, that allowed for such quick responses to take place. In their 2020 paper (Sininger et al., 2020), they expand on this strategy and suggest adjustments to current newborn hearing screening protocols that could lead to drastic time savings. Given that most children who are seen for a diagnostic ABR following a no clear response at the screening phase are normally hearing (false positives), measures can be taken in order to identify and discharged these infants quickly, as well as have a more efficient protocol to determine hearing thresholds for infants that may require amplification. The recommendations relevant to this study are highlighted below:

Begin testing with a wideband CE-chirp by ABR, to indicate appropriate starting levels for frequency specific testing. A wideband chirp gives higher amplitude responses than other broadband sounds due to maximized neural synchrony (Dau et al., 2000; Elberling et al., 2007). If a response to this chirp is detected, the next step is to begin at this level using frequency specific stimuli for threshold seeking, or 10-20dB above if not detected. If one ear one shows a lower threshold to the chirp, begin in that ear so masking can be applied to the opposite ear if necessary. Use Narrow Band level specific (LS) CE-chirp stimuli for threshold seeking, not only increase the amplitude of the response, but also to allow for the compensation needed to account for amplitude differences based on stimuli level. Kristensen & Elberling (2012) have shown these LS chirps to demonstrate a consistent amplitude advantage over clicks, as well as better response of the all peaks of the wave. Use of a dynamic epoch protocol – fixed

minimum of 800 epochs, but a flexible maximum of 6000 epochs for the ABR, and less than 60 seconds for the ASSR, in conjunction with the use of objective response detection. This allows for the system to stop averaging as soon as the required Fsp or q-sample value is reached, or the noise is low enough to justify an absent response. Whilst some current protocols (Aotearoa and worldwide) require a fixed number of epochs before confirming a response is detected/absent, a dynamic protocol will save time when the ABR amplitude is high and/or the background noise is low. The time saved for suprathreshold responses can then be used for those near or at threshold, which generally take more time to resolve as the signal amplitude is lower.[17] Regardless of the AEP used, protocol adjustments such as these could dramatically reduce test time with no loss to sensitivity.

2.9 Modified ABR Approaches

Since such protocols suggest starting with a broadband chirp stimulus in association with the ABR, and yet Sininger's earlier demonstration indicated significant time savings over the ABR are on offer via the binaural ASSR, one could start to wonder whether these two positions could be unified in some way. With the ABR remaining the gold standard for objective hearing testing, there has been extensive research on ways in which the test time can be decreased, and hence ways to help unify as described above. For example, there have been studies attempting to create an interleaved/interweaved stimulus protocol that allows for a lower test time overall, whilst maintaining diagnostic sensitivity by maintaining relatively long intervals between presentations to each ear. These studies are summarized below.

[17] See (Sininger et al., 2018; Sininger et al., 2020) for further expansion on time saving measures.

2.9.1 Interweaved ABR

Plourde et al. (1988) expanded on studies from the early 1980's that assessed the practicalities of interweaving or overlapping stimuli during ABRs. Interweaving is when two or more stimuli are sequentially presented, with the response of one stimulus recorded in the interval/s between the other stimuli. Picton et al. (1984) discussed an example of presenting clicks to both the left and right ears at an overall rate of 20/s, but alternating so that each ear only receives stimuli at a rate of 10/s. Whilst this interweaving was being untaken as part of studies to measure to measure evoked potentials from differing sources at one time (auditory, visual and somatosensory – for diagnosis of multiple sclerosis), this interweaving approach across modalities can be viewed as a predecessor to the current interleaving stimuli being studied presently, which is restricted to the auditory modality. One obvious potential advantage of an interleaving paradigm along these lines is that it may represent a relatively easy way to access a meaningful reduction of ABR test time. That is, the only alteration is a quasi-parallel delivery of the sounds for interleaving, while the key features of the ABR and associated aspects like response detection algorithms should remain the same or similar as monaural sequential stimulation.

2.9.2 Bilateral-simultaneous ABR (BiSi-ABR)

Maruthy et al. (2018) studied an interleaved ABR on 25 normally hearing adult participants. Using clicks, the researchers presented stimuli to both ears with an interaural time delay of 16ms. Each click pair therefore had a repetition rate of 30.1 clicks/second to each ear, with a total repetition rate of 60.2 clicks/second. This led to an interstimulus interval of 33.2. The researchers measured the BiSi-ABR in both a right-left condition and left-right condition to compensate for any order effects, then compared these results to a conventional ABR gathered using the same stimuli delivered with an ISI of 60.2ms. The results indicated that at suprathreshold levels (70 dB nHL) the latencies of Wave III and Wave V for the BiSi-ABR's were 'strikingly similar' to that of the conventional ABR. As the intensity decreased and moved closer to thresholds, the BiSi-ABR waveforms were close replicates of the

conventional ABR waveforms. Although test times were not a feature in the study, the researchers hypothesized that using the BiSi-ABR approach, test times for the ABR could be halved.

2.9.3 Parallel ABR

Polonenko and Maddox (2019) have also sought to reduce the test time for the ABR by introducing their Parallel ABR (pABR) measure. Randomized sequences of toneburst stimuli are presented quasi-simultaneously to both ears, allowing for measurement of five frequencies at once. A 'toneburst train' is created by placing 0.5-8 kHz tonebursts randomly in sequence. The data and waveform for each frequency can then be extrapolated out in offline analysis, due to the independent timing. They found that the morphology of the waveform closely resembled that of the conventional ABR, in terms of latency and amplitude of Wave V. The pABR exhibited a median test time of 4.6 minutes, versus a median of 30.1 minutes for the conventional ABR. A further study in 2022 by the same authors determined that the optimum presentation rate for the pABR was 40 Hz, with the total time for the pABR a mean of 7.7 minutes (Polonenko & Maddox, 2022), which is consistent with many NBHS protocols already in place. Overall, the pABR had shorter response times at lower levels of intensity, but longer response times at higher levels of intensity. Given the aim of NHSP is to determine hearing thresholds or provide a 'pass' of the test at low levels, the speed gains made at lower levels are of promise to reduce test time in a clinical setting (Polonenko & Maddox, 2019).

2.9.4 Interleaved ABR

Similar research has been underway at the University of Canterbury in recent years (Bencito, 2020; O'Beirne, 2015), supporting the hypothesis that presenting stimuli to both ears in a quasi-simultaneous way allows for a shorter acquisition time, without notable detriment in ABR morphology. Bencito (2020), utilised the 'Te Pihareinga' software developed by O'Beirne (2015), studied nineteen normally hearing adults 21-39 years of age (M = 26, SD = 4.52). Each listener received interleaved ABR stimuli at a suprathreshold level of 70 dB nHL under three conditions: the interleaved condition (both

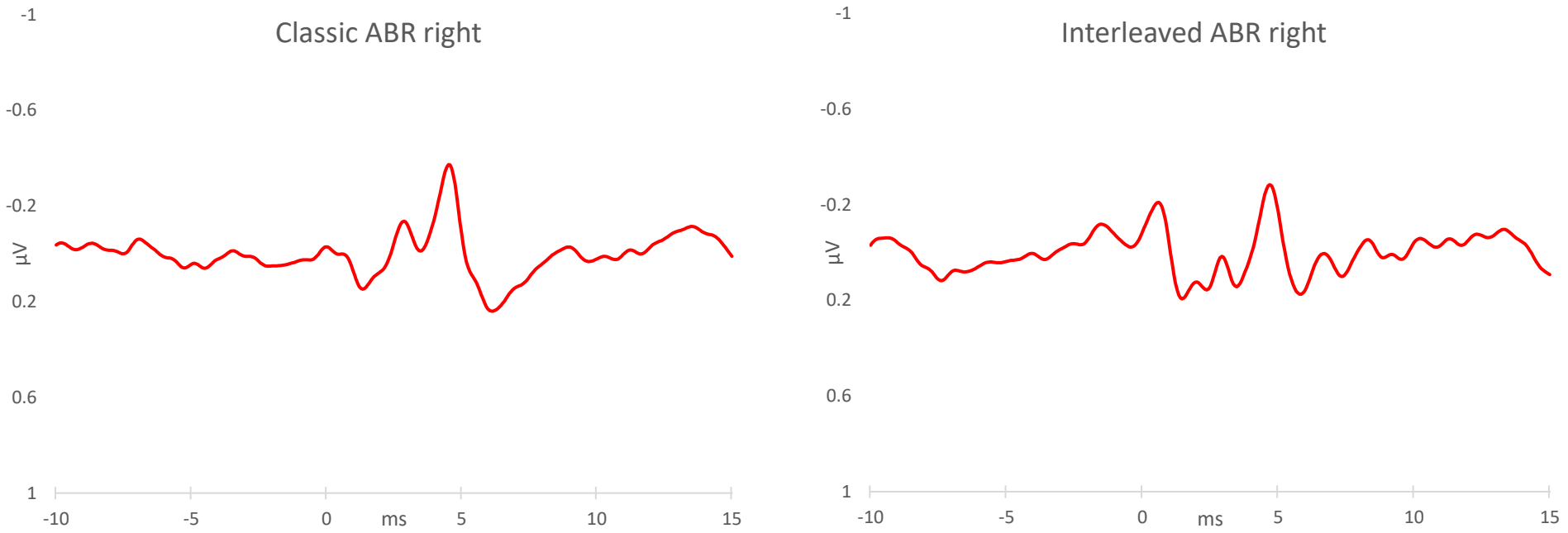
ears receiving stimuli in an interleaved fashion) monaural slow (right ear receiving stimuli at a rate the same as conventional ABR), monaural fast (stimuli delivered to the right ear only at the same rate as the interleaved rate). Bencito also examined the effects different stimulus repetition rates under each condition: 90.91, 76.92 and 45.45 clicks per second. Whilst all three conditions showed a similar wave V amplitude, the monaural fast condition showed significantly longer latencies for wave V than both the interleaved and monaural slow conditions. It was found that a rate of 90.91 clicks / second in the interleaved condition (45.5 clicks per ear / second) produced Wave V latency and amplitude similar to the conventional ABR, but with significant time savings Bencito (2020).

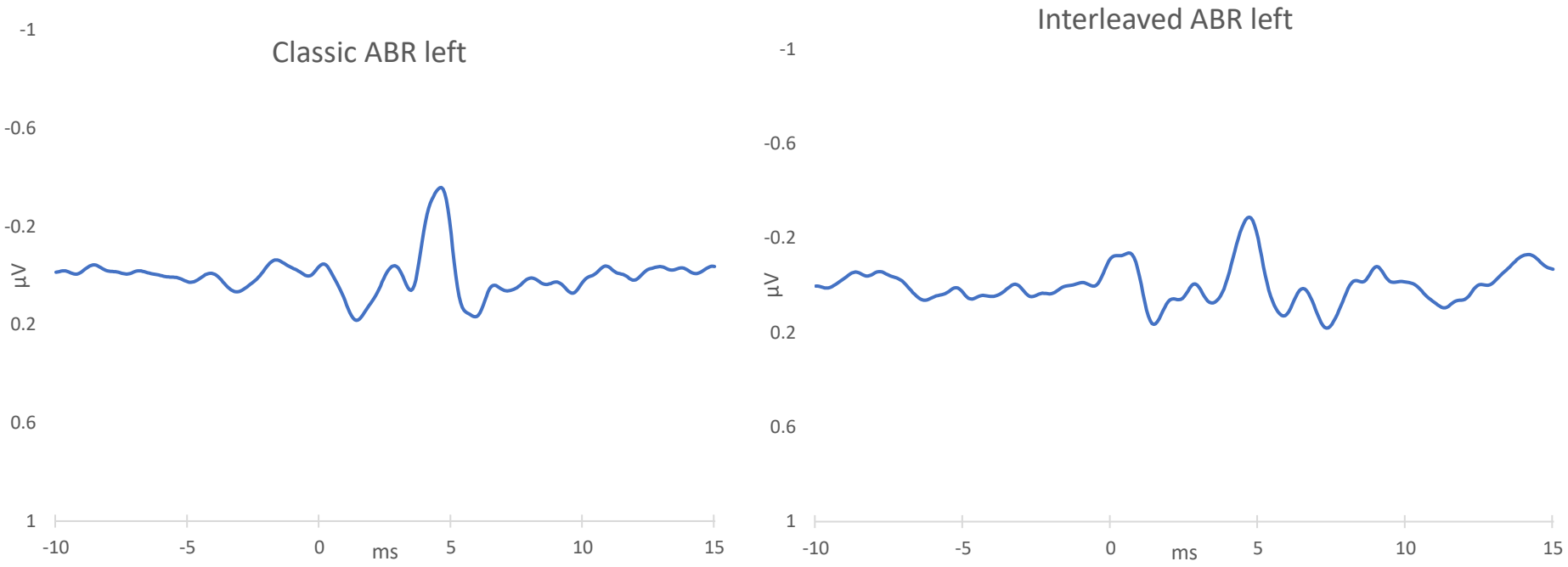
To further illustrate the concept of interleaved ABR, Figure 2.8 shows sample waveforms of the classic sequential, and interleaved approach (by ear) gathered on the same participant, in a single recording session. The amplitude of Wave V is clearly visible at 0.3 – 0.4 μV in both conditions, and the latency remains consistent at 5 ms post stimulus. The classic ABR has a slightly larger peak-to-peak amplitude with SN10 becoming more negative. A key observation though, is that the interleaved data were gathered in around half the time. Bencito (2020) chose to focus only on wave V amplitude and latency, due to its importance for newborn hearing screening. These findings were supported by Nofal (2022) who studied the interleaved ABR and interleaved cortical evoked potentials, and found the test times for the interleaved ABR in normally hearing listeners were significantly faster than the classic approach. Lien (2022) also studied the interleaved ABR and found that the amplitude and latency of wave V remained the same in listeners with sensorineural hearing loss, when compared to the classic approach. Interpeak latency and identification of other peaks within the interleaved waveform have not yet been studied.

This study will build on the work of (Bencito, 2020; O'Beirne, 2015) and utilise the interleaved ABR in a comparison study for speed and accuracy against the ASSR. This will be the first time it has been compared to another measure for speed, and utilised in a sensitivity study.

Figure 2.8

Classic and Interleaved ABR Waveforms by Ear





Note. 4000 epochs were gathered for each of the three recording conditions (classic right, classic left and interleaved) on the BioSemi ActiveTwo. The data was bandpass filtered from 80 - 1500 Hz and classically averaged.

2.10 Current Study

As discussed above, there has been a substantial amount of research undertaken using AEPs in order to improve newborn hearing screening programmes. Both the ABR and ASSR have been shown to have excellent correlation to behavioural thresholds, making them appropriate candidates for use in further research on the topic. There is an appetite to find a faster alternative to the conventional ABR, that maintains diagnostic sensitivity whilst reducing test time. The research by Sininger et al. (2018) suggests that the ASSR not only has speed advantages to the conventional ABR, but sensitivity of the threshold estimation has improved. However, in clinical practice, most audiologists are arguably more familiar with the ABR, and UNHS protocols have been written to reflect its use as the primary diagnostic tool. Alongside the ASSR (fastest measure) and conventional ABR (most versatile), we have emerging research supporting the further exploration of interleaved ABRs, as a means to reduce test time. It seems that a reasonable question arising from this observation is how the reduction in test time might influence wider recommendations when considering ASSR - perhaps the outright fastest way to gather the necessary threshold estimations. However, as far as the researchers are aware, the interleaved ABR has never been compared with ASSR in this way.

Therefore, the present work will compare both test time and the detection threshold provided by the ASSR and the ABR, using the same chirp stimuli for both measures. Participants will be normally hearing adults. By utilising the same stimuli and the same levels for both conditions, it should be valid to compare the relative sensitivity of both measures, as well the overall test time. The research questions and hypothesis are outlined below:

1). To compare test times between interleaved ABR and ASSR when using the same stimuli to obtain equivalent hearing test data.

H0 = There will be no difference in test times between the interleaved ABR and ASSR

H1 = There will be a difference in test times between the interleaved ABR and the ASSR

2). To compare the results from both the interleaved ABR and ASSR to determine the sensitivity of each.

H0 = There will be no difference in sensitivity between interleaved ABR and ASSR

H1 = There will be a difference in sensitivity between the interleaved ABR and the ASSR

3 Methods

3.1 Participants

Fifteen adult participants (*M* = 28.1 *SD* = 4.6; 11 females and 4 males) were recruited via printed advertising around the University of Canterbury campus. The advertising poster can be seen in Appendix A.

3.1.1 Exclusion Criteria

The exclusion criteria were:

1. Inability to comprehend behavioural hearing testing.
2. Hearing loss of a moderate (41 dB HL) level or greater, across the core frequencies of 0.5 kHz to 4 kHz. The level of stimuli used in for the ASSR and interleaved ABR would be below the hearing thresholds of these potential participants (see section 3.2.1)
3. A recent history of ear infection.
4. A history of neurological disorders, which may indicate changes to the structure of the auditory nerve or brainstem that could interfere with electrophysiological testing.
5. A skin condition prohibiting the application of surface sensors of the electrodes for measuring the ASSR and interleaved ABR results.

Preliminary procedures included a case history, otoscopic examination, middle ear function testing (226 Hz tympanometry) and Pure Tone Audiometry. These procedures were performed according to the New Zealand Audiological Society (NZAS) Best Practice Guidelines (New Zealand Audiological Society, 2018, 2021). Pure tone audiometry was performed using ER5 insert earphones at octave intervals in the range 0.25 - 8 kHz, and down to a minimum testing level of 15 dB HL. Thirteen participants had hearing sensitivity within the normal range (≤15 dB HL) at all frequencies tested. One participant had thresholds ≤15 dB HL in the right ear, and mildly raised thresholds in the left ear

(average core frequency threshold was 22.5 dB HL). One participant had raised thresholds at 6 kHz and 8 kHz in the right ear and 8 kHz in the left ear, but their core frequency average was <15 dB HL.

3.1.2 Sample Size Estimation

Previous studies comparing ASSR and ABR performance have featured sample sizes from 17 to >100, and participants with a range of different hearing levels (Michel & Jørgensen, 2017; Rance & Tomlin, 2006; Rodrigues & Lewis, 2010; Sininger et al., 2018; Van Maanen & Stapells, 2010).

Of particular relevance is a contemporary study by Sininger et al. (2018), in which the "Next Generation" ASSR was compared to the ABR for speed and sensitivity in newborn hearing testing. This study featured both normally hearing and hearing-impaired infants and children, in contrast to the present study which included normally hearing adult participants. However, in several key respects this study features similarities to the present research, including equivalent stimuli used in ASSR and ABR components (see section 3.3), and with respect to the type of automated response detection techniques used in ASSR and ABR (see section 3.5.2.2 and 3.6.2.2). Therefore, the effect sizes reported by Sininger et al. (2018) were used to estimate the present sample size requirements.

Sininger et al.'s 2018 study reported both test time and sensitivity differences between ASSR and ABR, with the latter in a frequency-specific way. The data with the largest discrepancies appeared to be in relation to stimuli delivered at 0.5 Hz, where a mean threshold difference between ASSR and ABR of 9.35 dB was reported (SD = 11.32 dB), leading to an effect size (dz) of 0.83. Based on a two-tailed parametric test at a significance level of 0.05, with 80% power, this suggests a sample size of 14 would be adequate. We therefore rounded the sample to 15 pragmatically. Note, this pragmatic approach means that the present study was powered to detect large differences in thresholds. In evaluating sensitivity of thresholds in this study, it is important to bear in mind what could be considered clinically significant - as opposed to statistically significant - differences. The smallest step size typically used

audiometrically is 5 dB, therefore any differences less than this may not be considered clinically significant when considering the sensitivity portion of the research question.

3.1.3 Informed Consent and Ethical Approval

All participants gave written informed consent. Upon registering interest in the in the study, potential participants were emailed a Participant Information Sheet (Appendix B) and Consent Form (Appendix C) to read before participating. Ethical approval was obtained by the University of Canterbury Human Research Ethics Committee, reference HREC 2022/24/LR (Appendix D).

3.2 Testing Conditions

Data from each participant was collected in a single 1.5-hour session at the University of Canterbury. The otoscopic examination, tympanometry and case history were performed in a quiet room, whilst the Puretone Audiometry, ASSR and interleaved ABR measurements were undertaken in an electrically shielded, sound treated booth that met ISO 8253-1:2010 ambient noise requirements for open ear audiometry down to 0 dB HL.

3.2.1 Study Design

The study design is a within-subject repeated measures design. All participants underwent both the ASSR and interleaved ABR testing, serving as their own control. Three different levels of stimulation were delivered during testing (20, 30 and 40 dB nHL) to generate an intensity series. The sequence of the testing was counterbalanced between participants to mitigate order effects. Order of testing can be seen in Table 3.1.

Table 3.1

Counterbalanced Sequence of Electrophysiological Testing

Participant ID #	Testing Sequence
1	ASSR 20, 30, 40, ABR 20, 30, 40
2	ASSR 30, 40, 20, ABR 30,40, 20
3	ASSR 40, 20, 30, ABR 40, 20, 30
4	ASSR 20, 30, 40, ABR 20 ,30, 40
5	ASSR 30, 40, 20, ABR 30, 40, 20
6	ASSR 40, 20, 30, ABR 40, 20, 30
7	ASSR 30, 40, 20, ABR 30, 40, 20
8	ASSR 20, 30 ,40, ABR 20, 30, 40
9	ABR 20, 30, 40, ASSR 20, 30, 40
10	ABR 30, 20, 40, ASSR 30, 40, 20
11	ABR 40, 20, 30, ASSR 40, 30, 20
12	ABR 20, 30, 40, ASSR 20, 30, 40
13	ABR 30, 40, 20, ASSR 30, 40, 20
14	ABR 40, 20, 30, ASSR 40, 30, 20
15	ABR 20, 30, 40, ASSR 20, 30, 40

3.2.2 Equipment

Electrophysiological stimuli were generated using Neurobehavioral Systems Presentation software (https://www.neurobs.com; version 22.1 Build 04.30.21) /) with EARTONE 3A insert headphones with foam tips, at same depth used for the puretone audiometry. Electrophysiological responses were gathered using the BioSemi ActiveTwo device. Two computers were used for stimuli presentation and acquisition. The Presentation computer was an HP Desktop-EGP9754 with a 64-bit operating system, x64-based processor and Realtek high-definition onboard soundcard. The acquisition computer was an HP Desktop-3E309FL with a x64 based processor. Data acquisition was performed on ActiView900, the BioSemi custom acquisition software.

3.2.3 Procedures

Once the preliminary tests had been undertaken and the participant was deemed eligible for the study, the electrophysiological measurements commenced. Participants were invited to sit in a comfortable, reclining chair and informed of what to expect during the testing. They were encouraged to relax, and even sleep if possible. Their skin was prepared for electrode attachment, using an alcohol wipe and Nuprep gel to ensure low impedance. Five electrodes were attached using electrolytic gel. The electrodes were set up in a two-channel montage with ipsilateral and contralateral mastoid (positive) referenced to the high forehead (negative). As the BioSemi instrument uses a driven-right-leg architecture (DRL), a common mode sense (CMS) electrode was placed on the low forehead, and a DRL electrode was placed over the right eyebrow. Driven right leg architecture refers to the active noise cancellation of ongoing interference such as 50 Hz mains inference. The CMS electrode senses the interference, and the DRL electrode injects the inverse of the current to cancel it out (BioSemi, n.d.).

The BioSemi device uses active electrodes, it is relatively tolerant of high impedances at the skin contact, and no impedance value is provided. Rather, the quality of electrical contact between skin and electrode is specified according to 'offsets,' which are the voltages measured between each active electrode and the CMS electrode. Low offsets suggest good quality signals will be obtained and measured. Electrode offsets were checked in the ActiView900 software and were within ± 40mV for all three active electrodes, the range recommended by the device manufacturer (Neurospec: Research Neurosciences, 2015). Once the set up was complete, the lights were turned off and the door closed, to encourage sleep and relaxation. An infrared camera and intercom ensured visual and two-way aural communication with the researcher outside the booth throughout the procedure.

3.3 Stimuli

3.3.1 The Don Chirp

A broadband chirp stimulus suitable for evoking both an ABR and ASSR was chosen for this study, containing frequency components from 0.1 – 8 kHz. A chirp stimulus is a rising pure tone epoch which takes in to account the cochlear travelling wave delay by delaying the timing of the higher frequencies relative to the low frequencies, therefore activating the entire basilar membrane simultaneously (Dau et al., 2000; Elberling et al., 2007). By compensating for the frequency dependent time delay of the basilar membrane, hair cells discharge simultaneously, preventing phase cancellation and leading to maximum neural synchrony (Dau et al., 2000; Sininger et al., 2020). In turn, this translates into faster electrophysiological response detection time and/or a better signal-to-noise ratio, and waveforms that exhibit larger amplitudes when compared to traditional (non-temporally compensated) stimuli such as clicks (Dau et al., 2000; Elberling et al., 2007; Ferm et al., 2013). These benefits have been demonstrated both for the ASSR (Elberling et al., 2007) and the ABR (Fobel & Daub, 2004).

