Diagnostic accuracy of CE Chirp

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LIST OF ABBREVIATIONS

ABR	auditory brainstem response
AABR	automated auditory brainstem response
AC	air conduction
AEP	auditory evoked potential
BC	bone conduction
BM	basilar membrane
CE-Chirp	Claus Elberling chirp
dBHL	decibel hearing level
dB nHL	decibel normalized hearing level
dB SL EML	decibel effective masking level
LS CE-Chirp	level-specific CE-Chirp
NTE	non-test ear
OE	occlusion effect
PTA	pure tone average
SRT	speech reception threshold
TE	test ear

FORMATTING

APA referencing style was utilized in this dissertation

ABSTRACT

The auditory brainstem response is an evoked potential that can be clinically used to estimate hearing sensitivity and to identify auditory nervous system pathology. Recently, there has been an increase in the implementation of the CE-Chirp stimulus in AABR equipment for neonatal hearing screening. The purpose of this study is to evaluate the diagnostic accuracy of the LS CE-Chirp-evoked ABR compared to the traditionally used click-evoked ABR for the identification of different degrees and configurations of sensorineural (SNHL) hearing loss.

An exploratory within-subject comparative research design was used. 49 ears with mild to moderate sensorineural hearing loss were assessed. Participants were assessed in a single session. Audiometric pure tone thresholds were obtained at 125-8000 Hz and ABR thresholds were measured using the click and LS CE-Chirp stimuli respectively. Click- and LS CE-Chirp-evoked thresholds were compared with each other and with behavioural pure tone average (PTA), high frequency average (HFA) and low frequency average (LFA). Diagnostic accuracy of the two ABR stimuli was also compared by using ROC curves.

Differences between click- and LS CE Chirp-evoked ABR, and behavioural thresholds were not statistically significant ($p>0.05$). The strongest significant correlation for ABR using clicks to behavioural thresholds was found at 2000 and 4000 Hz, whereas, the strongest correlation for LS CE-Chirp ABRs to behavioural thresholds was found at 1000, 2000 and 4000 Hz ($r>0.7$, $p<0.001$). A very strong, positive correlation was found between both click ($r=0.805$) and LS CE-Chirp ($r=0.825$) and the behavioural PTA ($p<0.001$). The mean differences for LS CE-Chirp were smaller than those of the click for PTA and low frequency range. ROC curves indicated better AUC values for the LS CE-Chirp at LFA and HFA compared to the click, also showing a narrower confidence interval and less variance than the click.

The predictive accuracy of the LS CE-Chirp-evoked ABR was slightly better than that of the click with reference to PTA, HFA and LFA thresholds; furthermore, it is less variable and more accurate than the click-evoked ABR with reference to HFA. Thus, the LS CE-Chirp is an accurate stimulus for estimation of hearing sensitivity using ABR when compared to the gold standard click stimulus for the purpose of identification of different configurations of SNHL.

Keywords: Auditory brainstem response, LS CE-Chirp, click, behavioral hearing threshold, sensorineural hearing loss

1. INTRODUCTION

Von Békésy (1960) stated that the human auditory system has high-frequency selectivity and is known for compressing an extensive range of sound levels into a detectable range (Harte, Pigasse, & Dau, 2009). These features can be explained by the tonotopic arrangement of the cochlea, resulting from a change in stiffness along the basilar membrane. The cochlea is arranged in such a way that the highest frequencies are found at the most basal end of the basilar membrane (BM) and the lowest frequencies are found at the most apical end of the BM (Harte et al., 2009). This means the traveling wave that is entering the cochlea has a greater length to travel before it reaches the low-frequency region of the cochlea in comparison to the high-frequency region.

The auditory brainstem response (ABR) is an auditory evoked potential that can be clinically used for estimation of hearing sensitivity (Bargen, 2015) and for identifying central and peripheral auditory nervous system pathology (Maloff & Hood, 2014; Mühler, Rahne, & Verhey, 2013). The click stimulus is typically used for obtaining ABRs (Cobb & Stuart, 2014; Gorga, Johnson, Kaminski, Beauchaine, Garner, & Neely, 2008; Maloff & Hood, 2014; Zirn, Louza, Reiman, Wittlinger, Hempel, & Schuster, 2014), as it has a rapid onset and is a broadband stimulus (Petoe, Bradley, & Wilson, 2010; Spankovich, Hood, Wesley, Grantham, & Polley, 2008). Because of this broad frequency spectrum, the click stimulus is thought to activate a broader area of the BM and elicit large amplitude responses. This is particularly applicable for the purpose of hearing screening as transient stimuli such as clicks elicit large amplitude responses which can be detected at low sensation levels (Hyvärinen, 2012; Johnson, 2002; Young Futures, 2014).

However, the click does not stimulate the entire cochlea at the exact same time (Petoe et al., 2010; Xu, Cheng, & Yao, 2014). The traveling wave takes some time to travel from the high-frequency region to the low-frequency region of the cochlea (Elberling, Don, Cebulla, & Stürzebecher, 2007; Zirn et al., 2014). Hence, there is a temporal delay between the highest frequency response and the lowest frequency response due to the tonotopic organization of the cochlea (Dau, Wegner, Mellert, & Kollmeier, 2000). Because the basal region is stimulated before the apical region, the neural activity of the low-frequency is phase-cancelled (Cebulla, Stürzebecher,

Don, & Müller-Mazzotta, 2012). Therefore, the click ABR response is mainly a reflection of more basal, high-frequency activity (Chertoff, Lichtenhan, & Willis, 2010; Cobb & Stuart, 2014; Maloff & Hood, 2014). Additionally, at lower intensity levels (near threshold); the waveform is likely to represent neural activity closer to the 1000-4000 Hz region. Hence, ABRs elicited by clicks do not provide information about the overall BM activity, which may result in a low-frequency or a mild to minimal hearing loss being missed (Maloff & Hood, 2014).

A way of compensating for the lack of lower frequency contribution is to use a CE-Chirp stimulus instead of a click stimulus (Dau et al., 2000; Elberling & Don, 2010). The CE-Chirp stimulus was designed to compensate for the cochlear traveling wave delay by sending lower frequency components in first and delaying higher frequency components(Cobb & Stuart, 2014; Ferm, Lightfoot, & Stevens, 2013; Young Futures, 2014; Zirn et al., 2014). Thus low-, mid-, and high-frequency regions of the cochlea are stimulated simultaneously, ensuring enhanced neural synchrony and therefore larger amplitude responses (Cobb & Stuart, 2014; Elberling & Don, 2010; Elberling et al., 2007; Keesling, Parker, & Sanchez, 2017; Petoe et al., 2010; Young Futures, 2014). The use of such a “rising frequency” chirp allows activity from lower frequency regions to be included (Dau et al., 2000). More recently, narrowband CE-Chirps (NB CE-Chirps) have been developed. These are octave-band limited CE-Chirp stimuli centered around 500, 1000, 2000 and 4000 Hz. Like the broadband CE-Chirp, the NB CE-Chirp ABR in adults has an amplitude that is significantly larger than its conventional tone pip counterpart (Rodrigues, Ramos, & Lewis, 2013). This should enable the acquisition of frequency-specific ABR results in a shorter amount of time (Ferm et al., 2013).