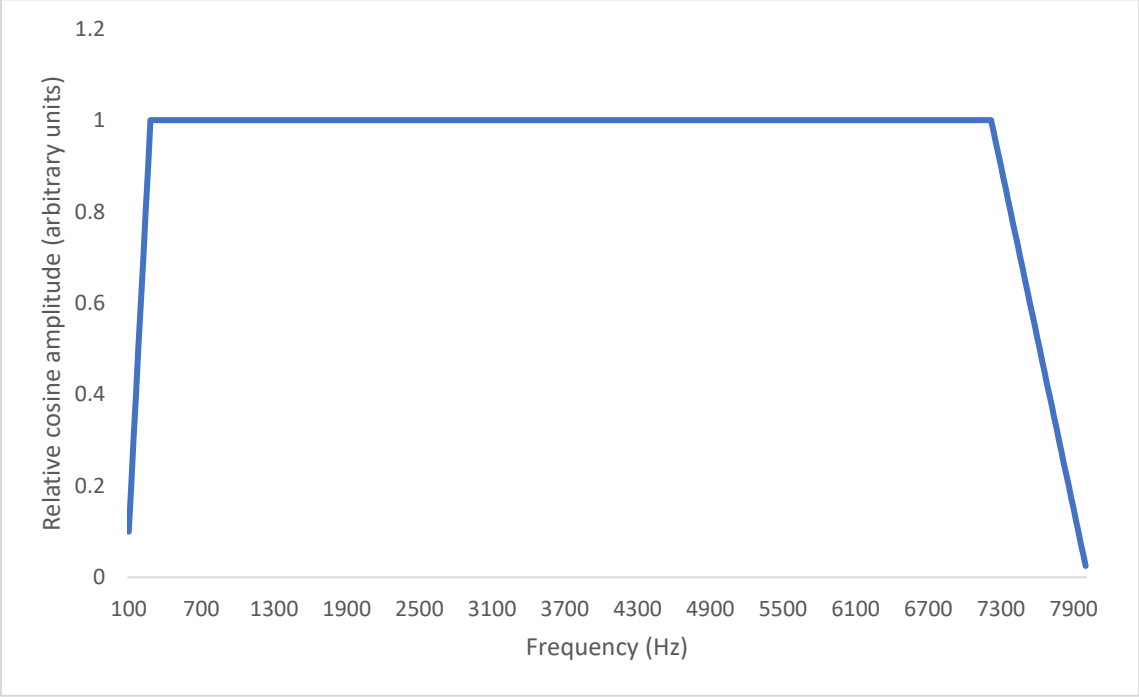
The chirp file for this study was programmed according to the methods described by Elberling et al. (2007), based on the latency function of the 'Don-model' for cochlear travelling wave delay. Briefly, Don et al. (2005) measured click-evoked ABRs in 38 normally hearing adults, using a derived band masking technique whereby ipsilateral masking noise at four progressively increasing band widths were used in conjunction with the not-masked condition to show the latency increase in mean Wave V values. This latency increase corresponds to the travelling wave delay for the associated frequency region. This data was plotted on a line of best fit (cochlear delay model) to determine the latency function of the cochlear phase delay. This model was recommended by Elberling et al. (2007) and later used as the basis of the commercially available CE-chirp (Elberling & Don, 2008), which has been widely adopted in clinical practice, such as with the Beraphone MB-11 newborn screening device stipulated for use in New Zealand's newborn hearing screening programme (Ministry of Health, 2016a).

3.3.2 Generation of the Don Chirp

Generation of the chirp occurs in the frequency domain and involves an array of cosines that were set at 20 Hz intervals in the range 100 – 8000 Hz. Each cosine was set with an inverse phase delay to compensate for the Don model delay, using the delay constants reported in Elberling et al. (2007), and then summed. Elberling et al. (2007) recommend designing each frequency component with equal amplitude (i.e. no windowing) but this has previously been shown to result in a 'ripple' effect (Sturzebecher et al., 2006) which can be addressed via reducing the amplitudes of the cosines with the highest and lowest frequencies. Sturzebecher et al. (2006) recommended a simple halving of the amplitude of the highest and lowest frequency cosines, but the present study implemented a more gradual roll-off according to the values in Figure 3.1.

Figure 3.1

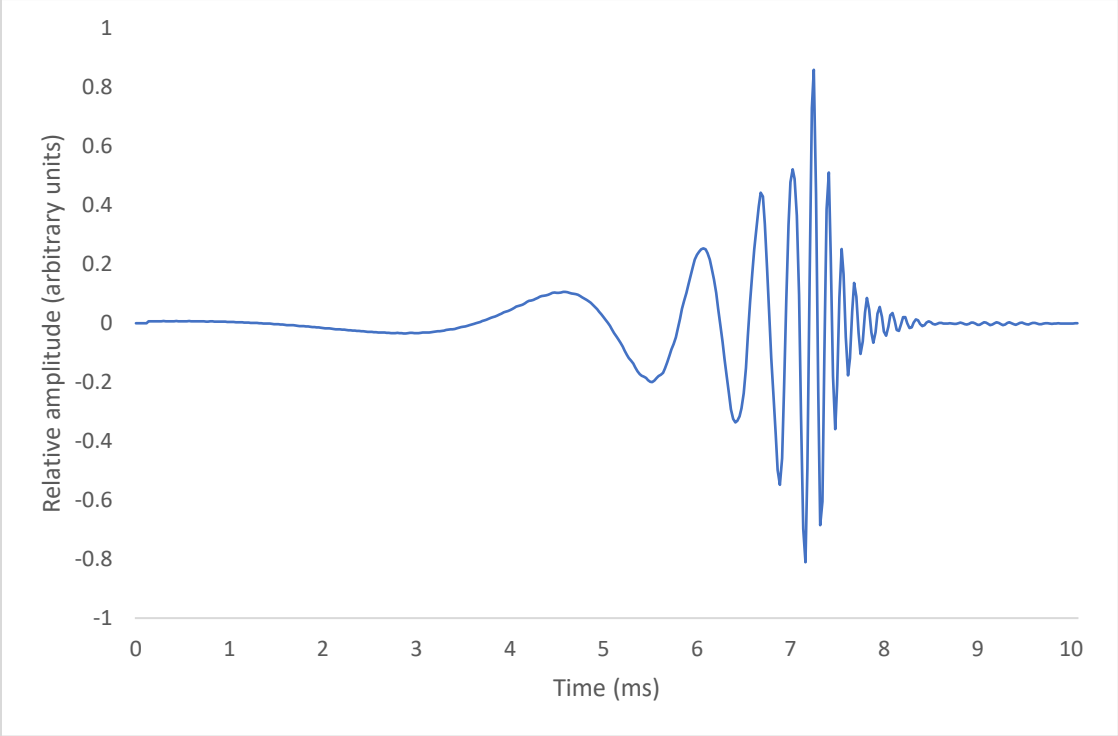
Cosine Amplitudes of the Chirp Frequencies



The stimulus was designed with a sampling rate of 44.28 kHz and exported as an audio file (.wav format) to the BioSemi software. A schematic depicting the chirp used in the present study is shown in Figure 3.2. The schematic spans 444 samples, around 10ms.

Figure 3.2

Frequency Content and Relative Amplitude of the Chirp



3.3.3 Calibration of the Don Chirp

Short duration stimuli used for ASSRs and ABRs, such as chirps, cannot be calibrated using an integrating sound level meter (SLM) in the same way that longer duration tones are. The shortest integration period of a SLM is typically the 'impulse' mode featuring an integration time of 35ms (International Electrotechnical Commission, 2002). This is substantially longer than a single instance of the ASSR or ABR stimuli, meaning each 35ms sampling period would be filled with longer silent periods

than stimuli. These silent periods would be integrated into the measured signal level. As a result, the measurement would underestimate the true sound pressure level, an effect known as 'undershoot.'

An alternative is the peak-to-peak equivalent method, which is used for calibrating short duration stimuli. This involves finding the peak-to-peak amplitude of the chirp that matches that of a long duration pure tone whose root-mean-square sound pressure level is known. The chirp used in the present study was calibrated apriori using this approach, and a full report of the calibration procedure is offered in Appendix E. Note, the report also includes calibration of stimuli not used in the present study. Therefore, an outline of the pertinent details relevant to the present study is repeated here. A Brüel & Kjær 2250 SLM was used to set a 1 kHz reference tone in the 711 occluded ear simulator (test cavity) to 90 dB SPL. The peak-to-peak amplitude of this signal was captured via an oscilloscope, to which the peak-to-peak amplitude of the chirp was matched. The linearity of the attenuator was then established, enabling chirps to be delivered at a range of known sound pressure levels. A secondary step involved converting the sound pressure levels (dB ppeSPL) to an audiometric scale (dB nHL). As there is no internationally agreed standard audiometric 'zero' for chirps (known as reference equivalent threshold sound pressure levels; RETSPLs) among the ISO family of standards (ISO 389), RETSPL data from Gøtsche-Rasmussen et al. (2012) was used instead. Note, this study followed the methods for determining RETSPLs described in ISO 389.9 to determine the reference equivalent threshold sound pressure levels of the CE-chirp (based of 20 stimuli/s). The findings indicate that 31.4 dB peETSPL is equivalent to 0 dB HL.

Note the source of the RETSPLs used relate to a CE-chirp via ER3A insert earphones, whereas the present study used a Don chirp. As noted earlier, while these two stimuli are closely related, a primary difference is the narrower bandwidth of the Don chirp. However, the EARTONE-3A insert earphones exhibit a relatively flat amplitude-frequency response only up to around 4 kHz, and above this point, the response rolls off at a rate of around 36 dB/octave (Elberling et al., 2012). This filtering of the high

frequency components of the stimuli suggests that RETSPLs for the Don chirp are unlikely to be meaningfully different from the CE-chirp when delivered by ER3A earphones.

3.4 Data Acquisition and Processing

Data collection and analysis was split in to two parts. Initial online recording of the participant's ASSR and interleaved ABR data, and subsequent offline analysis. This differs from the typical clinical scenario whereby data tend to be recorded and online-analysed concurrently. Therefore, the present study offers an offline-reconstruction of the response detection and waveform interpretation processes. Moreover, clinical scenarios that are concerned with threshold seeking can dynamically follow a decision-making algorithm whereas the present study followed a fixed protocol which always involved three presentation levels of the stimuli for both the ASSR and interleaved ABR.

3.5 Auditory Steady State Response

3.5.1 Online Processing

3.5.1.1 Stimuli Presentation

Chirp stimuli were delivered binaurally. The left ear was stimulated at a rate of 93.02 Hz ("93 Hz") and the right ear stimulated at a rate of 87.3 Hz ("87 Hz"). This paradigm featured the above-mentioned chirp with 441 samples, and this digitised sound was zero-padded at the beginning so that it contained either 475 samples (meaning 93 chirps could be appended into a 1 second period) or 505 samples (meaning 87 chirps could be appended into a 1 second period). Two audio files (.wav format) each of around 1 second in duration were therefore produced. Exact timing for each stimulus was determined based on the methods outlined by Rance (2008, pp. 20-21). Note, each resulting audio file contained an integer multiple number of chirps (94 and 88, respectively) so that each sequence would not be truncated, avoiding any acoustic transients). Therefore, the 87 Hz stimulus file lasted 1.07667

seconds and the 93 Hz stimulus file lasted 1.0145 seconds. The sounds were delivered continuously in a loop at each of the three presentation levels for a total of five minutes.

3.5.1.2 Acquisition of ASSR Data

BioSemi ActiView900 software was configured on the acquisition computer with a sampling rate of 16384 Hz and a bandwidth of 3334 Hz. Online filtering was from 0.1 to 8192 Hz, the Nyquist frequency.

3.5.2 Offline Processing

3.5.2.1 Filtering and Extraction of the ASSR

The raw ASSR data was processed offline using Brainstorm, on the MATLAB platform (Tadel et al., 2011). Data from each channel was first band pass filtered from 60-1000 Hz, with a 60 dB per octave slope. Data were then epoched based on triggering events from the moment of stimulus onset. This event information was used to form the basis of the epoch timing, to ensure that each epoch contained an integer number of response cycles. Data from the channel with the electrode ipsilateral to the ear of stimulation were epoched separately. Epoch duration was 10.07687 seconds for the right ear/right mastoid channel data (87 Hz). The left ear/left mastoid channel data (93 Hz) were epoched to a duration of 10.1045 seconds. This produced 30 epochs per ear, per stimulus condition. A 10 second epoch allows for narrow resolution (known as a 'bin') of the spectral energy around the modulation frequency when looking at the amplitude spectrum. Bin width for the left ear data was 0.09896588384 Hz and bin width for the right ear data was 0.09923682617 Hz. This frequency resolution is fine enough to differentiate the noise energy near the response (i.e., spectral averaging). Noise estimated from the bins surrounding the response frequencies is also used to determine the residual noise in the data (Rance, 2008, pp. 26-29). The epochs were then weighted to an estimate of their noise. Weighted averaging was chosen based on the work of John et al. (2001), who showed that weighted averaging gave the best SNR and

response detection probability for steady state responses, compared to other averaging and artifact rejecting protocols. Weighted averaging entails multiplying each amplitude value in the epoch by the inverse of the variance of amplitude values across that epoch. This approach assumes high noise epochs will have high variance and vice versa. 30 weighted epochs were then available for objective response detection.

3.5.2.2 Q-sample Automated Response Detection

An objective response detection procedure was performed in the frequency domain using a modified version of the Mardia (1972) q-sample testing approach (Cebulla et al., 2006). In the present implementation, epochs were transformed to the frequency domain via Fast Fourier Transform, and the modified q-sample statistic was applied to phase values and magnitudes of the first 6 harmonics (i.e., F0 + 5 multiples) in reference to the respective stimulus repetition rate (alternatively known as the modulation frequency).

The q-sample testing algorithm was set to perform 15 'checks' over the course of the 30 epochs, spanning the five-minute recording period i.e., a check was performed each time two epochs were added to the cumulative average (approximately 20 second intervals) (Cebulla & Stürzebecher, 2015; Stürzebecher & Cebulla, 2013). A response was only considered present if the q-sample statistic at the stimulus frequency exceeded the 99^{th} percentile of the null distribution (see below) for at least two consecutive checks. If the response was considered present for two consecutive checks, the time value of the first check was taken. This means the quickest a response could be detected was 20 seconds. However, there are some challenges to use of a lookup table, principally concerning the large number of data (no sound trials) required to generate an appropriate null distribution. As the current study utilised offline analysis on a different device, a bootstrapping method was used instead to approximate the null distribution (Chesnaye et al., 2018, 2021). That is, a bootstrapped null distribution was generated using the participant's own ASSR data, from 5 adjacent F0 frequencies relative to the response frequency (70-

120 Hz, plus associated harmonics), with both stimulus frequencies excluded from the null distribution. Using critical test values and/or bootstrapping allows for statistical testing can be performed repeatedly on sequential tests without eroding the statistical power of the results (Cebulla & Stürzebecher, 2015; Chesnaye et al., 2018).

3.5.2.3 Determining a Response Present, Absent and Inconclusive

A response was deemed present when the q-statistic at the response frequency (and harmonics) exceeded the 99th percentile of the values from the null distribution. Signal amplitude was defined by the amplitude in the cumulative averaged response in the bin corresponding to the fundamental frequency. Residual noise was calculated based on the mean amplitude across 60 frequency bins above and 60 bins below the stimulus fundamental frequency (skipping bins on and near the signal frequencies of each ear) in the cumulative averaged response. For the right ear (87 Hz) the residual noise was therefore the mean amplitude in the range 81-95Hz (excluding 87 and 93 Hz) and for the left ear (93 Hz) the residual noise was the mean amplitude in the range 85-99 Hz (excluding 87 and 93 Hz).

As there are no published residual noise values for the BioSemi ActiveTwo to determine a response absent, nor is there published data from New Zealand, we based the residual noise cut off values on the British Society Audiology figures for the Interacoustics Eclipse (British Society of Audiology, 2022). If the q-statistic remained below the critical value by the end of the recording run and the residual noise was below 10 nV then a response was deemed absent. If the q-statistic remained below the critical value by the end of the recording run and the residual noise was above 10 nV then a response was deemed inconclusive (British Society of Audiology, 2022).

3.6 Interleaved Auditory Brainstem Response

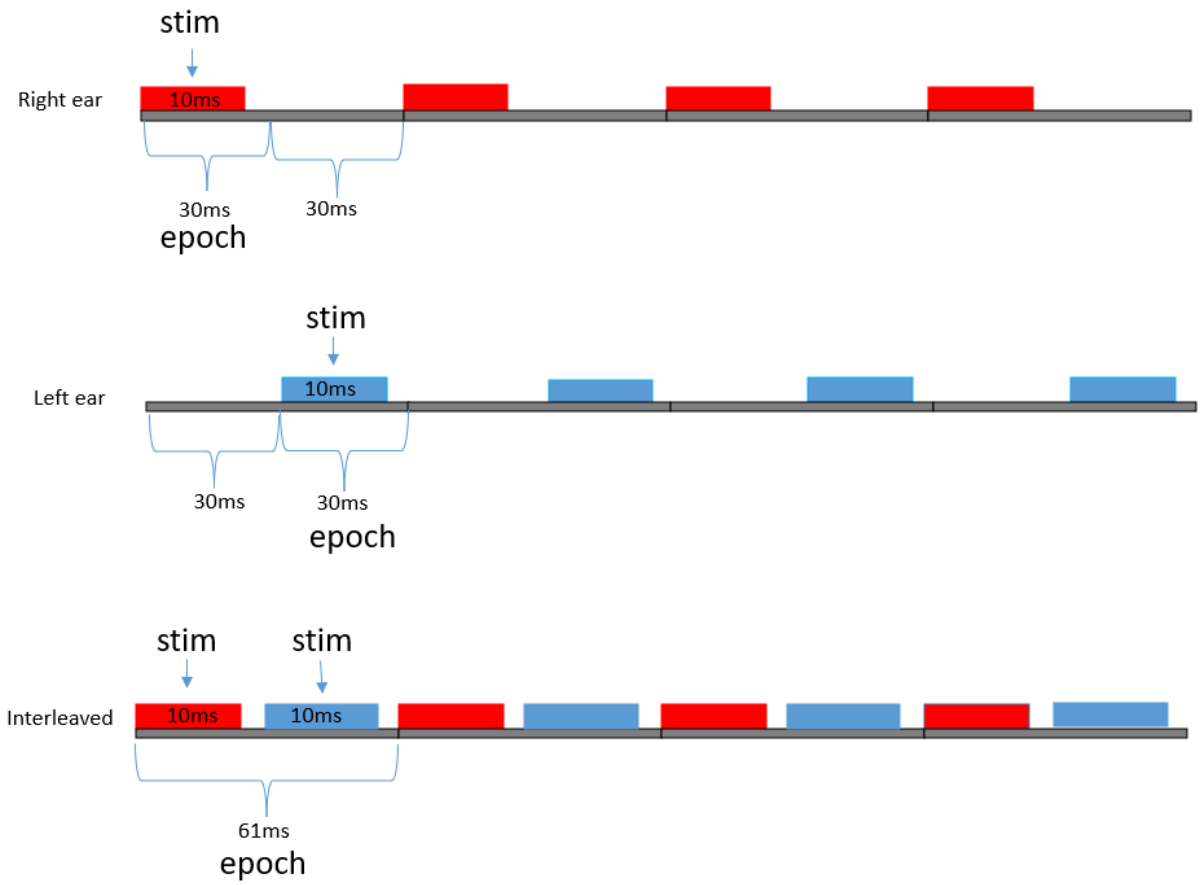
3.6.1 Online Processing

3.6.1.1 Stimuli Presentation

Chirp stimuli were presented in an interleaved fashion to the left and right ears in three conditions corresponding to the stimulus levels described in section 3.3 (20 dB, 30 dB and 40 dB nHL). The paradigm featured the above-mentioned chirp stimulus delivered via a wave containing 441 samples (10ms duration). Stimuli were presented at a rate of 16.4 Hz to each ear i.e., 61ms between the start of one stimulus to one ear, and the start of the next stimuli to the same ear. However, a stimulus was presented at an overall rate of 33 Hz i.e., only 30 ms between the start of one stimulus and the start of the next. Whilst the first ear was in silence, the second ear was receiving the stimuli. The sequence continued until 6000 chirps were delivered to each ear. Figure 3.3 shows a schematic of how the ABR stimuli was interleaved between the two ears.

Figure 3.3

The Interleaved ABR



3.6.1.2 Acquisition of the ABR

Raw electrophysiological data were captured at a sampling rate of 16384 Hz and a bandwidth of 3334 Hz were selected, identical to the ASSR data acquisition.

3.6.2 Offline Processing

3.6.2.1 Filtering and Extraction of Data

The raw interleaved ABR data was processed offline using Brainstorm, on the MATLAB platform (Tadel et al., 2011). Data from each channel was first band pass filtered from 80-1500 Hz, with a 60dB per octave slope. The data was epoched to a duration of 25.02ms each (the length of the wav. file plus 15ms for the ABR response), creating 6000 epochs per ear. The left ear/left mastoid channel was only

epoched for data corresponding to signals presented to the left ear, and the right ear/right mastoid channel was only epoched for data corresponding to signals presented to the right ear. A single-epoch weighted averaging approach was adopted whereby each amplitude value in the epoch is multiplied by the inverse of the variance of amplitude values across that epoch. This approach assumes high noise epochs will have high variance and vice versa. The approach is similar to the widely used Bayesian weighted average described by Elberling and Wahlgreen (1985), which addresses the fluctuation in noise over the course of the recording. Epochs with low noise are weighted statistically higher than those with high noise, with the final averaged waveform being more representative of the periods in which the noise was lower (Atcherson & Stoody, 2012). The Bayesian weighting approach is generally used to estimate variance across blocks of epochs (e.g., 256 epochs) (Elberling & Wahlgreen, 1985), but single epoch weighting was chosen for this study. The weighting approach of this study meant that no artifact rejection level needed to be determined apriori, as the epochs with high noise have already been appropriately down weighted (Don & Elberling, 1994). Only those epochs that exceeded the clipping level of the BioSemi amplifier were rejected (+/-262mV).

Objective ABR response detection was performed using the Fsp technique (Elberling and Don 1984) applied to the weighted epochs. In this technique, the variance at a single latency point across blocks of 250 epochs is compared with the variance within the cumulative averaged response via the following equation:

$$Fsp = \frac{Variance(averaged\ epoch)}{Variance\ (single\ point)}$$

In a clinical setting, the Fsp allows audiologists to dynamically determine the number of epochs needed to determine a 'response present' – or alternatively, a true 'response absent' – saving time when compared to fixed epoch numbers more commonly used in current protocols (Sininger et al., 2020). The Fsp value is updated every 250 epochs, and if a response is present, the value will grow as the residual noise reduces during averaging. Higher numbers indicate a better SNR, and eventually the

number may exceed some critical value corresponding to the response confidence (Sininger et al., 2020).

The single point used across each epoch was located at +18.75 ms relative to the stimulus onset to derive the noise calculation. The variance in the averaged epoch used to derive the signal calculation was based on five symmetrically spaced points spanning a 12.5ms range, which corresponded to the period of the lowest frequency content in the data (80 Hz). The latency range for these five points was +11.23 to 23.75ms. Therefore, as the Fsp value is updated every 250 epochs and the Fsp is a ratio of variances with an F distribution of 5 and 250 degrees of freedom in the numerator and denominator, respectively. Elberling and Don (1984) offered a conservatively derived critical value of 3.1, which corresponds to an estimate of the 99th percentile from a null distribution, albeit with data filtered with a high-pass cut-off of 100 Hz and a corresponding 10ms latency range.

3.6.2.2 Determining a Response Present, Absent and Inconclusive

The Fsp implementation provides an initial check after 250 epochs, or about 6 seconds into the recording sequence. This is the earliest theoretical response time. However, to bypass the risk of spurious findings from an inadequate sample size after only 250 epochs, it is common in clinical protocols to specify a minimum number of epochs above this point before the Fsp data are interpreted. Therefore, the Fsp findings were analysed only after 750 epochs, or 18.75 seconds. A response was only considered present if the Fsp value stayed above 3.1 for at least two consecutive checks. If the response was considered present for two consecutive checks, the time value of the first check was taken. This means the quickest a response could be detected was 18.75 seconds. A secondary feature of this strategy is that it ensured that initial checks occurred after a similar period between the ABR and the ASSR check sequence, to ensure a fair comparison with respect to the minimum possible detection time. The difference between 18.75 (ABR) and 20 seconds (ASSR) is not clinically significant, therefore will not likely impact overall interpretation of the detection time comparison.

Signal amplitude was defined according to the peak-to-peak amplitude of the ABR, typically Wave V to the following trough (SN10). An automated peak detection algorithm was used to define these peaks by finding the most positive and most negative points in the epoch within a latency range of +10 to +25ms relative to the stimulus onset. However, visual inspection of the waveforms was also carried out to address any anomalous findings, particularly where a post-auricular muscle response (PAMR) arose since these are usually much higher amplitude than the ABR. In these cases, the range was reduced to prohibit overlap with the PAMR (typically +10 to +20ms). Residual noise was based on the total variance of the epochs divided by the square root of the number of epochs. Again, there are no published residual noise values for the BioSemi Active Two or in the UNHSEIP protocol, so we again used values from the British Society of Audiology for the Interacoustics Eclipse (British Society of Audiology, 2019). If the Fsp statistic remained below the critical value by the end of the recording run and the residual noise was below 25 nV then a response was deemed absent. If the Fsp statistic remained below the critical value by the end of the recording run and the residual noise was above 25 nV then a response was deemed inconclusive (British Society of Audiology, 2019).

3.7 Analysis of Test Time and Sensitivity

3.7.1 Test Time

Total test time refers to the summed time (in seconds) it took to record a response from all three presentation levels (20dB, 30dB, 40dB) for each participant. Both ears were tested at once, and it is possible that there is a difference in test time between the participants left and right ears. In these cases, the test time is only as quick as the 'slowest' ear, therefore the longer time of the two was taken as the total time. For those participants that did not show a response at the end of the five minutes (ASSR) or 6000 epochs (ABR) the test time was recorded at the maximum value of 300 seconds. Test time results were then compared using parametric statistical analyses, after ensuring the data did not violate parametric assumptions.

3.7.2 Sensitivity Estimation

Threshold information was extrapolated in offline analysis, giving an idea of the sensitivity of both measures. As we did not test right down to threshold, nor did we dynamically seek threshold like a clinical procedure would and compare it to a behavioural audiogram (due to equipment restraints), we can determine the sensitivity of each measure through offline reconstruction of the determining factors. Utilizing the methods of Elberling & Don (1987), sensitivty estimation of the two methods can be undertaken in a two stage process. First, the AEP amplitude at each stimulus level is plotted against the residual noise and a line of best fit is applied to show the regression analysis between the two, and it can be extrapolated where the signal would fall in to the noise floor. Secondly, the statistical method of detection used for each AEP was applied (Fsp for the ABR and W-value for the ASSR) to determine exactly what level a reponse would be detected in dB nHL. This is deemed to be the threhsolds of each measure. The thresholds will then be compared to determine if one is more sensitive that the other (i.e. has a lower threhshold). In clinical audioloigy, thresholds are measured using 5 dB steps (Carhart & Jerger, 1959; Hughson & Westlake, 1944). A threshold of 13dB for exmaple, would be rounded up to 15dB. If both measures are within a 5 dB step size of each other, they will be considered to have the same sensitivity. As the threshold of sound perception reduces with the length of the stimulus (short duration sounds used to eliecit AEP's do not sounds as loud to the listener as a longer duration sound), the thresholds determined by this study are not true pyschacoustic thresholds, nor have the been compared to or corrected to behavioural thresholds. The research questions is simply asking at what point does the signal become unrecognisable in the noise, and at what point would it pass the statistical measures applied to be confirmed as a response.