The CE-Chirp stimulus may be of clinical use in assessing the integrity of the inner ear due to the following reasons. Firstly, CE-Chirps elicit substantially larger amplitude responses, which make the responses easier to interpret and identify at much lower intensity levels (near-threshold) and in turn decreases the test time (Bargen, 2015; Cebulla, Lurz, & Shehata-Dieler, 2014; Cobb & Stuart, 2014; Maloff & Hood, 2014; Mühler et al., 2013; Young Futures, 2014). Secondly, responses can be measured at higher levels of residual EEG noise and are reliable (Cobb & Stuart, 2014; Mühler et al., 2013). Thirdly, the chirp stimulus enables the representation of

overall basilar membrane activity in the ABR waveform, leading to more precise estimates of auditory thresholds, especially lower-frequency thresholds (Cobb & Stuart, 2014; Junius & Dau, 2005; Maloff & Hood, 2014). Another potential advantage, due to the fact that all frequency regions are included in the response, is the ability to identify pathology in any part of the cochlea. Thus, it does not matter what region (low-, mid- or high-) is affected by the pathology, it will likely result in affected amplitudes and latency of the CE-Chirp evoked ABR (Cebulla et al., 2012). In contrast, with the click stimulus, pathology in the mid- or low-frequency regions may not alter the amplitude and latency of CE-Chirp evoked ABR significantly.

The CE-Chirp stimulus, however, has some limitations. It is not adequate at higher levels of stimulation (>60 dB nHL) (Xu et al., 2014). The amplitudes of CE-Chirp-evoked ABR responses drop significantly lower when higher intensity levels are reached (Cho et al., 2015). This may be related to an upward spread of excitation (Dau et al., 2000; Elberling & Don, 2010). At lower levels of stimulation, each frequency component of the CE-Chirp excites an allocated, narrow area of the cochlea, but at higher levels of stimulation, the excitation spreads toward the basal end of the cochlea, which may lead to altered higher frequencies (Cho et al., 2015). Thus, at higher levels of stimulation, each allocated part on the basilar membrane is stimulated by a broader range of frequencies, creating desynchronization (Cho et al., 2015; Elberling & Don, 2008; Munch, Dau, Harte, & Elberling, 2014). The drop in response amplitude of the CE-Chirp ABR in comparison to the click ABR at higher levels of stimulation in normal hearing individuals suggests that there may be a higher level of stimulation at which CE-Chirps are no longer more effective than clicks (Elberling & Don, 2008). Elberling and Don (2010) therefore developed level-specific CE-Chirps (LS-Chirps) to overcome this. They found that shorter duration CE-Chirps are more effective at higher stimulation levels and longer duration CE-Chirps are more effective at low stimulation levels (<60 dB nHL). The CE-Chirp only took into account the duration of time the acoustic wave needs to travel through the cochlea's different frequency regions, whereas the direct approach takes into account the durational aspects, as well as the different stimulus intensity levels (Cargnelutti, Luis, Pinto, & Biaggio, 2016). The LS-Chirp was designed with varying durations for each stimulus level (changing every 5dB). The LS-Chirp is a broadband chirp with a magnitude spectrum equivalent to that of a click. The LS-Chirp should,

therefore, be used at higher stimulation levels (>60dB nHL) (Elberling & Don, 2010; Xu et al., 2014).

Another possible limitation of the CE-Chirp was suggested by Cobb and Stuart (2014). A decrease in sensitivity may take place when using the CE-Chirp for screening. The enhanced synchronization of different parts in the cochlea might lead to false negative results, meaning the overall responses measured from the cochlea might be adequate enough to pass the screening even when a hearing loss is present (Bargen, 2015).

In a recent comparison study by Maloff and Hood (2014), behavioral pure tone thresholds were compared to click- and CE-Chirp evoked ABR thresholds in individuals with normal hearing and sensorineural hearing loss. Twenty five normal-hearing adults and twenty five adults with sensorineural hearing loss participated. Maloff and Hood (2014) established that ABR thresholds to click and CE-Chirp stimuli do not differ markedly for either the normal-hearing, mild to moderate hearing loss, or mild to severe hearing loss groups. Wave V peak-to-peak amplitudes were greater for CE-Chirps than for clicks, especially at near-threshold intensity levels, for all groups. CE-Chirp evoked ABRs were closer to overall behavioral thresholds than click-evoked ABRs in all groups (Maloff & Hood, 2014). Furthermore, CE-Chirp evoked ABRs did not differ significantly from behavioral thresholds in the two hearing loss groups. Maloff and Hood (2014) came to the conclusion that CE-Chirp evoked ABRs are a useful means for determining physiologic response thresholds accurately, yielding a closer relationship to behavioral thresholds (Maloff & Hood, 2014). Maloff and Hood (2014) suggested that further studies were required to determine whether similar outcomes can be obtained in pediatric populations and whether outcomes can be generalized to individuals with specific degrees and configurations of hearing loss.

Similar findings were obtained in studies by Cebulla et al. (2014) and Mühler et al. (2013); they found that CE-Chirp-evoked ABR response amplitudes were significantly larger when compared to click-evoked ABRs. Cebulla et al. (2014) and Mühler et al. (2013) similarly concluded that due to the greater amplitudes elicited by CE-Chirps, the CE-Chirp stimulus yields reduced recording times, improved reliability and better quality of hearing sensitivity estimation, which is essential when testing

sedated infants. Mühler et al. (2013) also advised utilizing CE-Chirp-evoked ABRs rather than click-evoked ABRs for estimation of hearing sensitivity in the clinical setting, as they are much more reliable and can be measured at higher levels of residual EEG noise.

Zirn et al. (2014) conducted a study comparing click ABRs and NB CE-Chirp ABRs in children. Click and CE-Chirp ABRs were performed in 253 children and ABR results were analyzed in order to demonstrate the correlations between the two methods. The results showed notable correlations between ABRs obtained with clicks and NB CE-Chirps for both 2000 and 4000Hz chirps. In addition, no significant differences were observed between different age ranges or genders. Zirn et al. (2014) concluded that either method can be used for threshold estimation and recommended that the one measurement cannot be replaced by the other, but rather to perform measurements using both click- and CE-Chirp stimuli in order to obtain a complete illustration of the individual's hearing sensitivity.

Cobb and Stuart (2014) evaluated the test-retest reliability of CE-Chirp evoked ABRs in newborns. The findings in this study have shown good test-retest reliability for both ABRs to air- and bone-conducted CE-Chirps in newborns (Cobb & Stuart, 2014). With reference to the findings of Cebulla et al. (2014), Cobb and Stuart (2014), Maloff and Hood (2014), Mühler et al. (2013), and Zirn et al. (2014), one can reason, that the CE-Chirp stimulus may be equal or superior to the click stimulus concerning its ability to identify hearing loss and accurately estimate hearing sensitivity (Cobb & Stuart, 2014).

It is well established that the click is independent of low frequency hearing sensitivity (Cebulla et al., 2012; Chertoff et al., 2010a; Elberling et al., 2007; Petoe et al., 2010; Zirn et al., 2014). Therefore the CE-Chirp was designed to provide information from the entire cochlea. For this reason and due to the large response amplitude, the CE-Chirp is used in automated auditory brainstem response (AABR) equipment for the purpose of neonatal hearing screening (Young Futures, 2014). However, research on the correlation of CE-Chirp with different degrees and configurations of hearing loss is limited (Cho et al., 2015). Maloff and Hood (2014) brought into question the possibility of generalizing outcomes in normal-hearing individuals to those with hearing loss, because CE-Chirp stimuli are based on normal cochlear functioning

and advancements observed in adults with normal hearing may not be observed in adults with hearing loss. Studies looking at the sensitivity and specificity of chirp-evoked ABRs are also limited, and Bargen (2015) suggests that future studies should focus on this, especially in populations with hearing impairments, as most studies only focus on normal-hearing populations. This provides the basis to further explore if advancements, when using the LS CE-Chirp to estimate hearing sensitivity, observed in the normal-hearing population can also be observed in individuals with different degrees and configurations of hearing loss. The same can be said with regard to sensitivity; the comparative accuracy of the click versus LS CE-Chirp in normal-hearing individuals might be different to that of click versus LS CE-Chirp in individuals with hearing loss. This study therefore aimed to evaluate the diagnostic accuracy of the LS CE-Chirp-evoked ABR compared to the click-evoked ABR for the identification of different degrees of hearing loss.