3.7.3 Data Presentation

When presenting the data for this research, we have chosen to represent the grand average data using median values, as well as mean values in some instances. Whilst this may be an uncommon

approach, it is not without justification (Fox & Dalebout, 2002; Özdamar & Kalayci, 1999; Whitley & Ball, 2002). As discussed in section 3.5.2.1 and 3.6.2.1, weighted averaging was performed on the ASSR and interleaved ABR data during the offline processing of the within-subject data, removing the need for artifact rejection. Only those epochs above the limits of the BioSemi (+/-262mV) were removed. This means that some of the final responses show amplitudes that are outside of normal distribution. Whilst this data may or may not be spurious (small sample sizes often do not show normal distribution) (Fox & Dalebout, 2002), removal of this data would lead to an even smaller sample size, reducing the power of the study. Mean values can be biased by outliers in the data, skewing the final values presented in the Grand Averages (Fox & Dalebout, 2002). Median however, is less affected by outliers in the data, and reflects the centre of the data regardless of the shape of the distribution, giving a more reliable representation of the group data for sensitivity (Fox & Dalebout, 2002; Özdamar & Kalayci, 1999).

4 Results

4.1 ASSR Results

Grand-average power spectrums from the three stimulus levels are shown in Figure 4.1, averaged across the two recording channels for the purposes of display. Note, that as the stimuli to each ear were delivered at different rates and the FFT analyses were tailored to those rates (epoch lengths differed), when focusing on one frequency this would mean the response to the other would be spectrally averaged away. However, Welch's method for power spectral density estimation should be relatively immune to this effect. Therefore, for display purposes only, Welch's method was used to produce these figures, therefore the amplitude is shown in power (uV^2). The graphs below show only a snapshot of the frequency range (80 - 110 Hz) centred around the F0, and spikes for both ears can be viewed on one chart below. Both mean and median data are represented.

For the median data, the figures show spectral peaks at 87 and 93 Hz (corresponding to F0 for right and left ears), and the height of these peaks tends to increase from around 0.05 μV^2 to around 0.08 μV^2 as the stimulus level increases from 20 to 40 nHL, while the amplitude in the surrounding frequency bins (corresponding to residual noise) remains relatively constant around 0.038 μV^2 in these figures. An exception is the 87 Hz responses at 20 dB nHL which is not visible above the noise. Note the peak amplitudes appear somewhat greater at 93 Hz.

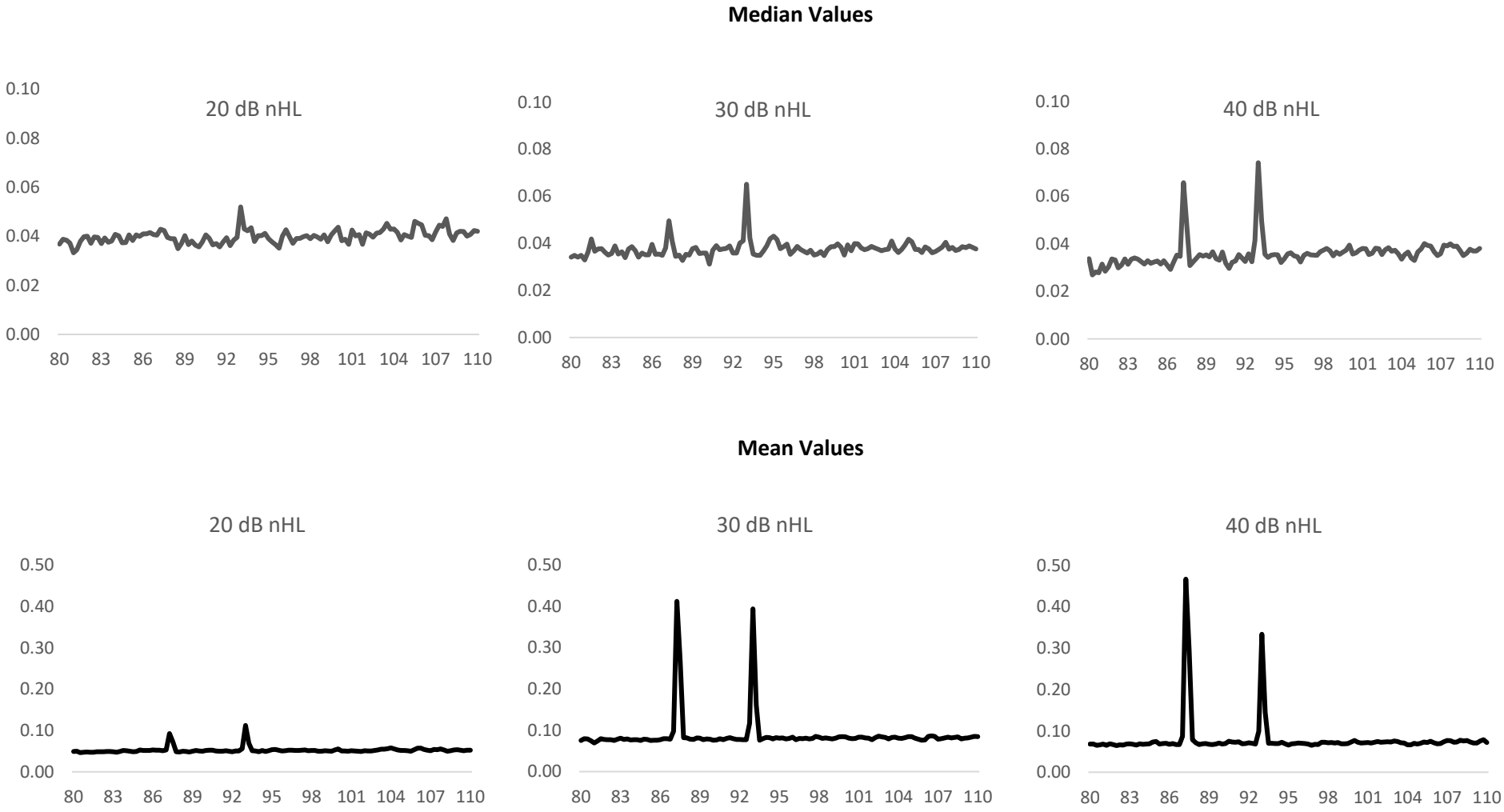
For the mean data, the spectral peaks are again in the expected locations (87 and 93 Hz) and the noise remains relatively constant at around 0.7μV^2. However, we do not see the expected increase in amplitude from 30 to 40 dB nHL. In fact, 30dB nHL appears higher than 40dB nHL, due to the skew caused by outliers in the data. In the 40dB nHL condition, the amplitude of the 87 Hz response is visibly higher than that of the 93 Hz response.

Note that these values differ from what is presented further in the results section, as they are representative of Welch's method and are showing power, not amplitude on the y axis.

4.1.1 Grand Averages

Figure 4.1

ASSR Grand Averages by Stimulus Level



Note. X axis denotes frequency and y axis denotes power of the response ($\mu V^{2)}$. Note the differing scales of the y axes (10 μV^2 for median and 50 μV^2 for mean).

4.1.2 ASSR Residual Noise

Figure 4.2 shows the residual noise data (nV) for each condition across the five minutes of recording time. The residual noise lowers progressively with each subsequent check, as the noise is cancelled through the averaging process (John et al., 2001). The residual noise values of each stimulus level follow the same pattern, as expected given participants received the ASSR stimuli in sequence in one session (in a counterbalanced order). Table 4.1 shows mean and standard deviation data for the residual noise.

Figure 4.2

Residual Noise Values of the ASSR by Stimulus Level

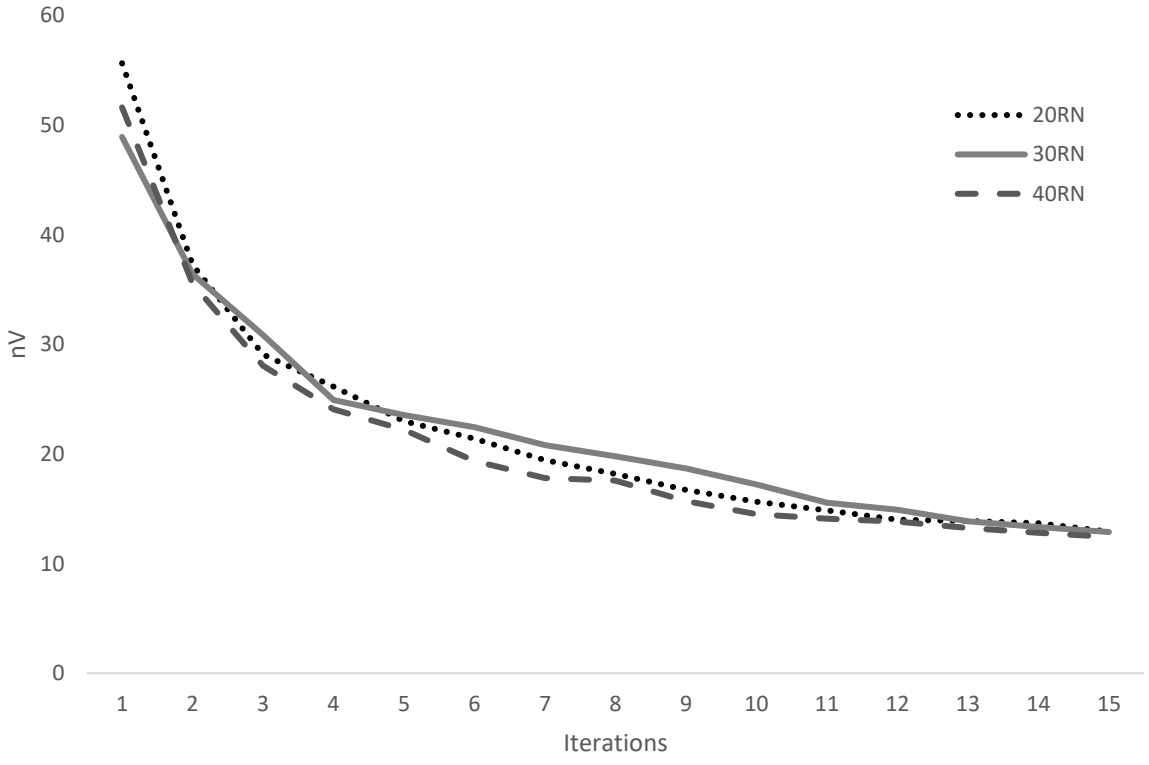


Table 4.1

Descriptive Statistics for the ASSR Residual Noise Values

Stimuli level	Mean	Standard Deviation
20nHL	12.92	11.65
30nHL	12.88	9.93
40nHL	12.43	10.84

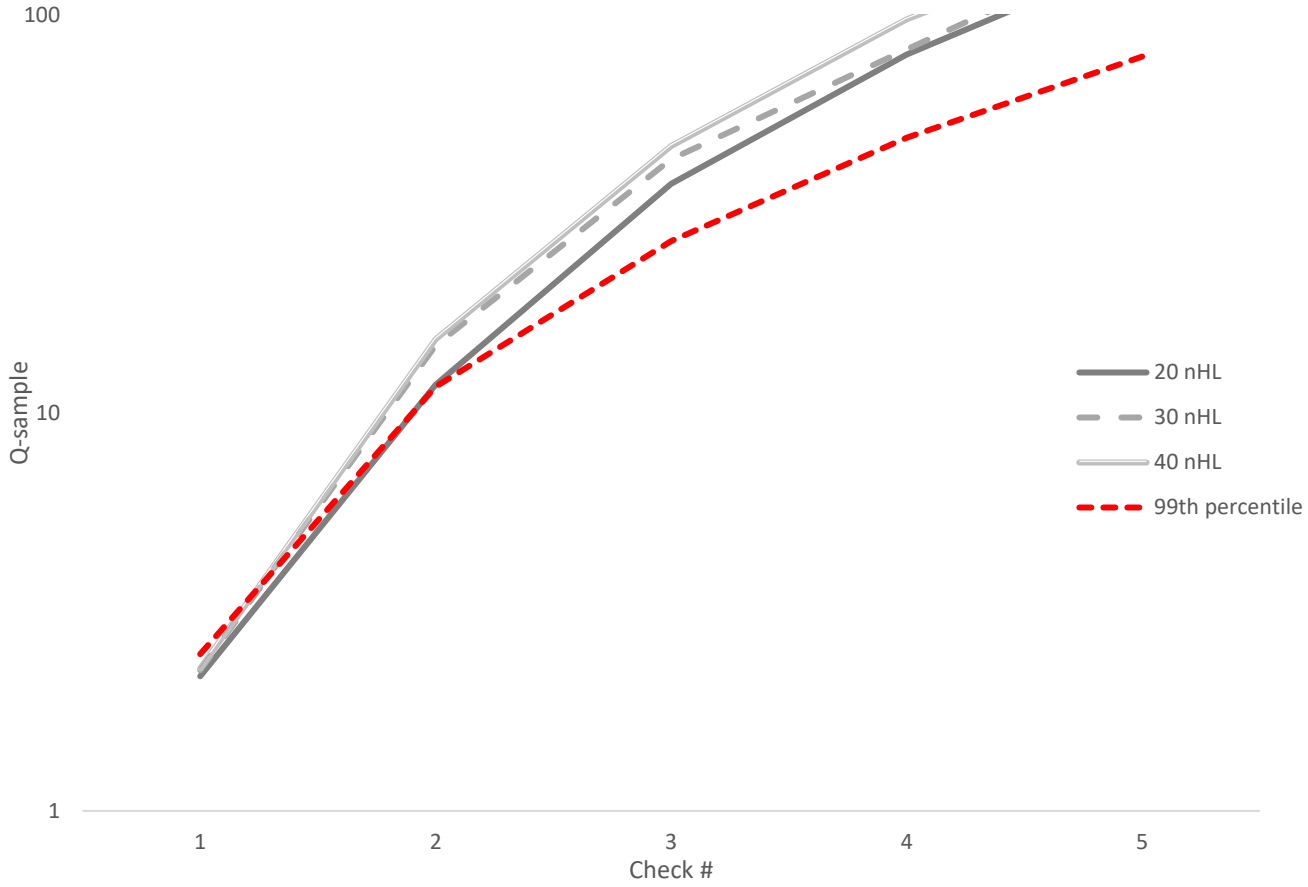
Note. Unit of measurement is nanovolts (nV).

4.1.3 Q-sample Data

Figure 4.3 shows the summed (median) Q-sample data for all participants in each condition. The red dotted line represents the 99th percentile, generated from the participants null values using the bootstrapping method. In practice the 99th percentile is not static, it shifts for each participant depending on the null values they generate (Chesnaye et al., 2018). The 99th percentile line shown in Figure 4.3 represents the average value from all participants at all three summed stimuli levels. On average, the q-sample statistic remains below the critical value by the first check in the sequence for all stimulus levels. However, by the second check, the response is detected in the 30 and 40 dB nHL conditions, and similarly by the third check at 20 dB nHL condition. Table 4.2 shows the mean and standard deviation information for the q-sample procedure.

Figure 4.3

Q-sample Data for the ASSR



Note. As the responses cross the critical value early in the test time, for easier visual representation only the first five checks are represented, spanning about 1 minute and 40 seconds of the 5-minute recording run. For the full table, see Appendix F.

Table 4.2

Descriptive statistics for the Q-sample Data

Stimuli level	Mean	Standard Deviation
20nHL	535.80	229.86
30nHL	647.57	627.43
40nHL	671.59	623.64
Averaged 99th	260.77	232.75

4.1.4 Response Present, Absent or Inconclusive

All participants showed bilateral responses to the 40db nHL stimuli, and the majority showed responses to the two lower-level stimuli. There were four missing responses in total, from three participants. Two of these occurred at 20nHL and two at 30nHL, which together account for 13% of the responses. All participants showed clear responses in at least one ear at the lowest stimulus level. As shown in Table 4.3, all the missing responses were deemed inconclusive, as the residual noise value at the end of the run was above the criterion cut off value of 10nV, meaning it is not possible to determine if the response was truly absent, or a small amplitude response hidden by noise.

Table 4.3

ASSR Absent or Inconclusive Responses

Participant	Ear	Stimuli Level	Residual Noise	Absent or Inconclusive
5	Right	30	11.91	Inconclusive
6	Left	20	37.14	Inconclusive
14	Right	20	12.63	Inconclusive
14	Right	30	16.15	Inconclusive

Although participant 5 showed an inconclusive result at 30 dB nHL for the right ear, the same listener exhibited a clear response at 20 dB nHL. To observe a response at a lower level suggests a response was likely present at 30 dB nHL in this instance. This is an example of how interpretation of the overall pattern can benefit interpretation of specific instances, even if those instances are inconclusive in isolation.

4.1.5 ASSR Test Time

Detection times for individual participants at all three levels, and total (summed) time can be seen in Table 4.4. Mean and median detection time decreased progressively as the stimuli levels were raised. Of note is that the mean and median test values diverge somewhat significantly, especially for

the 20nHL and 30nHL conditions. This is due to the test time for the missing responses (outlined in Table 4.3) which is recorded at the maximum test time of 300 seconds, meaning these outliers have more of an effect on the mean test time than the median.

Table 4.4

Total Test Time per Participant for the ASSR

Participant #	20 dB nHL	30 dB nHL	40 dB nHL	Total Time
1	160	60	80	300
2	120	20	20	160
3	120	80	100	300
4	180	120	120	420
5	100	300	100	500
6	300	100	40	440
7	60	40	40	140
8	40	20	40	100
9	40	40	40	120
10	100	40	40	180
11	80	40	100	220
12	40	20	20	80
13	60	60	60	180
14	300	300	40	640
15	20	40	40	100
Mean	114.67	85.33	58.67	258.67
Median	100.00	50.00	40.00	180.00
Standard Deviation	87.98	91.80	32.48	170.12

4.2 Interleaved ABR results

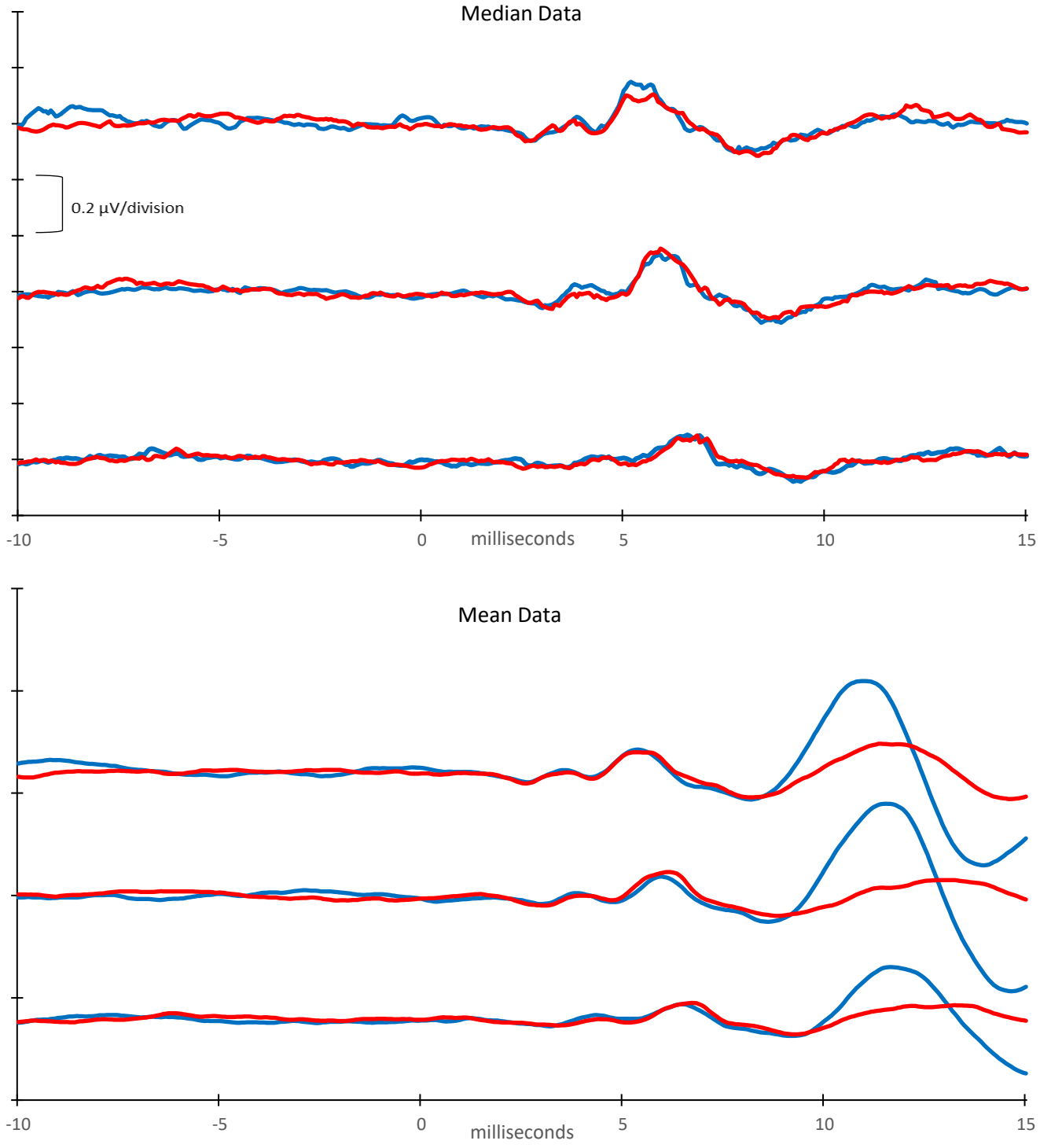
4.2.1 Grand Averages

Grand average interleaved ABRs for the three stimulus levels are shown in Figure 4.4. For the median data, the responses show expected ABR morphology with a wave V component occurring around 6ms in the 40 dB nHL condition, and progressively increasing in latency to around 7ms in the 20 dB nHL condition. Similarly, the peak-to-peak amplitude (wave V to SN10) reduced progressively from

around 0.5 µV to around 0.1 µV as the stimulus level reduces. Earlier peaks like wave III are apparent and these contribute to the variance within the averaged epoch that is detected by Fsp. When visual detection methods are used, these earlier peaks and the overall waveform morphology can assist (essentially via pattern recognition task for the clinician) in identifying ABRs and tracking them down to threshold. However, they do not contribute to the peak-to-peak estimate of signal strength when it is based on the Wave V to SN10 amplitude. Note the 10ms pre-stimulus baseline, which can also aid clinicians in visually differentiating a response but is not relevant for objective response detection and residual noise estimates based on the variance in the response range across epoch. The mean data shows a slightly different picture. Whilst wave V is still apparent at a similar amplitude and latency, the PAMR contributed by some participants is visible in the left (blue) trace. The PAMR is a high amplitude signal that is far larger than the amplitude of the ABR, so it must be excluded when determining the peak-to-peak ratio of the wave V and SN10 response. The PAMR can lead to a falsely high Fsp ratio, but does have clinical relevance as it shows the participants detection to sound, which is especially useful when the waveform may be difficult to interpret.

Figure 4.4

Interleaved ABR Grand Average by Stimulus Level



Note. Plotted in descending order from 40 – 20 dB nHL. The red line represents right ear data and the blue line represents left ear data.

4.2.2 Interleaved ABR Residual Noise

Figure 4.5 shows the residual noise data (nV) for each stimuli level, across the 6000 epochs. The residual noise lowers progressively with each subsequent check, as the noise is cancelled through the averaging process (John et al., 2001). The residual noise values of each stimuli level follow the same pattern, as expected given participants received the interleaved ABR stimuli in sequence in one session (in a counterbalanced order). Table 4.5 shows mean and standard deviation data for the residual noise.