2. METHODOLOGY

2.1 Research aim

The aim of the study is to evaluate the diagnostic accuracy of the LS CE-Chirp-evoked ABR compared to the click-evoked ABR for the identification of different degrees and configurations of hearing loss.

2.2 Research Design

This research study employed an exploratory within-subject comparative research design, yielding quantitative data. Quantitative data were collected as this study aimed to explain, predict and gain an in-depth understanding regarding the correlation between behavioural pure tone thresholds and the 2 different ABR thresholds (Leedy & Ormrod, 2010). The within-subject design allowed the direct comparison of click-evoked ABR thresholds, LS CE-Chirp-evoked ABR thresholds and behavioural pure tone thresholds for individual participants. Participants were assessed in a single session.

2.3 Ethical considerations

This study was approved by the institutional research ethics committee (GW20170218HS) prior to data collection (Appendix A). It is important to consider the ethical implications of all research, especially research where human participants are involved (SASLHA, 2011). The following ethical considerations were addressed to protect the well-being and rights of all participants during the research process:

2.3.1 Informed consent

All individuals were requested to give written informed consent (Appendix B) prior to any participant selection procedures or assessments. Information regarding the nature of the study, what participants could expect and what the rights of participants were throughout the research process was provided to participants verbally and in the form of an information letter (Appendix C). All participants were made aware that participation in the study is voluntary and that they have the right to withdraw at any time without any negative consequences.

2.3.2 Confidentiality and anonymity

Each participant was allocated an alphanumerical code to ensure anonymity and confidentiality. The participant's identity was therefore only known to the researcher. The results of the tests were kept confidential at all times and all

information was stored anonymously in an electrical format where only the code allocated to each participant was used for the purpose of identification.

2.3.3 Protection from harm

A researcher should at all times act in the best interest of participants and protect them from harm (SASLHA, 2011). The participants were not exposed to any emotional or physical harm or discomfort during the research process.

2.3.4 Plagiarism

The research report and study is the researchers own original work. Where secondary material was used, it was carefully acknowledged and referenced in accordance with the university requirements. A declaration against plagiarism can be found in Appendix E.

2.3.5 Release of findings

The research findings were made available to participants upon request. Participants were informed that the findings of this study will be made available to the scientific community in the form of a research article and that it will also be made available to students and lecturers at the Department of Speech-Language Pathology and Audiology in the form of a research dissertation. The results of the research will be stored at the Department of Speech-Language Pathology and Audiology for a minimum period of 15 years as this is policy at the University of Pretoria. A declaration for the storage of research data can be found in Appendix F. During this period data may be used for future research.

2.4 Participants

ABRs from 49 ears were tested and analyzed. The study group consisted of 37 participants with different degrees and configurations of SNHL (age range = 18-65 years, mean age = 44.55 years, SD = 16.03): 16 ears with moderate to mild reverse SNHL (mean 44.47 dB HL, SD 14.61) and 33 ears with mild to moderate sloping SNHL (mean 36.61 dB HL, SD 20.47). Participants were selected from pre-existing clients at the Vestibular Clinic of the University of Pretoria, Department of Speech-Language Pathology and Audiology using purposive sampling. Non-probability purposive sampling is when the researcher intentionally selects certain participants based on the presence of certain attributes; in this case, participants must have had a certain degree and configuration of hearing loss (Maxwell & Satake, 2006). Prior to

any participant selection procedures or assessments, all individuals were requested to give written informed consent (Appendix B). Information regarding the study and participant's rights were provided to individuals verbally and in the form of an information letter (Appendix C). Participants who were willing to partake in the study had an understanding of conversational English or Afrikaans as it was required of the participant to follow instructions during the behavioral hearing test. All participants were made aware that participation in the study is voluntary and that they may withdraw at any point in time. The following participant selection procedures were followed to determine if an individual fits the selection criteria:

- No middle ear pathology or excessive cerumen noted by means of otoscopic examination, utilizing a Welch Allyn pocket otoscope.
- No evidence of middle ear pathology as determined by type A tympanograms and present ipsilateral stapedius reflexes at 1000 Hz (Katz, Burkard, Hood, & Medwetsky, 2009).
- Participants had to present with a mild or moderate high frequency sloping hearing loss or with a mild or moderate reverse sloping hearing loss (125 – 1000 Hz ≥ 25 dB HL), unilaterally or bilaterally, as determined by a behavioral pure tone assessment. A high frequency sloping hearing loss was defined as a hearing loss where there was a greater than 20 dB shift from 500 to 2000 Hz. The presence of air-bone gaps resulted in participant exclusion.
- Participants did not present with any history of known neurological pathology at the time of testing, as the presence of a neurological pathology could affect the ABR-threshold estimates and compromise the reliability of results. ABR testing is a neurologic test that assesses the functioning of the auditory brainstem in response to an auditory stimulus. For the purpose of this study, a healthy neurological system is required as the focus of the study is to compare different stimulus types.

2.5 Data collection Material and Apparatus

Table1 and 2 provides a detailed summary of the equipment that was used during the study.

Table 1: Summary of equipment and material for participant selection

Equipment	Description
Welch Allyn pocket otoscope with reusable specula	Visual inspection to determine the condition of the external ear canal and tympanic membrane.
GSI Tympstar Middle ear analyser and a Y-226 Hz probe tone	Tympanometry was conducted with this device by placing a probe in the participant's ear and measuring the middle ear pressure, compliance and volume. Ipsilateral stapedial acoustic reflexes were also performed to assess the middle ear function and evaluate the integrity of the auditory nerve pathway.
Grason Stradler GSI 61 clinical audiometer with TDH-39 supra-aural headphones for air conduction and a B71 bone conductor for bone conduction calibrated in accordance with SANS 10154-1 (2012).	Behavioral pure tone thresholds were obtained at octave frequencies from 125 to 8000 Hz. Testing took place in a double-walled soundproof booth compliant with the standards required by SANS 10182 (2012). Pure tones were presented through TDH-39 supra-aural headphones to obtain air conduction (AC) thresholds and through a B71 bone conductor to obtain bone conduction (BC) thresholds.

Table 2: Summary of equipment and material for data collection

Equipment	Description
Case history	A short case history was filled out by each participant to obtain basic biographic information such as age, gender, duration of hearing loss and cause of hearing loss. The case history form can be found in Appendix D.
Grason Stradler GSI 61 clinical audiometer with TDH-39 supra-aural headphones for air conduction and a B71 bone conductor for bone conduction calibrated in accordance with SANS 10154-1 (2012).	Behavioral pure tone thresholds were obtained at octave frequencies from 125 to 8000 Hz. Testing took place in a double-walled soundproof booth compliant with the standards required by SANS 10182 (2012). Pure tones were presented through TDH-39 supra-aural headphones to obtain air conduction (AC) thresholds and through a B71 bone conductor to obtain bone conduction (BC) thresholds.
Interacoustics Eclipse EP 25 auditory evoked (AEP) response system with V1.3 software (Interacoustics A/S, Assens, Denmark) , calibrated in accordance with ISO 389-6 (2007), using NuPrep abrasive skin prepping scrub, Ten20 electrode paste, reusable gold cup electrodes and EarTone ABR insert earphones.	ABR measurements were made in order to estimate hearing sensitivity using the click and LS CE-Chirp stimulus respectively.