Figure 4.5

Residual Noise Values for the Interleaved ABR by Stimulus Level

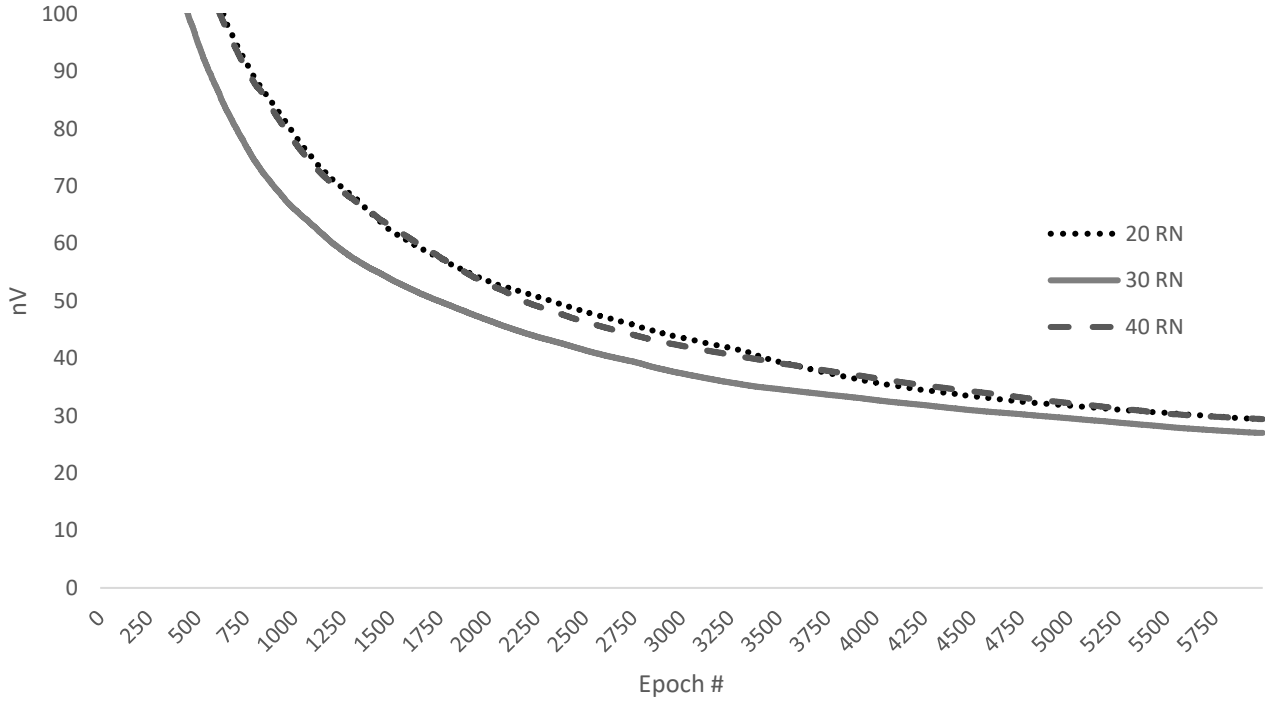


Table 4.5

Descriptive Statistics for the Interleaved ABR Residual Noise Values

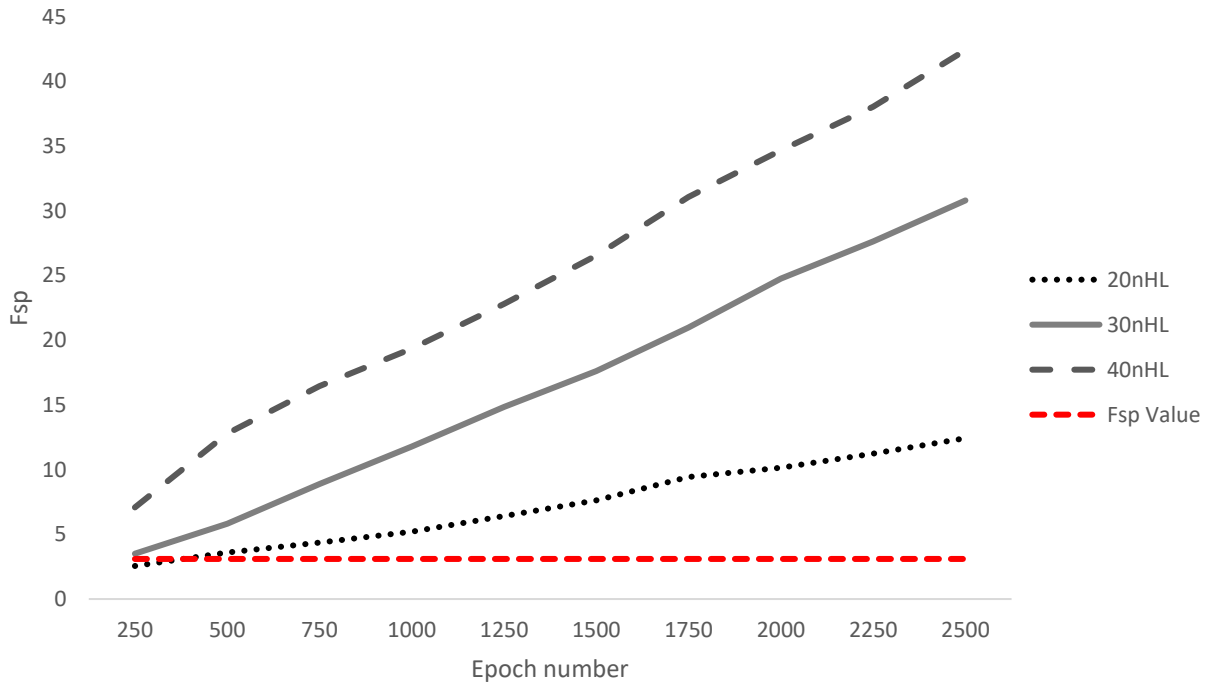
Stimuli level	Mean	Standard Deviation
20nHL	29.34	63.18
30nHL	54.66	72.65
40nHL	66.83	89.98

4.2.3 Fsp Data

Figure 4.6 shows the summed (median) Fsp data for all participants at each stimuli level. The red dotted line represents the Fsp value of 3.1. For the 30 dB nHL and 40 dB nHL stimuli levels, the Fsp is satisfied from the very beginning of the recording. For the 20 dB nHL stimulus level, the Fsp is reached by 500 epochs. Table 4.6 shows the mean and standard deviation information for the Fsp procedure.

Figure 4.6

Fsp Data for the Interleaved ABR



Note. As the responses cross the Fsp level early in the test time, for easier visual representation only the first 2500 epochs are represented. For the full table, see Appendix G.

Table 4.6

Descriptive Statistics for the Fsp Data

Stimuli level	Mean	Standard Deviation
20nHL	4.57	2.29
30nHL	13.31	6.34
40nHL	17.05	8.38

4.2.4 Response Present, Absent or Inconclusive

The Interleaved ABR produced eight missing responses in total. All bar one missing response was deemed inconclusive due to the residual noise of the test being above the cut off value of 25nV (Table

4.7). Most of the missing responses were at 30nHL and 40nHL when we had confirmed responses for these participants (participants 3, 13, 6 and 11) at lower stimuli levels. To observe a response at a lower level suggests a response was likely present at the higher levels. This is an example of how interpretation of the overall pattern can benefit interpretation of specific instances, even if those instances are inconclusive in isolation. Post Auricular Muscle Response (PAMR) was also seen in many of these waveforms, even when the response was not detected, suggesting they did in fact hear the stimuli. Participant 13 showed the only true absent response on the right at 30nHL, yet showed a response at 20nHL on this side, and again at 40nHL. This can be considered a true type II error of a false negative. Participant 5 had missing responses at 20dB in both ears, yet heard the higher-level stimuli. Whilst is it possible the stimuli were not heard by them at this lowest level, they also exhibit the highest residual noise values of all the missing responses, suggesting that participant movement or external noise may have played a part in the missing responses.

Table 4.7

Interleaved ABR Absent or Inconclusive Responses

Participant #	Ear	Stimuli Level (nHL)	Residual noise (nV)	Absent or Inconclusive
3	Left	40	32.46	Inconclusive
5	Left	20	37.13	Inconclusive
5	Right	20	32.24	Inconclusive
6	Right	40	30.83	Inconclusive
6	Left	40	27.48	Inconclusive
11	Left	20	26.74	Inconclusive
11	Right	40	30.03	Inconclusive
11	Left	40	26.20	Inconclusive
13	Right	30	23.24	Absent

4.2.5 Interleaved ABR Test Time

Detection time for all three levels of interleaved ABR stimuli and total (summed) time can be seen in Table 4.8. Median detection time decreased progressively as the stimuli levels were raised, as expected. However, the mean detection time did not show the same pattern. As there were more inconclusive responses at the 40nHL stimuli level, the test time for these participants (taken at the 300 seconds, when the testing reached 6000 epochs) has skewed the mean time upwards. As this was a set duration test time, we were unable to dynamically choose whether to change or stop recording in such instances where the residual noise was high. Ramifications of this will be examined in Discussion section 5.4.

Table 4.8

Total Test Time per Participant for the Interleaved ABR

Participant #	20nHL	30nHL	40nHL	Total Time
1	118.75	25.00	56.25	200.00
2	93.75	31.25	18.75	143.75
3	75.00	131.25	300.00	506.25
4	131.25	18.75	18.75	168.75
5	300.00	93.75	43.75	437.50
6	81.25	100.00	300.00	481.25
7	37.50	18.75	62.50	118.75
8	18.75	18.75	18.75	56.25
9	56.25	50.00	18.75	125.00
10	87.50	25.00	25.00	137.50
11	300.00	31.25	300.00	631.25
12	18.75	18.75	18.75	56.25
13	93.75	300.00	68.75	462.50
14	31.25	37.50	18.75	87.50
15	18.75	18.75	18.75	56.25
Mean	97.50	61.25	85.83	244.58
Median	81.25	31.25	25.00	143.75
Standard Deviation	84.06	70.47	106.00	186.89

4.3 Total Test Time Comparison

The total (summed) test times for the ASSR and interleaved ABR can be seen in Figure 4.7. Mean, median and standard deviation for both measures can be seen in Table 4.9. Statistical analysis of the test time comparison was performed on IBM SPSS Statistics software version: 28.0.1.0 (142). Firstly, normality testing was undertaken on the test time data to ensure normal distribution of the values. Shapiro-Wilk and Kolmogorov-Smirnov were performed to check for parametric assumptions of normality and homogeneity. Both tests were non-significant ($p > 0.05$). Skewness and kurtosis were also within normal ranges for normality. The full set of normality testing undertaken can be seen in Appendix H.

Figure 4.7

Total Test Time Comparison of the ASSR and Interleaved ABR

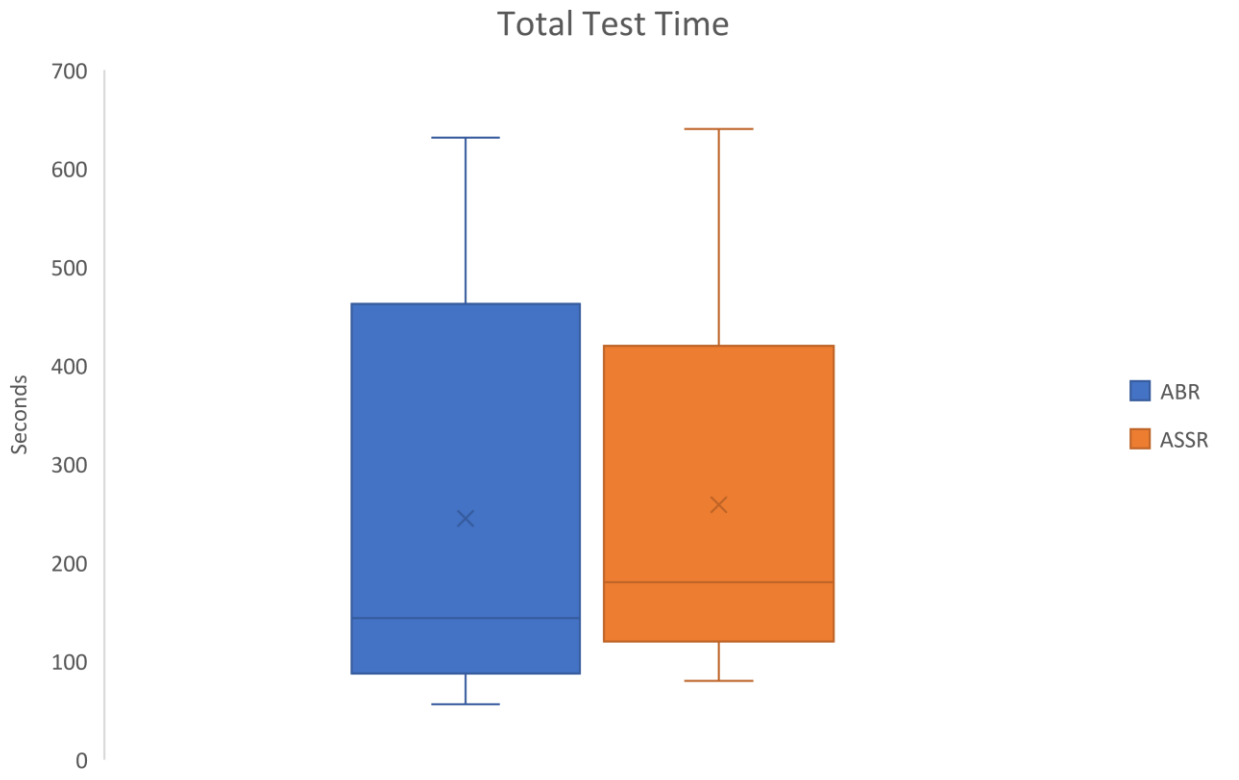


Table 4.9

Descriptive Statistics for the ABR and ASSR Test Time

	ABR	ASSR
Mean	244.58	258.67
Median	143.75	180.00
Standard Deviation	198.08	170.12

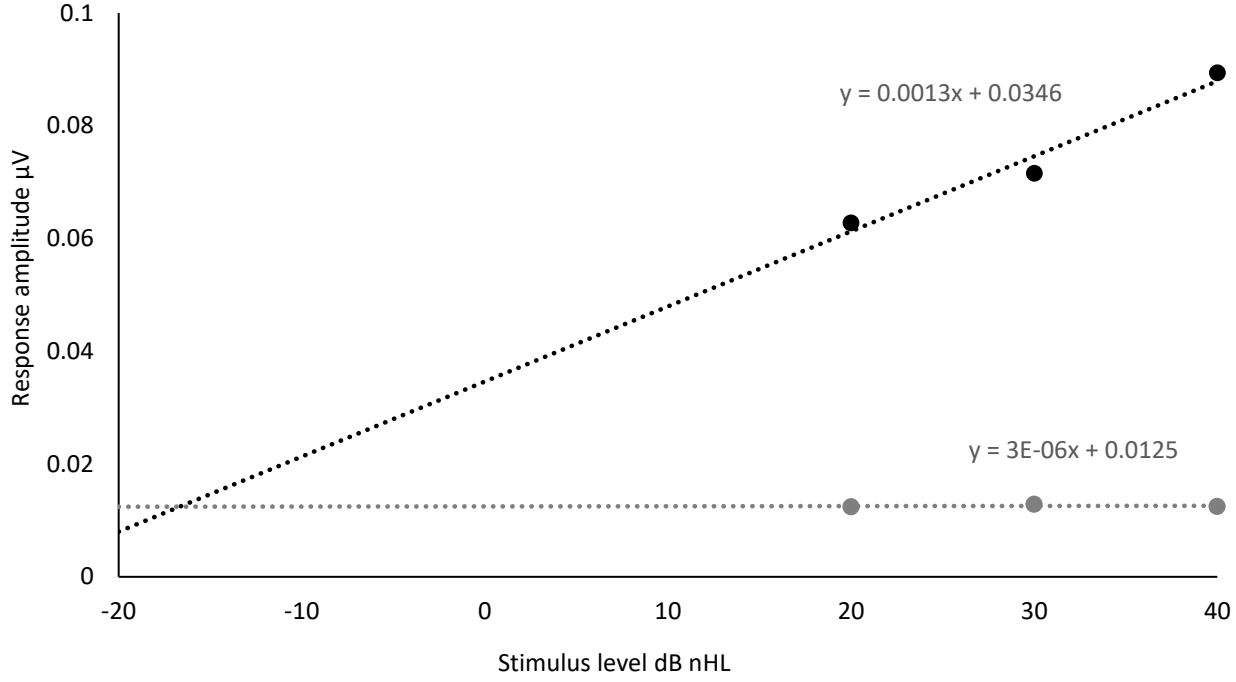
A paired sample t-test was performed to compare mean test times and results considered statistically significant if $p < 0.01$. Preliminary tests did not indicate any violations of parametric assumptions (see Appendix H). The findings indicate there is no statistically significant difference in total test time needed to acquire the same intensity series either via the ASSR or the interleaved ABR ($t_{14} = 0.2$; $p = 0.81$)

4.4 Threshold Comparison

The second research question of this study aimed to determine the sensitivity of hearing thresholds estimated by the ASSR and the interleaved ABR. Figure 4.8 shows the amplitude intensity plot for the ASSR data. The median amplitude values at the end of the 5-minute recording period for all participants are plotted on the diagonal (black) line, and the median residual noise values on the horizontal line (grey). A linear growth function is demonstrated via the line of best fit ($y = 0.0013x + 0.0346$), with the amplitude of the responses increasing monotonically with the stimulus level. Plotting the data in this way allows for extrapolation of where the signal would fall in to the noise floor, without testing right down to threshold for all participants. The signal disappears into the noise floor at -17 dB nHL (SNR of 1).

Figure 4.8

Amplitude Sensitivity Plot for the ASSR and Residual Noise



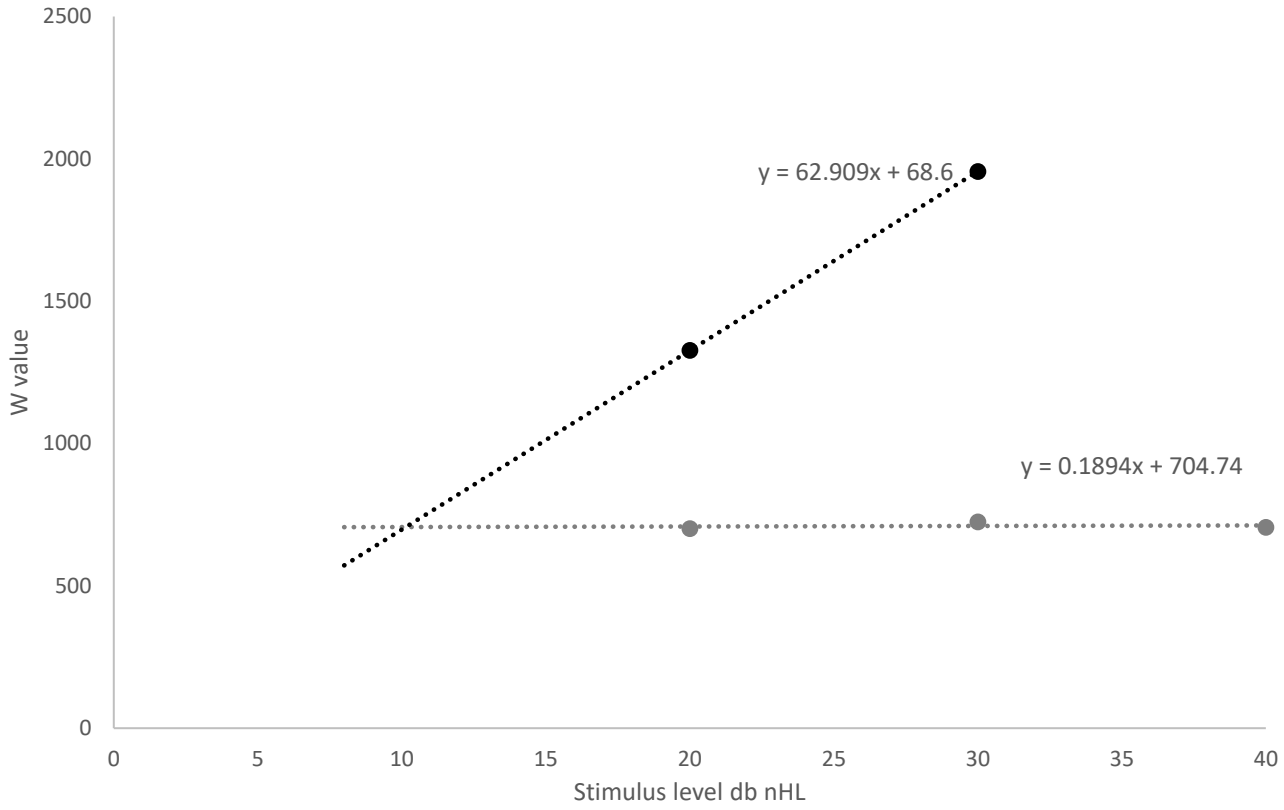
Note. The black line represents the merged response amplitudes of all participants at the three stimulus levels. The grey line represents the median residual noise at each stimulus level.

Figure 4.9 shows the threshold estimation for the ASSR. The criterion for a Clear Response is based on the median q-sample data gathered from all participants, which was set to a 99% confidence interval, which is plotted along the x-axis. The black line shows the w-value data for the 20dB nHL and 30dB nHL conditions. A growth function is demonstrated via the line of best fit (y = 0.0013x + 0.0346). Interestingly, the median 40 dB nHL response is of a smaller amplitude than the 30 dB nHL. We have excluded the 40dB nHL data from this plot as including it creates a shallower growth function, skewing the results to suggest a much lower threshold. It would have been helpful to test at higher stimuli levels (say 50 dB nHL and 60 dB nHL) for the same participants, to confirm that there is in fact, a linear growth

pattern and that the results from 40 dB nHL are simply spurious. The intercept of the two lines (where the w-value would have crossed the 99th percentile and be considered a Clear Response) is 10 dB nHL.

Figure 4.9

Threshold Estimation for the ASSR

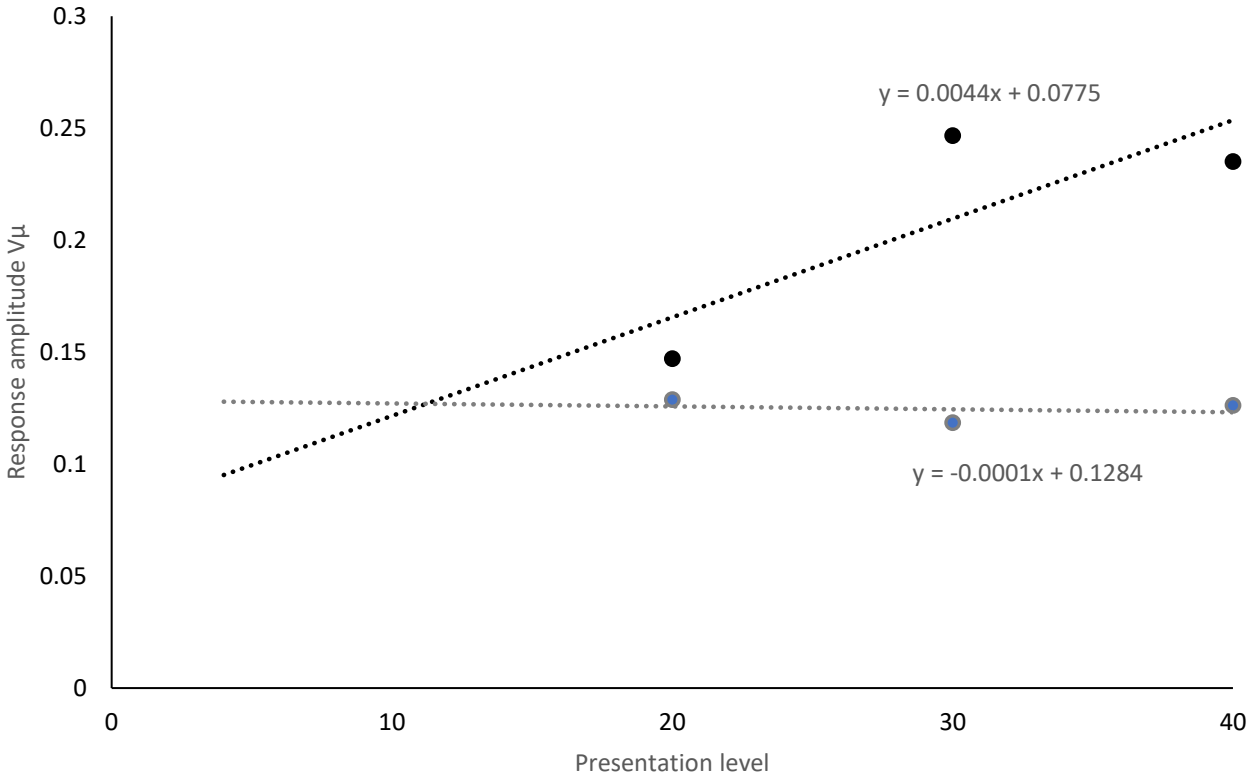


Note. The black line represents the median critical values of all participants at the three stimulus levels. The grey line represents the median W value for all participants at each stimulus level.

Figure 4.10 shows the amplitude intensity plot for the interleaved ABR data. The median amplitude values at the end of the 5-minute recording period for all participants are plotted against the median noise values at the end of each run. The signal disappears into the noise floor at 11 dB nHL (SNR of 1).

Figure 4.10

Amplitude Sensitivity Plot for Interleaved ABR and Residual Noise

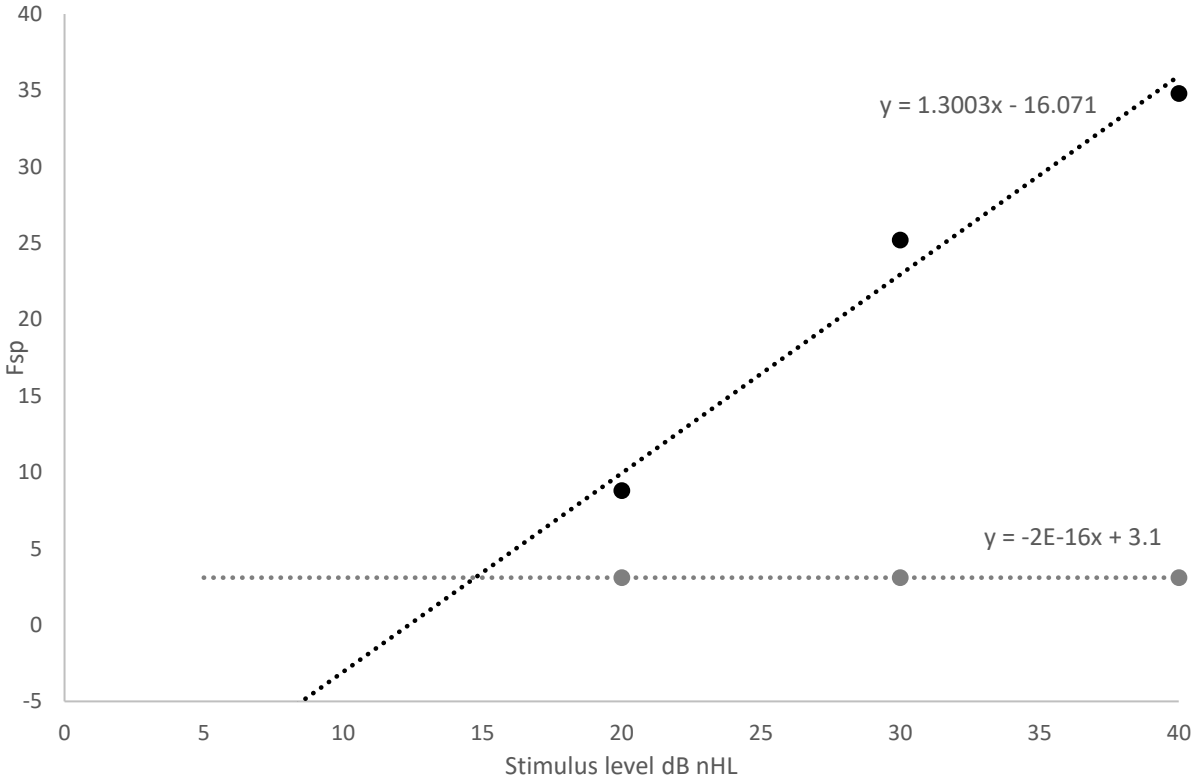


Note. The black line represents the median response amplitude of all participants at the three stimulus levels. The grey line represents the median residual noise at each stimulus level.

Figure 4.11 shows the threshold estimation for the Interleaved ABR. The criteria for a Clear Response is based off the Fsp value of 3.1. A linear growth function is demonstrated via the line of best fit (y = 1.3003x - 16.071). The intercept of the two lines (response would have crossed the Fmp value of 3.1 and be considered a Clear Response) is 15 dB nHL.

Figure 4.11

Threshold Estimation for the Interleaved ABR



Note. The black line represents the median Fsp values of all participants at the three stimulus levels. The grey line represents Fsp value of 3.1.

5 Discussion

The aims of the current study were to undertake a performance comparison between ASSR (arguably the current 'gold standard' in terms of test time) and the interleaved ABR, in the hope of informing their prospective use in newborn hearing testing. The purpose of comparing these two measures is to shed light on easily-accessible modifications to current method in widespread use (the ABR), as this is seen as relatively time consuming, and often the necessary results to determine hearing thresholds cannot be obtained in one appointment. If studies such as these can find a measure that is otherwise equivalent to current ABR approaches, but is more time efficient, it may be a viable alternative to the current methods in place. To the best of the author's knowledge, this is the first study to compare the ASSR to the interleaved ABR with this objective in mind. The main hypotheses were to determine if there was a difference in test time between the ASSR and the interleaved ABR, or if there was a difference in sensitivity between the two measures. A summary of the key findings of this study are:

- No statistically significant or clinically significant difference in test time between the ASSR and the interleaved ABR.
- The ASSR response detection technique was relatively more sensitive than the interleaved ABR, suggesting responses could be detected down to 10dB nHL on average, whilst the ABR approach suggested responses could be detected down to 15 dB nHL in normally hearing listeners.

Therefore, the current study does not reject the null hypothesis for test time. For sensitivity, the data support the alternative hypothesis– there is a difference in sensitivity between the ASSR and the interleaved ABR.

5.1 Test Time Findings

5.1.1 ASSR Test Time

The present study delivered stimuli at three levels (20 dB nHL, 30dB nHL and 40 dB nHL - using the same RETSPL), and the mean test times were 114.67, 58.67 s and 85.33 s respectively. Median scores were somewhat lower, at 100, 50 and 40 seconds respectively. In newborn hearing screening, the chirp stimulus is usually delivered at 35dB nHL, and studies in the published literature also utilise this stimulus level.

Cebulla and Stürzebecher (2013) describe mean test times for ASSR detection utilising an MB11 Berphone, which is used in Aotearoa New Zealand for newborn hearing screening, and an using an approach with parallels to the present work. In this study, the researchers utilised a similar chirp stimulus at 35dB nHL, albeit delivered monaurally. The stimuli were delivered at a range of repetition rates between 20 Hz and 100 Hz, with the overall aim of determining the optimal repetition rate for use in newborns. Based on a cohort of 116 infant listeners, the mean detection time for the 90 Hz (the closest stimulus repetition rate to that utilised in this study) was 32 seconds, and a median test time of 22 seconds, which are substantially lower than the test times found presently. Cebulla and Stürzebecher's study utilised eight harmonics for response detection, compared to five harmonics in the present study. Along with the use of monaural stimulus presentation, and infant rather than adult listeners (infants tend to have smaller heads thus larger evoked potential amplitudes) the use of more harmonics tends to decrease the test time (Cebulla et al., 2006), which may explain the difference in mean test times observed in this study.

Cebulla et al., (2006) also compared a range of one sample and q-sample tests to determine which showed the best test performance in terms of time and sensitivity, this time in adults. Participants were fifty-seven adults between 20 – 64 years of age (*M* = 42 years of age) with hearing in the normal range, or with sensorineural hearing loss between mild to moderately severe at least of the core

frequencies. Tone specific stimuli were delivered at 30 dB nHL for the normally hearing listeners, and 30dB SL for the listeners with hearing loss, at a rate of 90 Hz. The version MQSTV4 (a modified Mardia q-sample test with both ranked and unranked spectral phases and amplitudes used to detect a response, and six harmonics), was the closest in design to the objective detection used in this study. The MQSTV4 detection test showed a median detection time of 28 seconds for a multiple stimulus ASSR, and 42 seconds for AM stimuli. This is in comparison to our 50 seconds for the same level stimulus. Median test times in this study varied widely, depending on the data used for objective detection, showing the importance of choosing the right detection parameters in order to produce a shorter test time.

5.1.2 Interleaved ABR Test Time

Test time for the interleaved ABR has not previously been measured in the research (Bencito, 2020; Lien, 2022; Nofal, 2022). This is the first time it has been used for test time and sensitivity analysis, but it can be compared to the previous study by Sininger et al. (2018). Both studies captured ASSR and ABR using a similar study design with the same listeners and equipment used for each condition, with the stimuli begin delivered in a counterbalanced order. Although Sininger et al. (2018) delivered frequency specific chirps to the two ears, compared to the broadband chirps delivered to two ears in the present study, in both studies the ASSR and ABR were elicited using the same stimuli. Both also utilised similar objective measures for response detection (Fsp/Fmp for the ABR, q-sample testing for the ASSR).

Sininger et al. (2018) elicited the ABR using the classic, sequential stimulation and found a significant difference in test time between the ASSR and ABR (the ABR taking 30% longer than the ASSR to capture the same information). In the present study in which the interleaved ABR was instead utilised, there was no difference found between the two measures. The results of this research suggest that the interleaved ABR may have closed the gap previously found by the two measures in methodologically similar studies. Whilst no statistically different time difference was found, this is a null finding. We have not determined that the two test times are the same, simply that we have not found a

difference. Further studies of test time comparison of the two measures, particularly with lower-level stimuli, would be beneficial.

5.2 Sensitivity Findings

The sensitivity protocol for this study was based off the work of Elberling & Don (1987), who studied 10 normally hearing adults to determine ABR threshold sensitivity, and compare it to the participants psychoacoustic thresholds elicited using the same stimulus parameters. They highlight that that the relationship between the two depends strongly on the methodological characterises of the two tests – the number of sweeps, level of background noise, and the detection method used.

In this study, the same (or similar, in the case of objective response detection) methodical characteristics were used for the two electrophysiological conditions, making it as fair a comparison as possible. The threshold of the ASSR was found to be at 10 dB nHL, compared to the interleaved ABR at 15dB nHL. This suggests the ASSR is more sensitive that the interleaved ABR in terms of threshold detection. This aligns with the study by Sininger et al., (2018) which concluded that threshold estimation is lower by the ASSR than the ABR. However, correction factors (which were drawn from differing protocols and research) were applied the thresholds obtained in that study, and the researchers suggest that may have had an impact on the difference they found between the two measures. Sininger et al., (2018) also noted this was in contrast to other studies comparing the ASSR and the ABR (Rance et al., 2006; Van Maanen & Stapells 2010). Further comparison studies between the ASSR and interleaved ABR in a wider variety of populations (infants, those with hearing loss) are necessary to help determine if this sensitivity difference is supported.

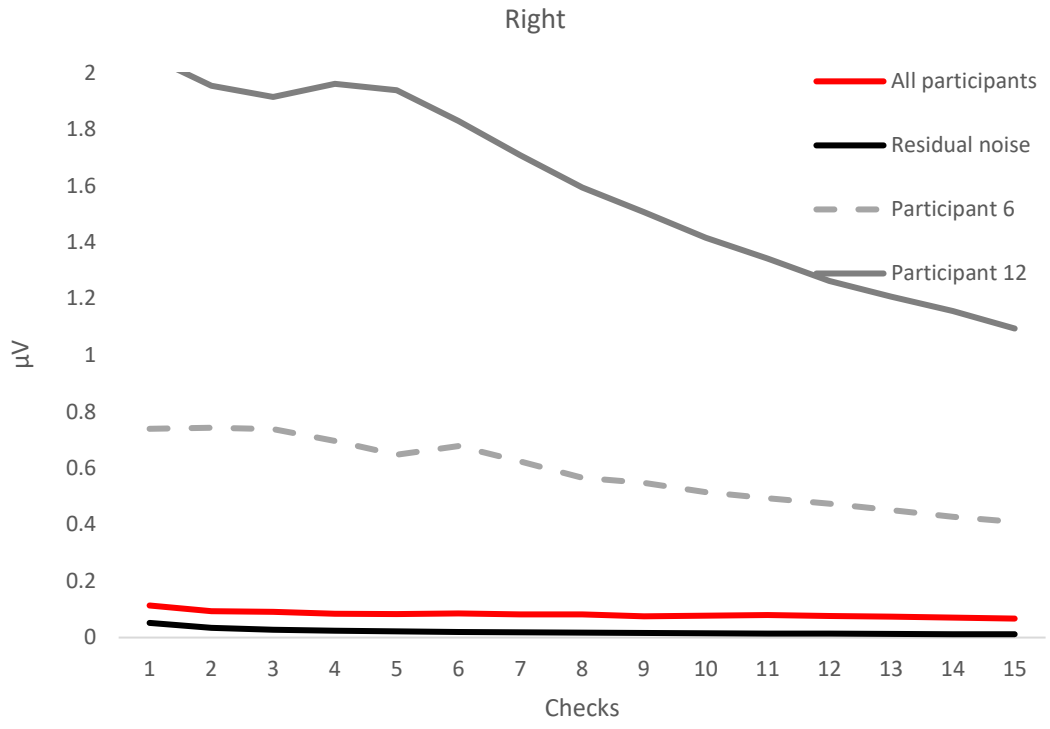
5.3 Other Findings of Interest

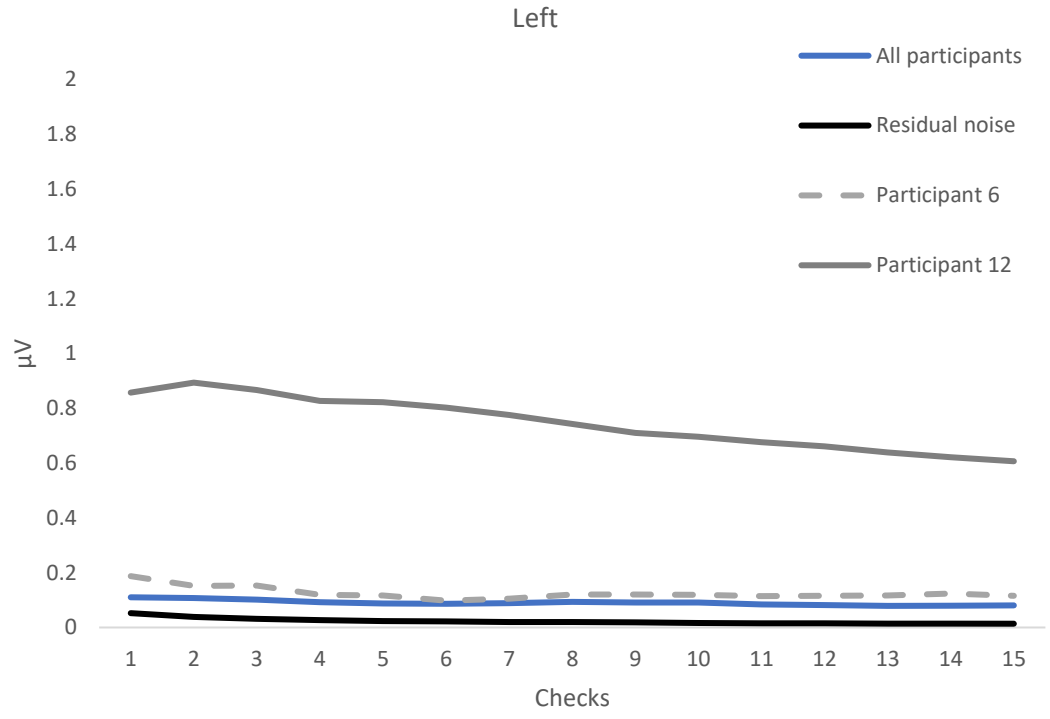
5.3.1 Anomalous ASSR Findings

Amplitude of the ASSR responses were largely as expected, however there were spurious results from participants 6 and 12. Both participants showed responses at amplitude levels that were higher than expected for a true response. Participant 12 showed responses well above the expected level in both ears, and participant 6 in the left ear. Figure 5.1 shows the summed left and right responses for these two participants across the 15 checks/five minutes, compared to the average response of all participants and the average residual noise. The typical pattern seen is that of a small drop in amplitude of the F0 after the first couple of checks, as the averaging process removes any noise that was at the F0 and leaves only the true signal. Whilst participant 6 and 12 follow this pattern, their responses are well above the amplitude expected, even at the end of the averaging.

Figure 5.1

ASSR Responses Showing Outliers





One possibility for such high amplitudes is the data reflect stimulus artifact produced by the insert earphones (Campbell et al., 2012). When the electrical driving voltage is delivered to the transducer, an electromagnetic field is generated around the transducer. The pattern of this field will reflect the stimulus, so for example it would repeat at 93 or 87 Hz. Although the amplitude of the field drops away expoentially with distance (inverse sequare law), in some cases the field induces a current in the recording electrode wires, for instance if they become too close to the transducer. As the ASSR is assessed in the frequency domain, there is no corresponding possibility to note artefactual responses like in the ABR, when waveform morphology is inspected. These were simply considered 'present' responses by the q-sample testing. In this study, it was only when reconstructing the responses offline and tracking their amplitude that the high amplitude responses become obvious through visual interpretation. However, most ASSR software in clinical use does not utilise such visual interpretation, instead relying solely on statistical analysis to determine response presence or absence. Whilst this is largely seen as a positive aspect of the ASSR, in that it prevents bias and human error from colouring an audiologist's conclusions, this observation also highlights the potential for misleading outcomes inherent in statistical measures too. Whilst statistical measures should remain the first port of call for response detection, utilizing the ASSR amplitude plot as a secondary check could be one means to allow for such 'responses' to be identified by the tester, and we suggest its use should be routine during all ASSR assessments.

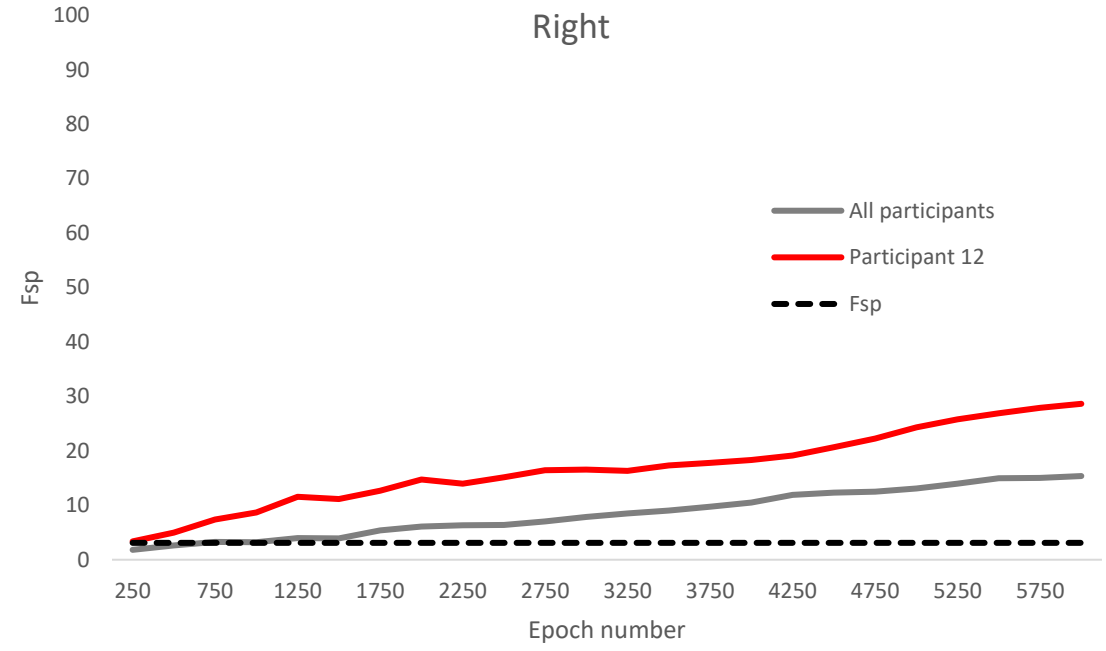
5.3.2 Anomalous interleaved ABR Findings

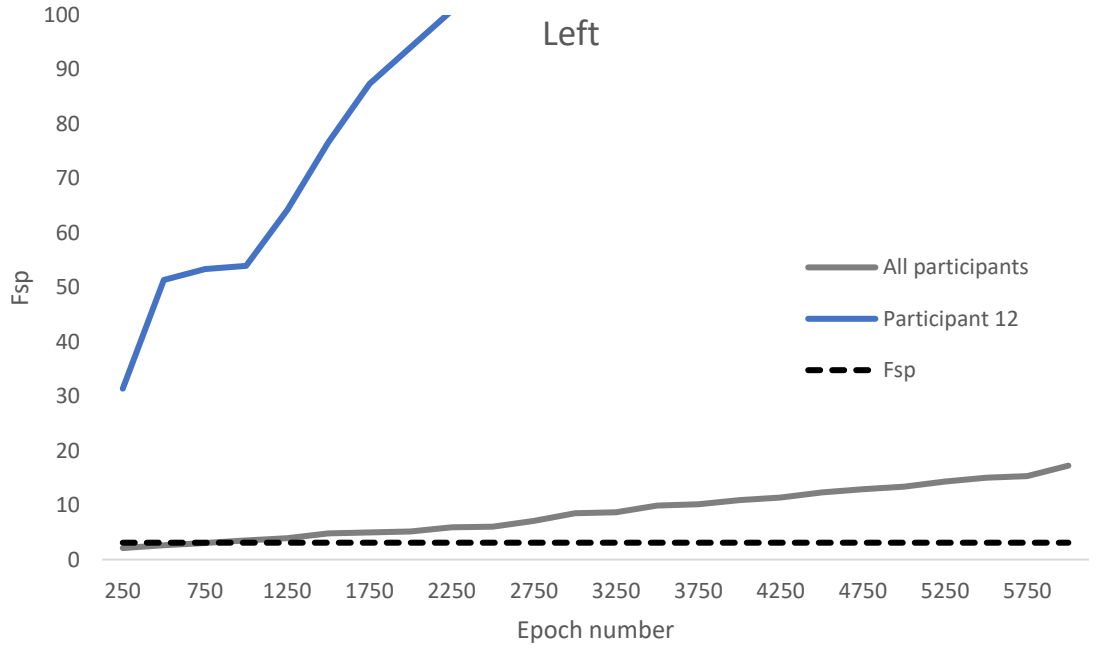
These anomalous findings for participants 6 and 12 prompted a check of their interleaved ABR data. If stimulus artifact was present for ASSR findings, it was likely to be present for the ABR results as well, given all stimuli were delivered in one session (in a counterbalanced order). In the ABR, stimulus artifact produces a visual artefact on the trace that looks like the chirp (or other) stimulus, if waveform morphology is being examined. If the artefact strays into the Fsp detection range then an inflated value

will occur (Campbell et al., 2012). As we determined the ABR responses in this study using the objective methods of Fsp and an automated peak to peak detection algorithm, individiual waveforms were not analysed (only the grand averages). Inflated Fsp values would allow for an ABR response to be detected very early on in the recording as the Fsp value would likely be satisfied within the first few checks. Participant 6 had detection times and Fsp values within the normal range. However, participant 12 had a detection time of 18.75 seconds for each stimulus level (i.e., the quickest time available, with response being determined as present by the very first check). Figure 5.6 shows the summed left and right responses for participant 12 across all 6000 epochs, compared to the average response of all participants and the Fmp criterion value of 3.1. The above examples show that errors can occur when using these objective methods only, without other checks in place. In a clinical scenario, most software allows for the Fsp/Fmp value to be viewed by the audiologist, and an extremely high value such as this may alert them to the presence of stimulus artifact during the recording. This option that was not available to us when using the BioSemi, a limitation of the study. We suggest the use of objective detection as a first measure, followed by waveform analysis and identification of wave V following the end of the recording run to determine the validity of the response as suggested by Sininger et al., (2018).

Figure 5.2

Interleaved ABR Fsp Values Showing Outliers





5.3.3 Artifact Rejection

As mentioned in Methods Section 3.6.2, this study did not utilise artifact rejection during response recording, instead relying on Bayesian weighting to prevent any unwanted noise from impacting on the averaged response (Elberling & Wahlgreen, 1985). ASSR responses vary between participants, however they are generally smaller than other AEP's, ranging from 30μV-100μV depending on the stimulus, participant state and the algorithms used to detect a response. Sininger et al. (2018) used an artifact rejection level of 40nV in their comparison study. Earlier studies focusing on ASSR response detection and the British Society of Audiology Practise Guidelines suggest a more conservate artifact rejection level of 20μV. Getting the balance right for the artifact rejection level is difficult – too low and true responses can be averaged out, too high and those with destructively high noise may still be included (Don & Elberling, 1994). This approach means only those responses that exceeded the clipping level of the BioSemi (+/-262mV) were rejected. The ASSR epochs were 10 seconds long, compared to the 25ms of the interleaved ABR epochs. Longer epochs allow for better spectral averaging (Rance, 2008); however, the likelihood of the epoch being disrupted by noise and therefore downweighed during averaging is far higher, purely due to the fact the ASSR epoch is 400 times longer than the interleaved ABR epoch. This may explain some of the spurious results at the ASSR 40dB nHL condition, with noisier epochs being down weighted more often, affecting the summed signal amplitude seen.

5.4 Test Time of a Dynamic Protocol vs Fixed Time

Due to equipment constraints, the present study followed a fixed protocol which always involved three presentation levels of the stimuli for both the ASSR and interleaved ABR. In a clinical scenario concerned with threshold seeking, audiologists can dynamically follow a decision-making algorithm. Test time may then change, due to decisions made by the tester during the testing. For

example, when SNR ratio is unfavourable or response amplitude is spurious, the audiologist could stop the testing, decrease the artifact rejection level, or reposition the headphones. Whilst this may help to create better quality waveforms, the stopping and starting of each of these measures will no doubt increase test time compared to the fixed protocol used in this study.

5.5 Next Steps

Further research for the interleaved ABR could look at the use of LS NB CE-chirps to determine if the speed advantages and waveform morphology are maintained with frequency specific thresholds. Additionally, an intensity series could be performed on participants with sensorineural hearing loss, to determine if the interleaved ABR produces expected morphology in this population. Lien (2022) did not find a difference in morphology between normally hearing and hearing loss groups, however the stimulus level used was 70dB nHL, well above threshold for both groups. Further data could be gathered in infants to determine normative latency and morphology of an interleaved paradigm. Whilst it is not expected there would be a difference between the interleaved and conventional ABR – as this was not shown in adults - infants are the population in question for the benefits of this data. Extending data gathering to infants in a further research project may help inform whether the interleaved ABR could reduce test time for newborn hearing screening programmes.

This study utilised ‘bootstrapping’ to determine the critical value for the ASSR. In future, the use a ‘table look up’ based off the work of Cebulla and Stürzebecher (2015); Stürzebecher and Cebulla (2013) could be implemented, as it has been in clinical ASSR software already. This would require creating of no sound trial data from participants prior to the electrophysiological testing.

As mentioned above, further studies of test time and sensitivity between the ASSR and interleaved ABR could be undertaken to determine which presents the best option for potentially replacing the ABR in UNHS protocols, especially comparing electrophysiological threshold to behavioural thresholds.

6 Conclusion

The interleaved ABR and ASSR both offer speed advantages to the current ABR protocol, and there is no speed advantage to utilising one over the other. Use of either of these measures could lead to significant time savings for the diagnostic portion of the newborn hearing screening protocol in Aotearoa New Zealand, but only if their sensitivity can match that of the ABR.

Sensitivity estimation showed the ASSR can resolve thresholds at lower levels than the interleaved ABR. However, the evidence for the reliability of the ASSR threshold estimation is still undergoing research, and there is not yet a body of evidence strong enough to conclude its sensitivity when compared to the traditional ABR. As commercial ASSR systems are not yet in widespread use, there is significant variability in the testing systems available, in both their verification and statistical detection methods. Interleaved ABR research is still in its infancy, but, similar to the ASSR, shows promise for use in newborn hearing screening due to time savings.

Further research on the ASSR and interleaved ABR to determine threshold sensitivity and test time when undertaking a dynamic threshold seeking protocol would be an excellent next step in determining which measure may present the best option in terms of diagnostic accuracy vs speed for newborn hearing screening protocols in Aotearoa and worldwide.

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Appendix A

Study Advertisement

UNIVERSITY OF CANTERBURY
Te Whare Wānanga o Waitaha
CHRISTCHURCH NEW ZEALAND

Would you like a free hearing test?

Are you aged over 18?

Participants must have no current ear infections, no issues with ear wax or history of neurological and balance issues.

We are conducting a study evaluating the speed and accuracy of two electrophysiological tests that measure hearing levels.

This research will help inform newborn hearing screening protocols and hopefully make diagnosis of infant hearing loss faster.

If you are interested in participating in the research, please contact any of the following:

Penelope Bundy (Audiology student)
Email: pbu44@uclive.ac.nz

Dr. Michael Maslin (Supervisor)
Email: mike.maslin@canterbury.ac.nz

Dr. Greg O'Beirne (Co-supervisor)
Email: Gregory.obeirne@canterbury.ac.nz

APPROVED BY THE UNIVERSITY OF CANTERBURY HUMAN RESEARCH ETHICS COMMITTEE ON 20/05/2022.

Appendix B

Participant Information Sheet

Department: *School of Psychology, Speech and Hearing*
Phone: *03 369 4333*
Email: *pbu44@uclive.ac.nz*
Date: *08/04/2022*
HREC Ref: *HREC 2022/24/LR*

An evaluation of speed and accuracy of audiometry via the Auditory Steady State Response and Auditory Brainstem Response.

Information Sheet for participants

Principle Supervisor: Dr. Mike Maslin
Co-supervisor: Dr. Greg O'Beirne
Master of Audiology Research Student: Penelope Bundy

Kia ora,

You are invited to participate in a research study on the comparison of the Auditory Steady State Response (ASSR) and the Auditory Brainstem Response (ABR) in terms of determining hearing thresholds accurately and quickly. This study is being carried out by Master of Audiology student Penelope Bundy, under the supervision of Dr. Mike Maslin from the University of Canterbury | Te Whare Wānanga o Waitaha (UC).

Background

As hearing loss is considered a major public health issue, newborn hearing screening programmes are in place in many countries worldwide, including New Zealand since 2010. The earlier hearing loss is detected, the earlier interventions can begin, giving the child the best chance at developing language and comprehension skills, either spoken or signed.

If an infant does not show a clear response during a hearing screen performed shortly after birth, they are referred to an Audiologist for a full hearing assessment using an electrophysiological technique called the Auditory Brainstem Response (ABR). Electrophysiological techniques automatically measure

responses to sounds, so are used in populations that are unable to give behavioural responses (e.g. pressing a button when they hear a beep). During the ABR, sound is played to the patients' ears, and the corresponding brain wave activity is measured using sensors placed on the skin. It is a non-invasive and painless process; however, it requires the patient to be very still and quiet (ideally asleep) as the brainwaves are very small, and can easily be swamped by the sound of the patient's movements. The ABR is considered to be very accurate when measured correctly on a sleeping or very still patient. However, it is slow to perform as the audiologist must perform multiple measurements of each ear, at varying sound pitches and loudness levels to determine thresholds accurately. This can take several hours, and is generally longer than an infant sleep cycle. This means that often, the infant and their family have to attend multiple appointments before the audiologist can give accurate information about the infants hearing status.

There is however, other electrophysiological techniques that can be performed to determine hearing thresholds that are faster than the ABR. One is the Auditory Steady State Response (ASSR) and it measures a different area of brain activity from the ABR. The measurement of the ASSR is quicker, as multiple sounds can be tested at once, making significant time savings. Additionally, work at UC has led to the development of an interleaved ABR, which tests both ears at once without apparent loss of accuracy. To date there has been no comparison of the interleaved ABR or ASSR to determine the speed and accuracy of both. They are promising techniques for use in newborn hearing screening that could vastly speed up diagnosis of hearing loss.

Why have you received this invitation?

You are invited to participate in this research because you have responded to a request for participants. Your participation is voluntary (your choice). If you decide not to participate, there are no consequences. Your decision will not affect your relationship with me, the University of Canterbury or any member of the research team.

What is the purpose of this research?

In order to determine if we should recommend either the interleaved ABR and/or ASSR as the preferred technique, we need to measure them on a population that can also give behavioural information about their hearing thresholds, otherwise we have no point of comparison to determine their accuracy. Therefore, this research needs to be conducted on adults first before it can be tested on infants.

The information from this study will help to inform newborn hearing screening protocols in New Zealand and worldwide.

What is involved in participating?

Preliminary testing to determine eligibility

If you choose to take part in this research, you will be asked to attend a single session at the University of Canterbury. To confirm your eligibility for the study we will first perform a few tests:

1. Some questions about your ear health.
2. Otoscopy. This involves a visual check of your ear drum and ear canal with an ear light and enables identification of any obvious signs of abnormality such as blockage or an ear infection. This takes about a minute.
3. Middle ear function check. This is a check to see how the ear drum is moving and whether there is any infection or fluid present in the middle ear space. This takes about a minute.

4. Puretone audiometry testing to determine your hearing thresholds. This requires sitting in a soundproof booth wearing headphones, and pressing a button when you hear a sound. This takes about fifteen minutes.

Measurement of the ABR and the ASSR
During the ABR and ASSR testing you will be asked to sit in a reclining chair and relax. Skin surface sensors will be placed on your earlobes and forehead. These sensors record electrical activity from your brain in response to sound, which will be played to you via headphones. The activity is present naturally when we hear sounds. When applying the sensors, I will first gently rub your skin underneath the sensor with an exfoliating paste to ensure a good contact. The sensors are then attached onto the skin with some clinical tape. Sounds of varying pitch and level will be played to you in a random order, but never loud enough to cause discomfort or damage to your hearing. It is expected this process will take up to 2.5 hours.

Are there any potential benefits from taking part in this research?
We do not expect any direct benefits to you personally from participating in this interview. However, the information gathered will potentially benefit newborn hearing screening protocols. And, you will get a free hearing test!

Are there any potential risks involved in this research?
We are not aware of any risks to participants in the research. All of the procedures are routine clinical tests of hearing (or similar to those used routinely) and are non-invasive. I estimate that your participation will take around 2.5 hours total, ideally performed in one session.

What if you change your mind during or after the study?
You are free to withdraw at any time. To do this, please let me know either during the study or after you have finished. I will remove any information you have provided up to that point from the data set if it is still possible.

What will happen to the information you provide?
All data will be anonymous. We will not be able to identify you or link your identity with any information you provide once the session is completed. I will store all study data in password-protected files on the University of Canterbury computer network or in lockable cabinets in lockable offices. Your consent form or any piece of information that identifies you will be kept separate from the raw data. Access to the consent forms will be restricted to the project supervisor and research student. All data will be destroyed five years after publication of study findings.

Will the results of the study be published?
The results of this research will be published in a Master's thesis. This thesis will be available to the general public through the UC library. Results may be published in peer-reviewed, academic journals. Results will also be presented during conferences or seminars to wider professional and academic communities, and may be submitted for peer reviewed publication. You will not be identifiable in any publication. A summary of results will be sent to all participants who request a copy of these.

Who can you contact if you have any questions or concerns?
If you have any questions about the research, please contact: *Penelope Bundy: pbu44@uclive.ac.nz*

If you have any concerns about this project, please contact*: Mike Maslin mike.maslin@canterbury.ac.nz*

This study has been reviewed and approved by the University of Canterbury Human Research Ethics Committee (HREC). If you have concerns or complaints about this research, please contact the Chair of the HREC at human-ethics@canterbury.ac.nz).

What happens next?
Please review the consent form. If you would like to participate, please sign and return the consent form to pbu44@uclive.ac.nz

Appendix C

Participant Consent Form

UNIVERSITY OF CANTERBURY
Te Whare Wānanga o Waitaha
CHRISTCHURCH NEW ZEALAND

Department: School of Psychology, Speech and Hearing
Phone: 03 369 4333
Email: pbu44@uclive.ac.nz
Date: 25/03/2021
HREC Ref: HREC 2022/24/LR

An evaluation of speed and accuracy of audiometry via the Auditory Steady State Response and Auditory Brainstem Response

Consent Form for Participants

- ☐ I have been given a full explanation of this project and have had the opportunity to ask questions.
- ☐ I understand what is required of me if I agree to take part in the research.
- ☐ I understand that participation is voluntary and I may withdraw at any time without consequences. Withdrawal of participation will also include the withdrawal of any information I have provided should this remain possible.
- ☐ I understand that any information or opinions I provide will be kept confidential to the research student and the project supervisors, 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.
- ☐ I understand that these results may be published in an academic journal.
- ☐ I understand that all data collected for the study will be kept in locked and secure facilities and/or in password protected electronic form. I understand the data will be destroyed after five years.
- ☐ I understand the risks associated with taking part and how they will be managed.
- ☐ I understand that I can contact the researcher Penelope Bundy (email: pbu44@uclive.ac.nz) or supervisor Dr. Mike Maslin (email: mike.maslin@canterbury.ac.nz) for further information. If I have any complaints, I can contact the Chair of the University of Canterbury Human Research Ethics Committee, Private Bag 4800, Christchurch, (email: human-ethics@canterbury.ac.nz).
- ☐ I would like a summary of the results of the project.
- ☐ By signing below, I agree to participate in this research project:
  Name:_____ Signed:_____ Date:_____

Email address (for report of findings, if applicable):_____
Please email the signed copy of this form to Penelope Bundy on pbu44@uclive.ac.nz

Appendix D

Human Research Ethics Committee Approval

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

Ref: HREC 2022/24/LR

20 May 2022

Penelope Bundy
School of Psychology, Speech and Hearing
UNIVERSITY OF CANTERBURY

Dear Penelope

Thank you for submitting your low-risk application to the Human Research Ethics Committee for the research proposal titled “An Evaluation of Speed and Accuracy of Audiometry via the Auditory Steady State Response and Auditory Brainstem Response”.

I am pleased to advise that this application has been reviewed and approved, **subject to the following:**

In the Advertisement, please amend “Human Participants Ethics Committee” to “Human Research Ethics Committee”.

With best wishes for your project.

Yours sincerely

Dr Dean Sutherland
Chair, Human Research Ethics Committee

Appendix E

Calibration of the Chirp Stimuli

Calibration report for short-duration signals delivered by insert earphone, for Cortical Auditory Evoked Potentials (CAEPs) and Auditory Brainstem Responses (ABRs)

MinChul Park and Michael Maslin
21 February 2022

Measurement items

- Brüel & Kjær 2250 sound level meter (SLM). 711 on top socket and rear output.
- GRAS 711 occluded ear simulator: Microphone s/n 0083336 and coupler s/n 0119816.
- 1 kHz 94 dB acoustic calibrator s/n 3025572 (calibration due date 04 Feb 2023).
- General purpose oscilloscope
- Interacoustics AC40 clinical audiometer (s/n 148943) calibrated according to ISO389-2, with ER5-A insert phones (as a cross-check).

Device setup & stimuli to be measured

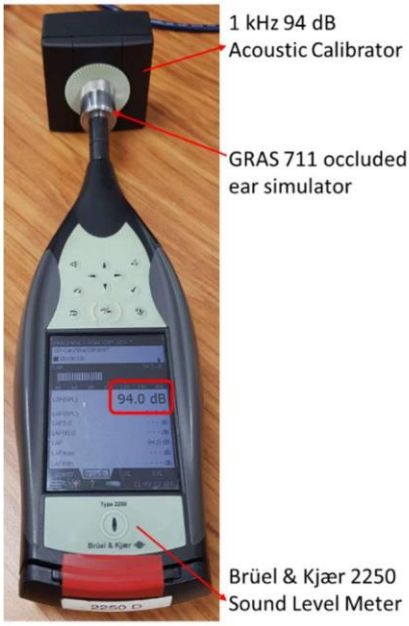
- Neurobehavioural Systems Presentation running on Windows 10 PC (HP EliteDesk 800 G1 TWR with 8192 MB RAM and 3.16 GHz Intel i7 processor) and delivering output via RealTek High-Definition Audio onboard soundcard.
- Left ER3-A insert phone with 10 Ohm impedance (s/n 59803) coupled with ER3-14 sponge.
    - Continuous 1 and 4 kHz pure tones
    - Continuous white noise
    - 1 kHz tonebursts for CAEPs (80 ms, including 5 ms onset/offset) o 4 kHz tonebursts for ABRs (1.25 ms, 2-1-2 cycle)
    - Don chirp for ABRs (0.1 – 8 kHz)

1. Checking the calibration of measurement system

A 94 dB SPL signal from the acoustic calibrator was delivered to the GRAS 711 coupler. The reading on the Brüel & Kjær 2250 SLM was then confirmed as 94 dB SPL as per Figure 1.

Figure 1.

Checking the calibration of the Brüel & Kjær 2250 SLM. The acoustic calibrator presented a 1 kHz 94 dB SPL pure tone signal through the GRAS 711 coupler and the SLM displayed this as 94 dB SPL.



2. Cross-check of stimulus measurement system using AC40 Audiometer with continuous 1 kHz pure tones

A second cross-check was performed using a series of 1 kHz pure tones delivered at a range of levels from a calibrated AC40 pure tone audiometer. The measured readings were then compared to the derived readings.

All measurements were performed in a sound-treated booth. The AC40 audiometer was used to deliver 1 kHz pure tones to the 711 coupler. Sound Pressure Levels (SPLs) were recorded and noted down from the display on the SLM screen. The measured values were compared to known values in a 711 coupler (artificial ear) as described in ISO 389.2. The audiometer dial setting + RETSPL (Figure 2, showing RETSPLs from ISO 389.2) allows derivation of the value in such a cavity. Measured and derived values are displayed in Table 1.

Table 1

*Measured and derived sound press level values. *dB dial + RETSPL, but irrespective of microphone sensitivity. The measured output is consistently about 2 dB below the derived output. However, the 94 dB SPL calibrator check was correct.*

dB dial	dB SPL output	Derived SPL*
90	93	95.5
80	82.7	85.5
70	72.5	75.5

60	62.5	65.5
50	53.1	55.5

Figure 2

Reference Equivalent Threshold Sound Pressure Levels from ISO 389.2

Table 1 — Reference equivalent threshold sound pressure levels in an acoustic coupler conforming to IEC 126 and in an occluded-ear simulator conforming to IEC 711

Frequency Hz	RETSPL (ref. 20 µPa)[a] dB	
	Acoustic coupler (IEC 126)	Occluded-ear simulator (IEC 711)
125	26,0	28,0
160[b]	22,0	24,5
200[b]	18,0	21,5
250	14,0	17,5
315	12,0	15,5
400[b]	9,0	13,0
500	5,5	9,5
630	4,0	7,5
750	2,0	6,0
800[b]	1,5	5,5
1 000	0,0	5,5
1 250	2,0	8,5
1 500	2,0	9,5
1 600[b]	2,0	9,5
2 000	3,0	11,5
2 500	5,0	13,5
3 000	3,5	13,0
3 150[b]	4,0	13,0
4 000	5,5	15,0
5 000	5,0	18,5
6 000	2,0	16,0
6 300	2,0	16,0
8 000	0,0	15,5

[a] Values are rounded to nearest half-decibel.
[b] Values for these frequencies are derived by interpolation.

3. Output report

SPLs and oscilloscope readings for the following stimuli were measured for left transducer only:

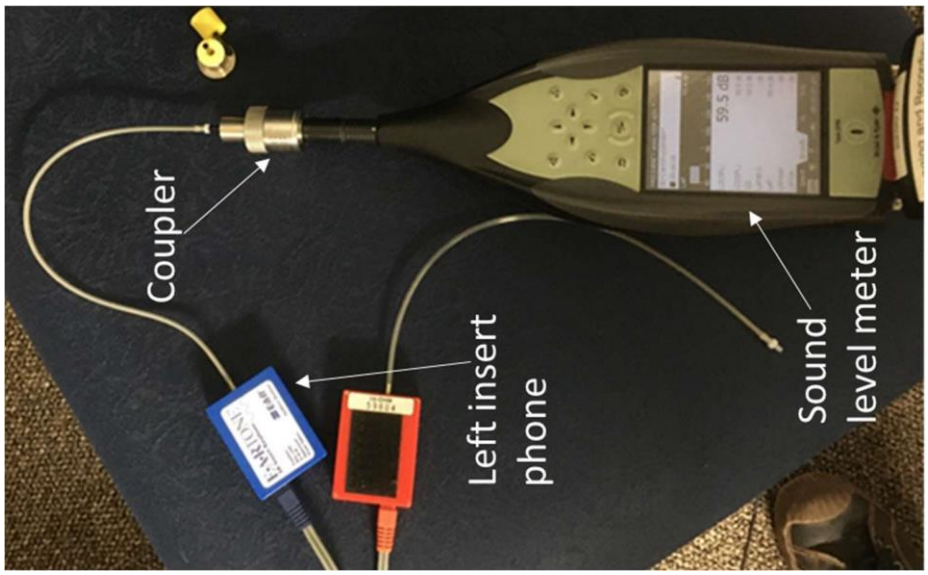
- 1 kHz pure tones
- White noise
- 4 kHz Tonebursts for ABRs (2-1-2 cycle)
- Don chirp for ABRs (0.1-8 kHz)
- 1 kHz tonebursts for cortical EPs (80ms, including 5 ms onset/offset)

When measuring the stimuli from Presentation, the insert earphones were connected to patch panel port 10 (left transducer) and port 9 (right transducer). The external side of the patch panel was then

connected to the rear socket of the PC sound card. This setup is to be used in practice. The left insert phone was connected to the 711 coupler as per Figure 3 and Figure 5.

Figure 3

Left insert ear phone set up with the 711 coupler / sound level meter



3.1. Pure tones

A series of continuous 1 kHz reference pure tones were generated by Presentation and delivered to the coupler. Results are displayed Table 2, for data spanning the top half of the attenuator range (0 to 0.5). An input/output function (I/O function) based on the results is displayed in Figure 4. The attenuator setting in Presentation software was used to control the output level, with the 'global' audio settings on the Window's PC set to "100". Note, Presentation attenuator works between 0 and 1 (0 = as dB/100). To adjust sound levels, it is practical to use up to 3 decimal places. The first, second and the third decimal points of the attenuator value adjusts the sound level in steps of 10, 1 and 0.5 dB respectively.

Table 2

Output check for continuous 1 kHz pure tones

Attenuator Setting	dB SPL output (Left)	dB SPL (A) output (Left)
0	100.5	100.5
0.1	90.2	90.2
0.2	80	80
0.3	69.6	69.7
0.4	59.5	59.5
0.5	49.9	49.5

Figure 4

I/O function based on Table 2 which shows linearity from 0 to 0.5 with x-intercept approximately at 0.988 (i.e., when attenuator value = 0.990, dB SPL ≈ 0)

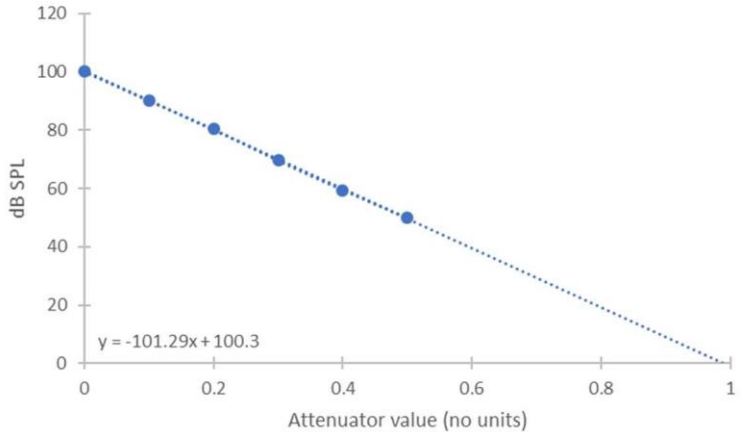


Figure 5

Input cable carrying driving voltage to the insert transducer, which then converts this to sound pressure level. The 711 coupler + sound level meter converts this sound pressure level to output voltage

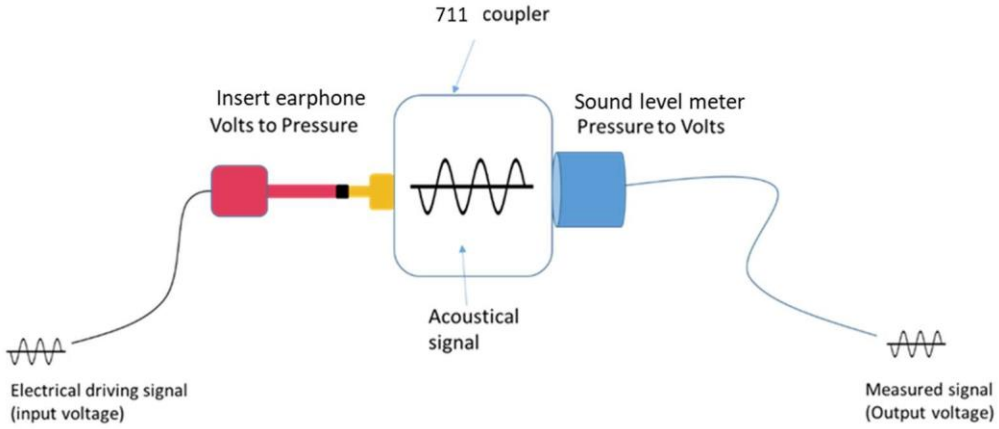
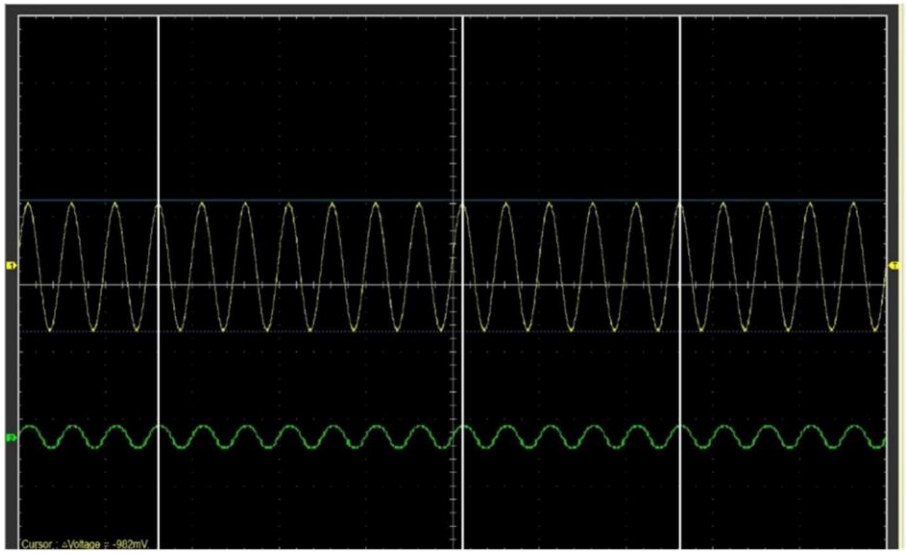


Figure 6 shows the input voltage to the insert transducer and the output voltage from the sound level meter microphone, for a 1 kHz pure tone. This is useful to gauge the faithfulness of the transduction.

Figure 6

1 kHz calibration tone signal at 100 dB SPL. Input (green) voltage and output (yellow) voltage according to the schematic drawn in Figure 5. Time base at 2 ms. The white lines were drawn to show consistency in phase. The sound level meter was set to +20 dB socket gain to produce a clean waveform on the scope



3.2. White noise levels

Output levels for white noise (continuous) stimuli were measured in the same way as described above. SPLs were recorded using the SLM and viewed via the oscilloscope. These data are displayed in Table 3, and an i/o function is displayed in Figure 7. As with Figure 6, Figure 8 shows the relationship between the input voltage to the insert transducer and the output voltage from the sound level meter microphone for the continuous white noise stimulus – useful in observing the faithfulness of the transduction.

Table 3

Continuous white noise levels at varying attenuator levels recorded in dB SPL (Z) and (A). The resulting i/o function is displayed in Figure 7. Note similarity between dB SPL and dB SPL (A) values. This may be because of the frequency response of the insert phones, removing the high/low frequency ends of the noise thus making SPL measures similar to A

Attenuator setting	dB SPL (Z)	dB SPL (A)
0	96.2	96.4
0.1	86.2	86.2
0.2	76.1	76.6
0.3	66.1	66.5
0.4	56.1	56.2
0.5	46.5	46.2

Note. Similarity between dB SPL and dB SPL (A) values. This may be because of the frequency response of the insert phones, removing the high/low frequency ends of the noise thus making SPL measures similar to A

Figure 7

dB SPL (Z) values for continuous white noise stimuli at different attenuator levels showing linearity with x-intercept approximately at 0.964 (i.e. when attenuator value = 0.964, dB SPL (Z) ≈ 0). dB SPL (A) values are not shown as the two are very similar

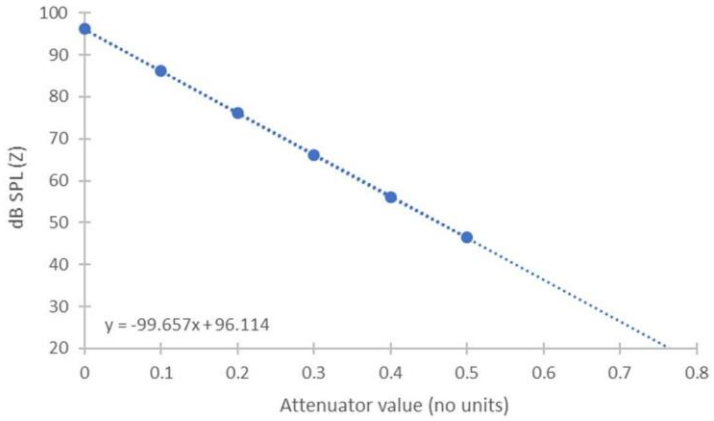
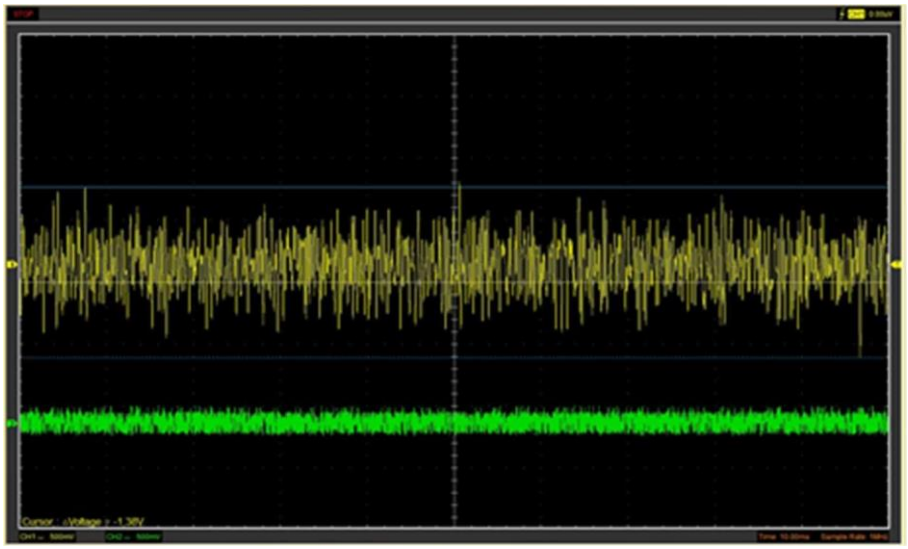


Figure 8

Continuous white noise signal at 96.4 dB SPL (A) showing input voltage as green and output voltage as yellow. Time base is at 10 ms.



3.3. 1 kHz tone burst (80ms)

Output levels for 80ms tone burst stimuli used for CAEPs were measured in the same way as described above. That is, SPLs were recorded using the SLM and viewed via the oscilloscope. The SLM was set to impulse mode (35 ms integration period) to enable acoustic as well as peak-to-peak-equivalent-SPL

(ppeSPL) measurements of the tone bursts. These data are displayed in Table 4 and an i/o function is displayed in Figure 9. However, the attenuator settings used in the research are based on ppeSPL data.

Table 4

1 kHz tone burst dB SPL values at varying attenuator settings

Attenuator setting	dB SPL (impulse)
0	91.5
0.1	81.2
0.2	70.9
0.3	60.8
0.4	50.9
0.5	41.3

Figure 9

dB SPL values for 80 ms 1 kHz tone bursts at different attenuator levels showing linearity with x-intercept approximately at 0.907 (i.e. when attenuator value = 0.907, dB SPL ≈ 0)

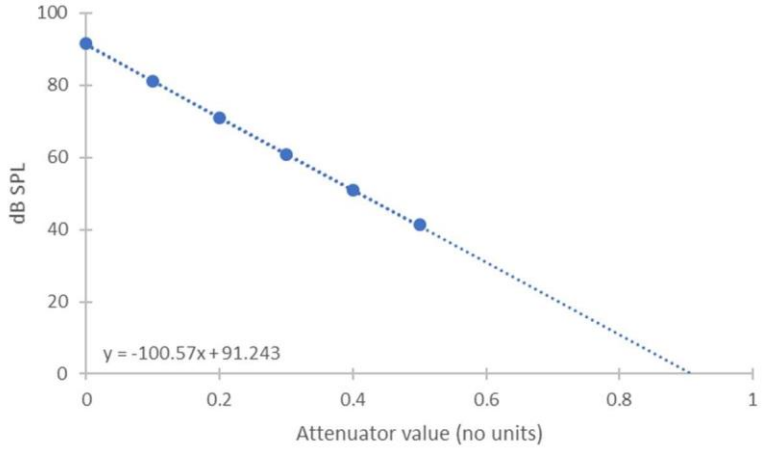


Figure 10

Continuous 1 kHz pure tone at 70 dB SPL with peak to peak voltage at 307 mV with +40 dB socket gain from the SLM. Time base is 5 ms

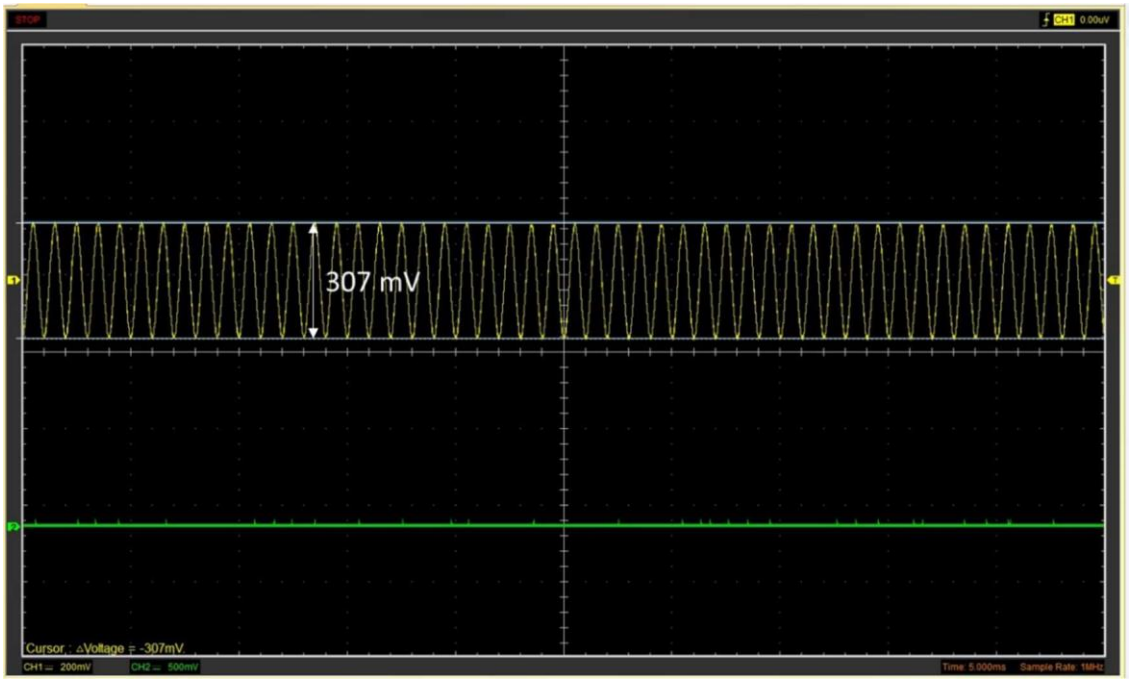
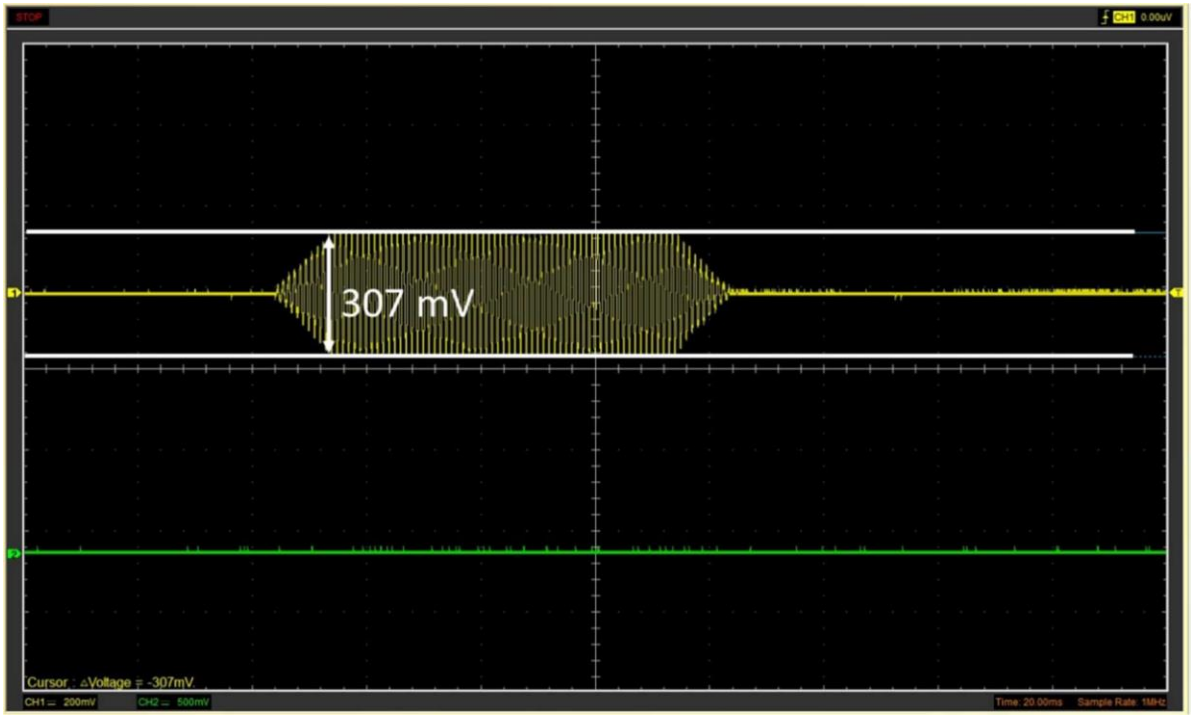


Figure 11

1 kHz 80 ms tone burst calibrated to 70 dB ppeSPL with +40 dB socket gain from the SLM. Peak to peak voltage at 307 mV, time base at 20 ms



To achieve the ppeSPL (70 dB), the reference tone and the tone burst required different attenuator settings. For the reference/continuous tone, the attenuator was set to 0.295. For the 1 kHz tone burst, the attenuator was set to 0.215. That is, to achieve the 70 ppeSPL for the 1 kHz tone burst to match to the continuous 1 kHz pure tone, the attenuator value in Presentation had to be set to 0.295 and 0.215 for the continuous tone and tone burst respectively. The resulting output voltage for each stimulus is displayed in Figure 10 and Figure 11 respectively.

Figure 12

Continuous 1 kHz pure tone at 55 dB SPL with peak to peak voltage at 507 mV with +60 dB socket gain from the SLM. Time base is 10 ms

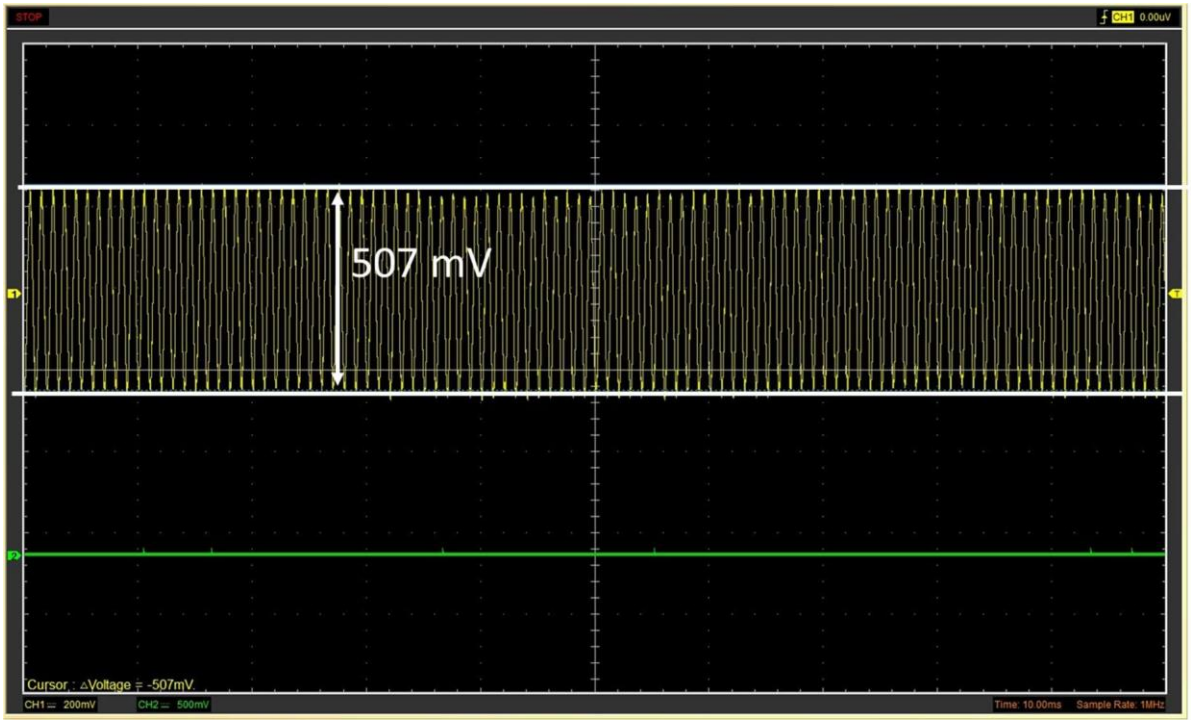
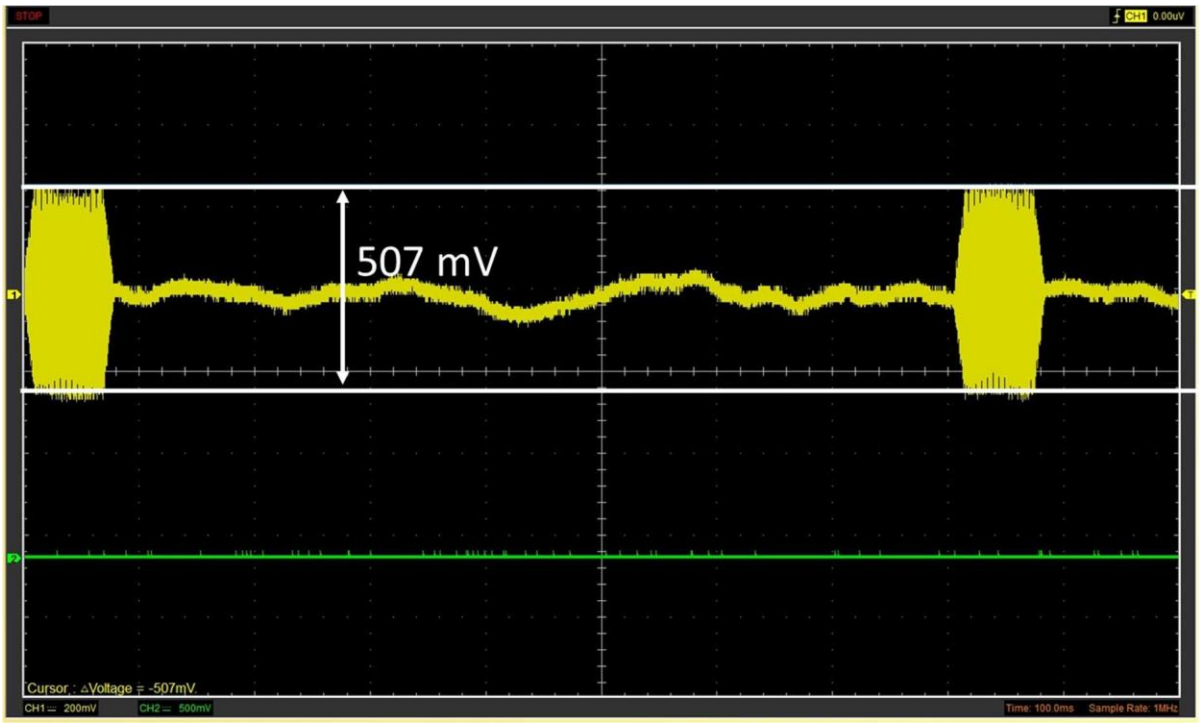


Figure 13

1 kHz 80 ms tone burst calibrated to 55 dB ppeSPL with +60 dB socket gain from the SLM. Peak to peak voltage at 507 mV, time base at 100 ms



Similarly, with the example above, to achieve the 55 dB ppeSPL, the continuous tone and the tone burst required different attenuator settings, 0.45 and 0.37 respectively. That is, to achieve the 55 ppeSPL for the 1 kHz tone burst to match to the continuous 1 kHz pure tone, the attenuator value in Presentation had to be set to 0.45 and 0.37 for the continuous tone and tone burst respectively. The resulting output voltage for each stimulus is displayed in Figure 12 and Figure 13 respectively. Note for the 55 dB SPL levels (high attenuator values) the waveforms are less stable due to noise. The only way these waveforms could be viewed at all was via the socket gain feature of the Brüel & Kjær 2250 SLM.

3.4. 4 kHz tone burst (2-1-2 cycle)

Output levels for 4 kHz tone burst stimuli used for ABRs were measured in the same way as described above (i.e., SPLs were recorded using the SLM and viewed via the oscilloscope). The SLM was only used to measure the 4 kHz reference tone, while the tone bursts were matched using the ppeSPL method.

Due to the inherent difficulties of measuring the short duration stimuli down at 70- and 55-dB SPL, it was decided to match the 2-1-2 tone burst stimuli to a pure tone at 100 dB SPL and extrapolate attenuator values for the required stimulus levels based on the linearity of the attenuator as shown by Figure 4, Figure 7 and Figure 9.

Table 5

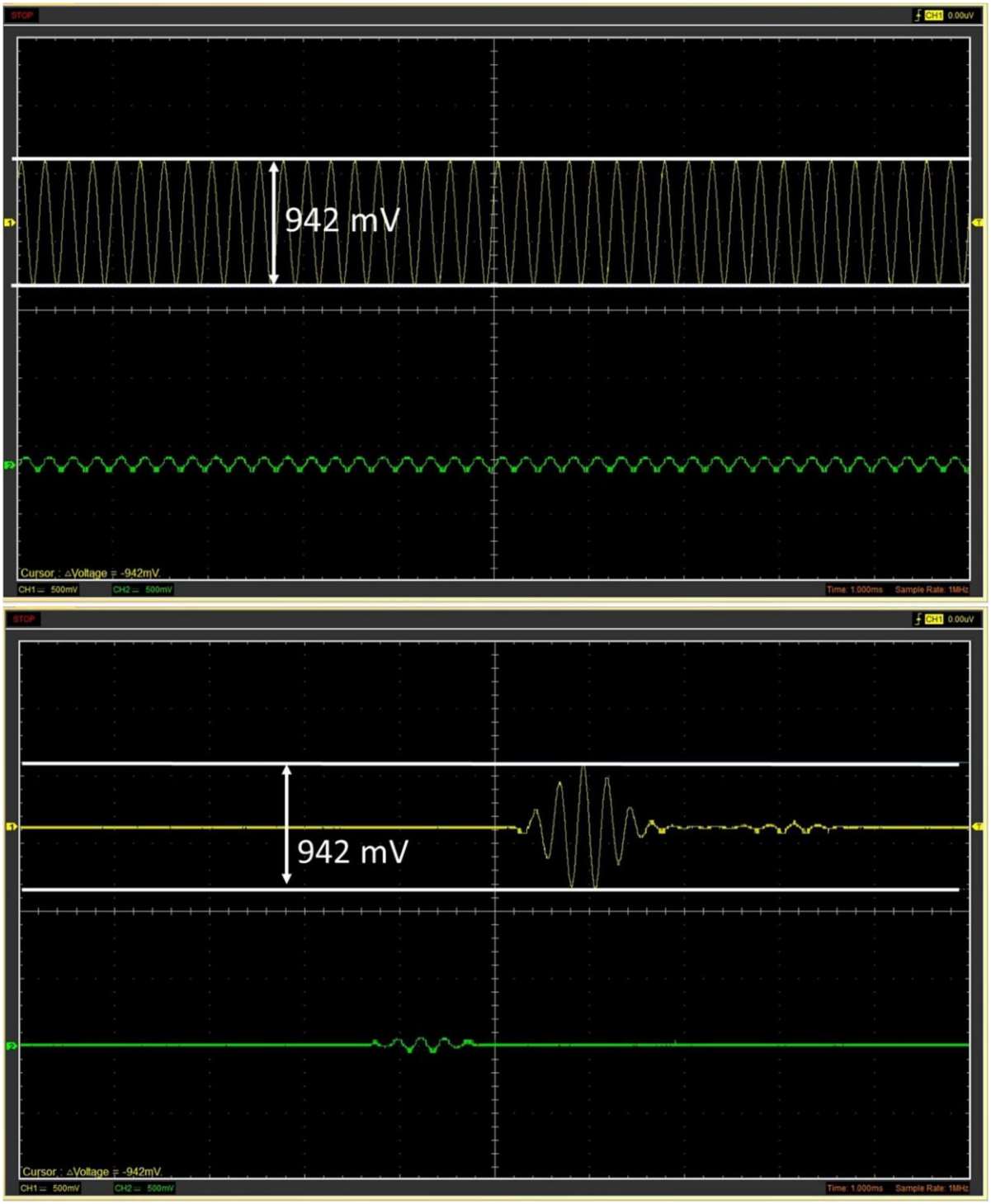
Attenuator values for 4 kHz reference tone and tone bursts (dB SPL)

dB SPL	4 kHz Reference tone	4 kHz Toneburst
dB		
100	0.055	0.045
95	0.105	0.095
90	0.155	0.145
85	0.205	0.195
80	0.255	0.245
75	0.305	0.295
70	0.355	0.345
65	0.405	0.395
60	0.455	0.445
55	0.505	0.495
50	0.555	0.545

For a 100 dB SPL stimulus the reference tone attenuator value was set to 0.055 and the tone burst attenuator value was set to 0.045. The reference and tone burst input/output voltages are shown in Figure 14.

Figure 14

100 dB SPL 4 kHz continuous tone (top) and corresponding 80 ms tone burst (bottom) showing the same peak-to-peak voltage. With the socket gain set to +20 dB, this was 942 mV. Yellow – output voltage and green – input voltage. Time base at 1 ms

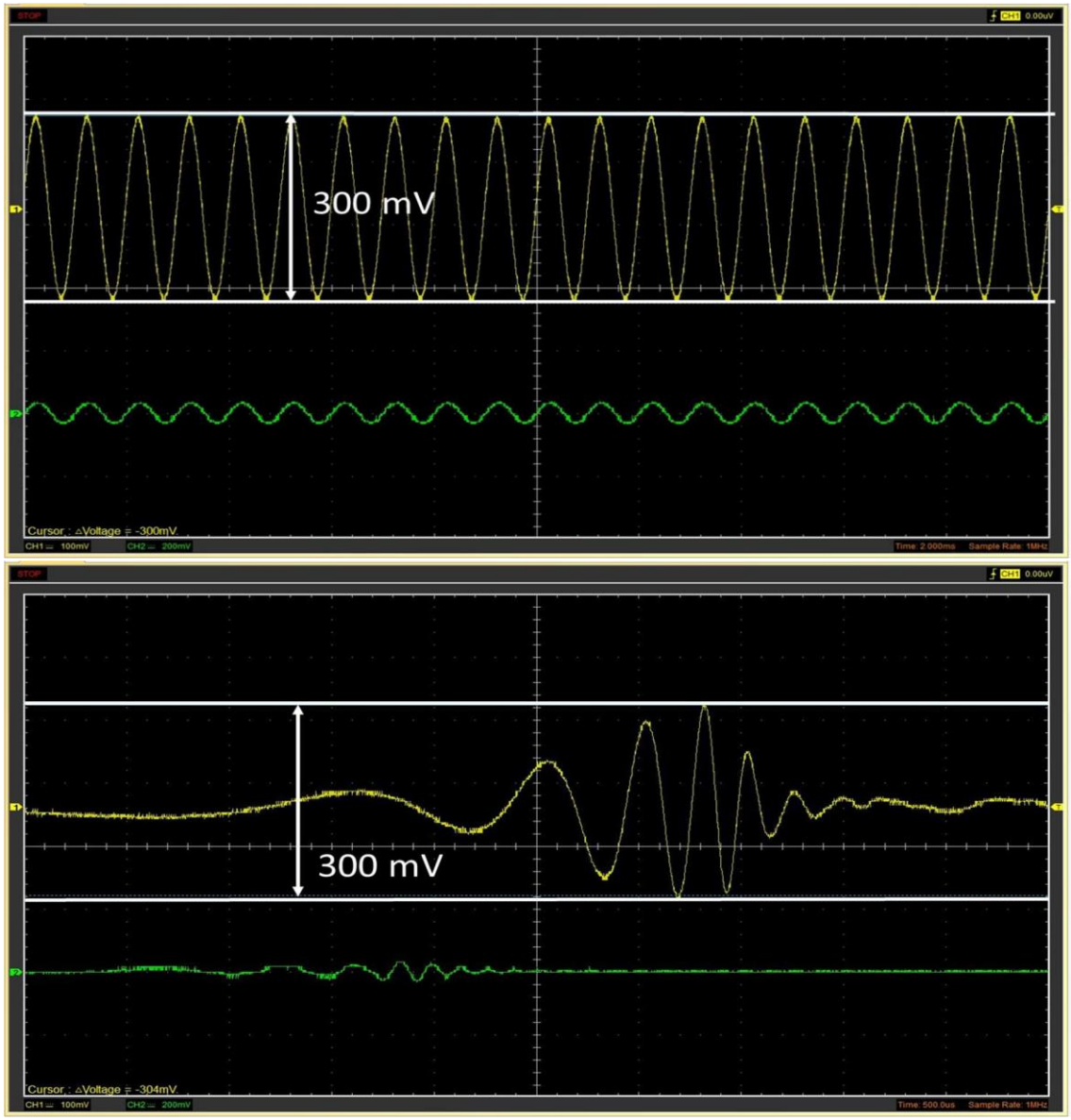


3.5. Don chirp (0.1 – 8 kHz)

Output levels for broadband chirp stimuli used for ABRs were measured in the same way as described above. The SLM was only used to measure the 1 kHz reference tone, while the chirps were matched using the ppeSPL method. Due to the inherent difficulties of measuring the short duration stimuli down at 70- and 55-dB SPL, it was decided to match the chirp stimuli to a 1 kHz pure tone at 90 dB SPL and extrapolate attenuator values for the required stimulus levels based on the linearity of the attenuator as shown by Table 6.

Figure 15

90 dB SPL calibration tone (top – time base 2 ms) and corresponding chirp stimulus (bottom – time base µs) showing the same peak-to-peak voltage. With the socket gain set to +20 dB, this was 300 mV. Yellow – output voltage and green – input voltage



For a 90 dB SPL stimulus the reference tone attenuator value was set to 0.095 and the chirp attenuator value was set to 0.09. The reference and chirp input/output voltages are shown in Figure 15.

Table 6

Attenuator values for 1 kHz reference tone and chirp stimulus (dB SPL)

dB SPL	1 kHz Reference tone	Chirp
90	0.095	0.090
85	0.145	0.140
80	0.195	0.190
75	0.245	0.240
70	0.295	0.290
65	0.345	0.340
60	0.395	0.390
55	0.445	0.440
50	0.495	6.490

4. Attenuator values to be used in research – CAEPs

For CAEP research, 80 ms 1 kHz tone bursts at 45 and 60 dB nHL will be used. RETSPL for 1 kHz tone burst (80 ms) = 5.5 dB. Note that the initial plan was to conduct research with stimuli at 55- and 70dB SPL, hence the levels in the Figures above. After pilot testing, it was decided to revise the stimulus levels to 45 and 60 dB nHL.

Table 7

Attenuator values for 1 kHz tone burst at 45 and 60 dB nHL in varying conditions

Attenuator Values for 45 dB nHL Tone burst		Attenuator Values for 60 dB nHL Tone burst	
In Quiet	0.41	In Quiet	0.26
Noise (dB SPL)		Noise (dB SPL)	
35 [+10 dB SNR]	0.612	50 [+10 dB SNR]	0.463
40 [+5 dB SNR]	0.563	55 [+5 dB SNR]	0.413
45 [0 dB SNR]	0.513	60 [0 dB SNR]	0.363
50 [-5 dB SNR]	0.463	65 [-5 dB SNR]	0.313
55 [-10 dB SNR]	0.413	-10 dB SNR]	

4.1. Attenuator values to be used in research – 4 kHz ABRs

For 4 kHz ABR, 45 and 60 dB nHL will be used and RETSPL for 4 kHz tone burst = 32.5 dB.

Table 8

Attenuator values for 4 kHz tone burst at 45 and 60 dB nHL in varying conditions

Attenuator Values for 45 dB nHL Tone burst		Attenuator Values for 60 dB nHL Tone burst	
In Quiet	0.27	In Quiet	0.12
Noise (dB SPL)		Noise (dB SPL)	
35 [+10 dB SNR]	0.612	50 [+10 dB SNR]	0.463
40 [+5 dB SNR]	0.563	55 [+5 dB SNR]	0.413
45 [0 dB SNR]	0.513	60 [0 dB SNR]	0.363
50 [-5 dB SNR]	0.463	65 [-5 dB SNR]	0.313
55 [-10 dB SNR]	0.413	70 [-10 dB SNR]	6.236

4.2. Attenuator values to be used in research – Chirp ABRs

For chirp ABR, 45 and 60 dB nHL will be used and RETSPL for chirp = 31.5 dB. Note due to output limitation, the chirp at "70" dB nHL is only at 66.5 dB nHL (at maximum attenuator setting).

Table 9

Attenuator values for chirp stimulus at 45 and 60 dB nHL in varying conditions

Attenuator Values for 45 dB nHL Tone burst		Attenuator Values for 60 dB nHL Tone burst	
In Quiet	0.225	In Quiet	0.075
Noise (dB SPL)		Noise (dB SPL)	
35 [+10 dB SNR]	0.612	50 [+10 dB SNR]	0.463
40 [+5 dB SNR]	0.563	55 [+5 dB SNR]	0.413
45 [0 dB SNR]	0.513	60 [0 dB SNR]	0.363
50 [-5 dB SNR]	0.463	65 [-5 dB SNR]	0.313
55 [-10 dB SNR]	0.413	70 [-10 dB SNR]	0.263

5. Trigger timing and Jitter check

Triggers are 5V TTL impulses sent via the parallel port from the Presentation PC to the Biosemi data acquisition PC. These triggers are essential in the process of aligning epochs during data analysis with the time that stimuli were delivered to the listener in reality. If there is a timing delay then the latency of observed evoked responses will not be accurate. If there is a timing variability ("jitter") then evoked responses will not be apparent as they will be removed during the signal averaging process (which relies on a response that is time-locked to the signal). Due to stacking and other background operating system activities, a common observation is that there is a timing difference between trigger and stimulus. In

complex scenarios which taxes the PC resources (memory/processing power), there may also be a timing jitter.

The association between signal and trigger were assessed in the present setup using two channels of the oscilloscope. Channel 1 (driving voltage to the transducer) data was obtained by delivering the stimulus input voltage directly to the oscilloscope. Channel 2 (trigger signal) data was also obtained by delivering the trigger impulse directly to the oscilloscope. The 37-pin parallel port cable was disconnected from the Biosemi device and the (male end) pins carrying the trigger impulse were identified from the "pin map" shown in the Biosemi user manual. The present study transmits the 5V TTL on port 1 (see Figure 16).

Figure 16

Biosemi USB Trigger Interface connection (37 pins male Sub-D). Port 1 signal (trigger impulse) is carried by pin 1. Pin 37 is the ground

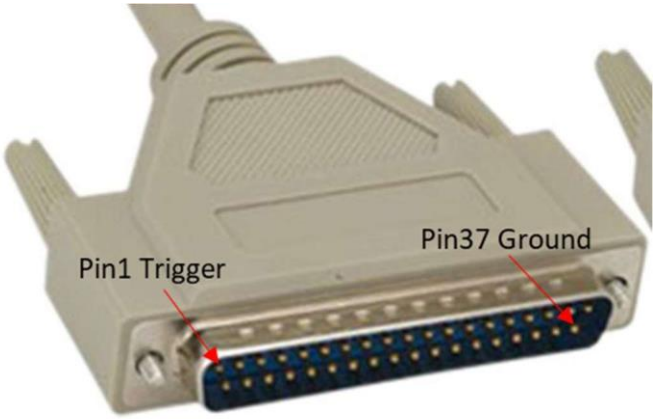


Figure 17 shows the timing association between trigger and 1 kHz tone burst stimulus. There appears to be an approximately 1.94 ms offset between the trigger onset and the stimulus onset. This would cause the ensuing auditory evoked potentials to have an apparent latency increase of 1.94 ms compared to the expected. However, a 1.94 ms correction can be applied during the analysis pipeline. Figure 18 shows multiple triggers and stimuli. A consistent 1.94 ms offset can be observed. These data suggest that there is minimal/no latency jitter. For the purposes of demonstration, only data from 1 kHz tone bursts are shown but the below observation is consistent in 4 kHz tone bursts and the chirp stimulus, showing no latency jitter.

Figure 17

Timing delay between trigger (yellow) and toneburst stimulus (green) shown on a 10 ms time base. The y-cursors (vertical blue lines) indicate an ≈ 1.94 ms delay between the onset of the trigger and the onset of the stimulus

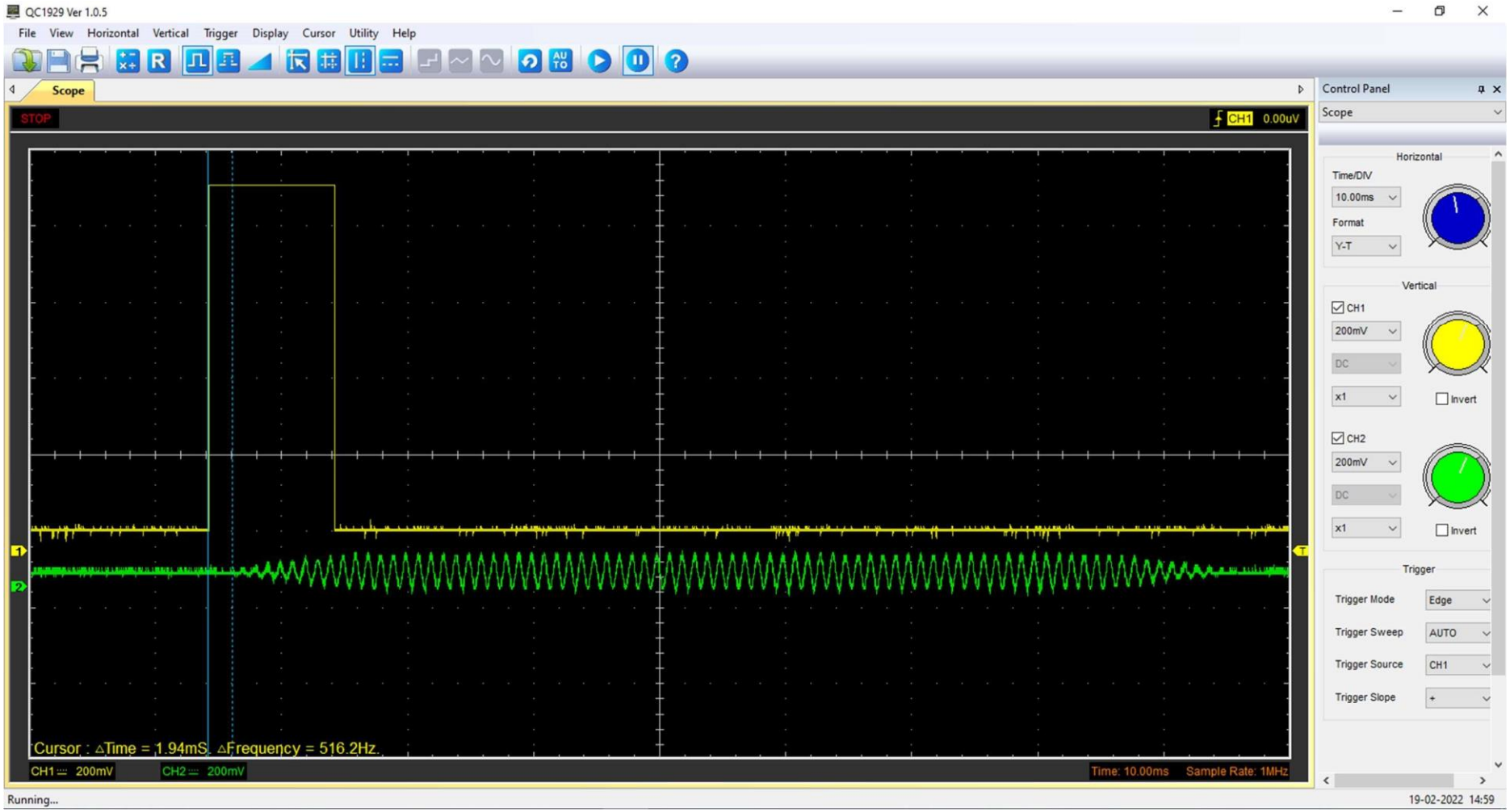
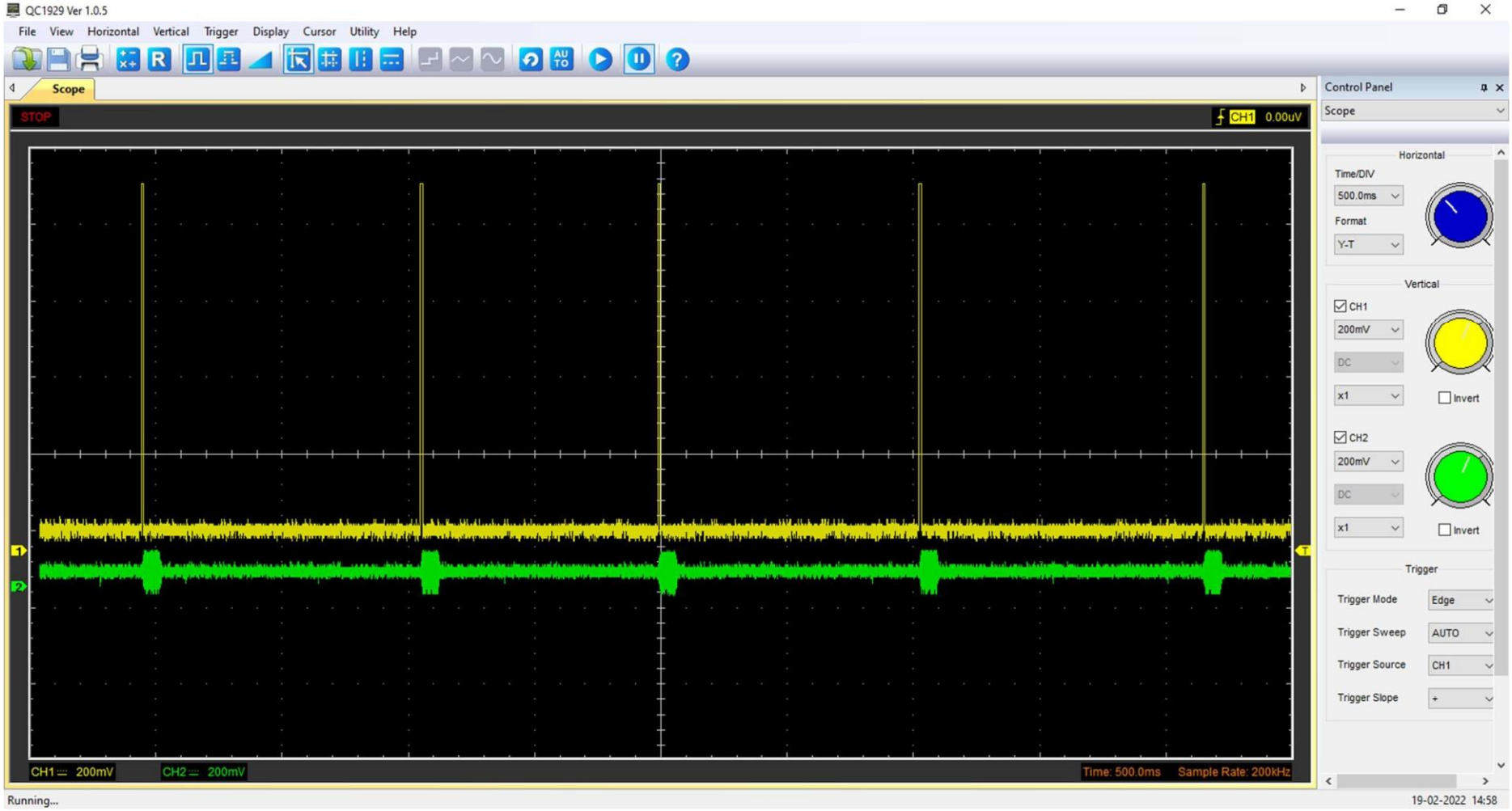


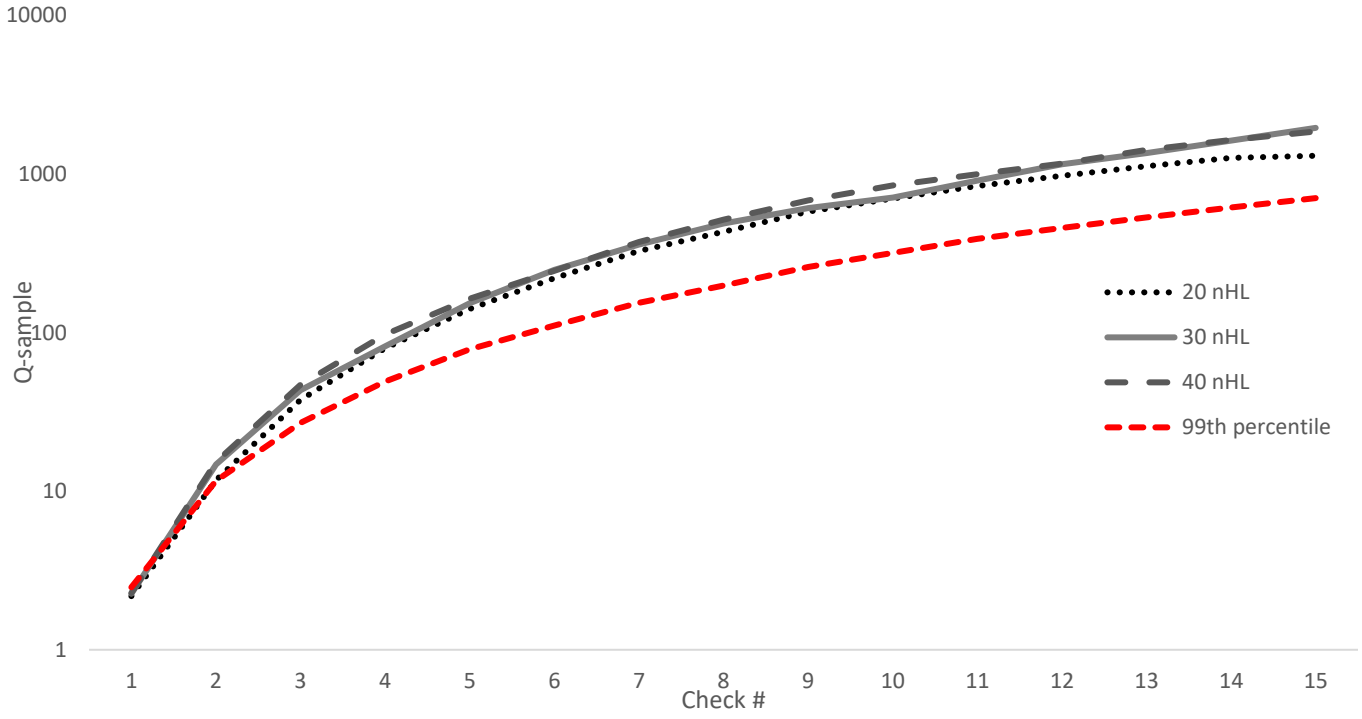
Figure 18

Multiple triggers (yellow) and toneburst stimuli (green) shown on a 500 ms time base. The offset between the trigger and stimulus is consistent



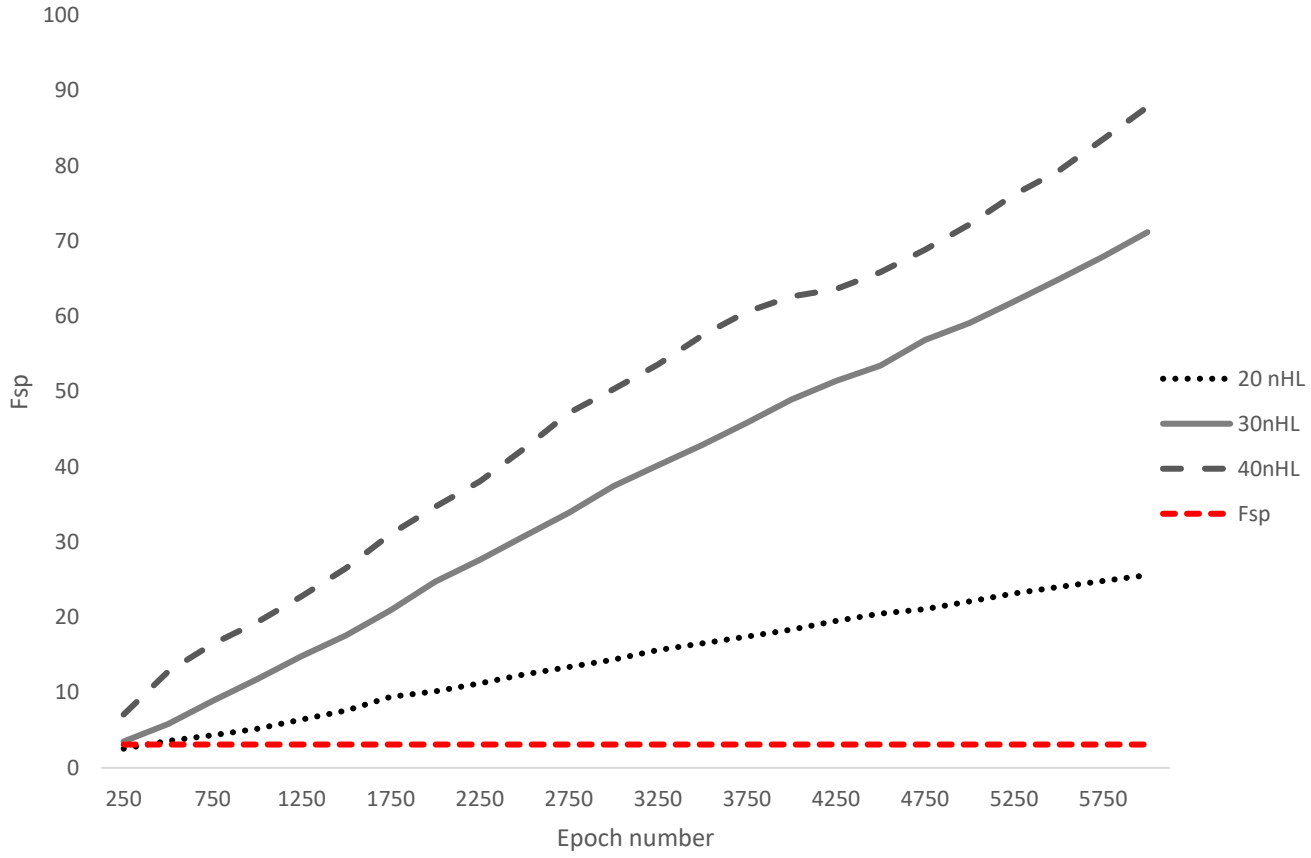
Appendix F

Complete Q-sample Data for the ASSR



Appendix G

Complete Fsp Data for the Interleaved ABR



Appendix H

Results for normality testing performed on the test time data, performed on SPSS

Case Processing Summary

	Cases					
	Valid		Missing		Total	
	N	Percent	N	Percent	N	Percent
Difference	15	100.0%	0	0.0%	15	100.0%

Descriptives

			Statistic	Std. Error
Difference	Mean		-14.08	56.88
	95% Confidence Interval for Mean	Lower Bound	-136.08	
		Upper Bound	107.91	
	5% Trimmed Mean		-7.80	
	Median		-23.75	
	Variance		48530.46	
	Std. Deviation		220.30	
	Minimum		-552.50	
	Maximum		411.25	
	Range		963.75	
	Interquartile Range		103.75	
	Skewness		-.43	.58
	Kurtosis		2.30	1.12

Extreme Values

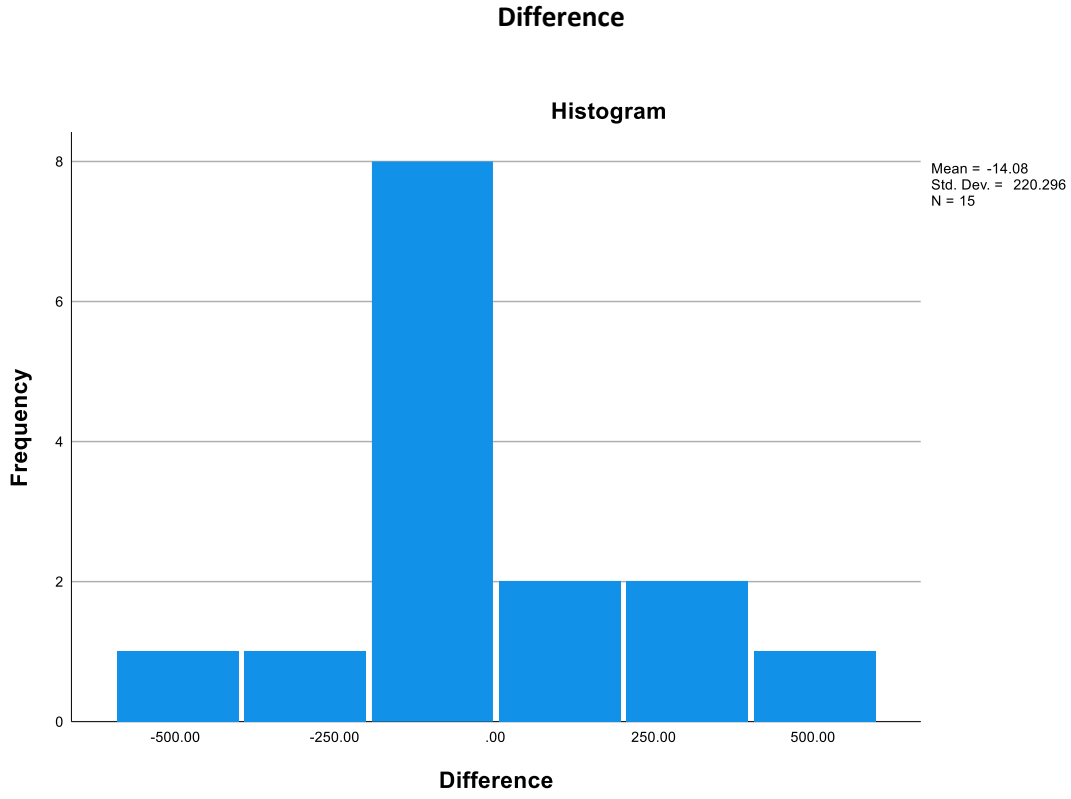
			Case Number	Value
Difference	Highest	1	11	411.25
		2	13	282.50
		3	3	206.25
		4	6	41.25
		5	9	5.00
	Lowest	1	14	-552.50
		2	4	-251.25
		3	1	-100.00
		4	5	-62.50
		5	15	-43.75[a]

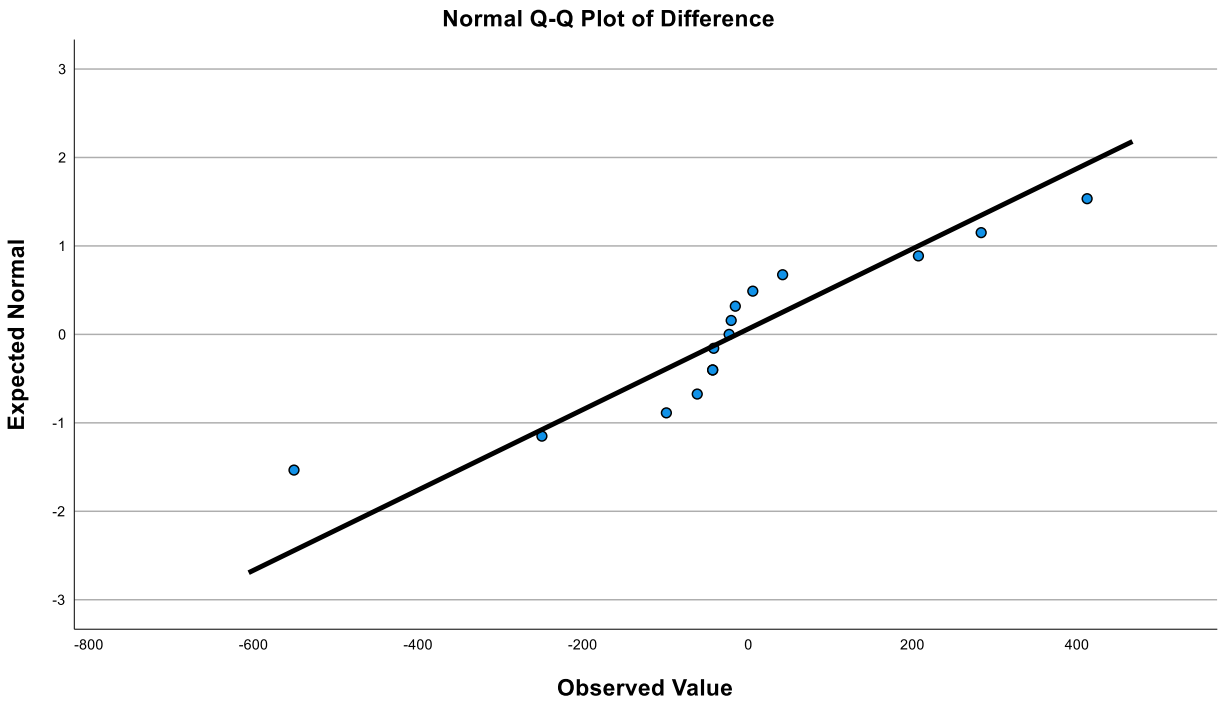
a. Only a partial list of cases with the value -43.75 are shown in the table of lower extremes.

Tests of Normality

	Kolmogorov-Smirnov[a]			Shapiro-Wilk		
	Statistic	df	Sig.	Statistic	df	Sig.
Difference	.215	15	.061	.892	15	.073

a. Lilliefors Significance Correction




Normal Q-Q Plot of Difference
Expected Normal
3
2
1
0
-1
-2
-3
-800
-600
-400
-200
0
200
400
Observed Value