2.6 Procedure

Participants were assessed in a single session consisting of an otologic examination (otoscopic examination, acoustic immittance measurements, and behavioural pure tone assessment) and ABR measurements. Prior to each test, participants were provided with a short explanation on what is expected of them and what the tests entail. The procedures for participant selection and data collection comprised of the following:

2.6.1 Procedures for participant selection

Otologic examination

- An otoscopic examination was performed bilaterally to determine the condition of the external ear canal and tympanic membrane. The participants' ear canal

and outer ear was visually inspected to rule out any obvious pathology such as discharge, or excessive wax build-up.

- Tympanometry was conducted by placing a probe in the participants' ear to determine the middle ear functioning with regard to middle ear- pressure, volume and compliance. Ipsilateral stapedial acoustic reflexes were also performed to assess the middle ear function and evaluate the integrity of the auditory nerve pathway. Abnormal tympanograms or absent ipsilateral stapedial acoustic reflexes at 1000 Hz resulted in participant exclusion. Normative data by Katz et al. (2009) was used to interpret the results. If ipsilateral stapedial acoustic reflex could not be measured at 1000 Hz, conductive pathology was excluded by the presence of air-bone gaps.

Behavioral pure tone hearing assessment

- Behavioral air conduction thresholds were obtained bilaterally at octave frequencies from 125 to 8000 Hz. Pure tones were presented through TDH-39 supra-aural headphones in both ears respectively. Bone conduction thresholds were obtained where the air conduction thresholds exceeded 10dB HL by presenting tones through a B71 bone conductor. Masking was applied where needed (Katz, Chasin, English, Hood, & Tillery, 2015). The initial masking level for BC was considered as 10 dB SL EML above the AC threshold of the non-test ear (NTE), plus the correction factor for the occlusion effect (OE) in the case of normal hearing or a sensory neural hearing loss in the NTE. The OE was considered to be 15 dB at 250 and 500 Hz and 10 dB at 1000 Hz. The noise level was increased in 5 dB steps, after which the threshold was checked in the test ear (TE). If there was no change in the threshold for three consecutive EMLs, it was taken as the threshold. The presence of air-bone gaps resulted in participant exclusion. Testing took place in a double-walled soundproof booth. During behavioral audiometry, participants were required to co-operate and respond consistently. The participant was requested to indicate each time he/she heard the tone. Threshold response was defined as the lowest intensity where the stimulus is audible to the participant. A pure tone average (PTA) was calculated by calculating the average of hearing sensitivity thresholds at 500, 1000 and 2000 Hz.

- Speech reception thresholds (SRT) were also obtained, using recorded spondee word lists, in order to ensure the reliability and validity of the behavioural pure tone thresholds. The PTA and SRT did not differ by more than +/- 6 dB (Stach, 2010). If a discrepancy of more than +/- 6 dB was present the results were deemed as unreliable and it resulted in exclusion from the study.

2.6.2 Procedures for data collection

Behavioral pure tone hearing assessment

Behavioral air conduction thresholds were obtained bilaterally at octave frequencies from 125 to 8000 Hz. Pure tones were presented through TDH-39 supra-aural headphones in both ears respectively. Testing took place in a double-walled soundproof booth. During behavioral audiometry, participants were required to co-operate and respond consistently. The participant was requested to indicate each time he/she heard the tone. Threshold response was defined as the lowest intensity where the stimulus is audible to the participant. A pure tone average (PTA) was calculated by calculating the average of hearing sensitivity thresholds at 500, 1000 and 2000 Hz.

ABR measurements

ABRs were performed using the Interacoustics Eclipse EP25 auditory evoked (AEP) response system with V1.3 software (Interacoustics A/S, Assens, Denmark) calibrated in accordance with ISO 389-6 (2007). Calibration was done by measuring the ppeSPL (peak-to-peak equivalent sound pressure level) using a sound level meter and oscilloscope. Testing took place in a sound treated room. Auditory brainstem responses are objective and did not require the co-operation of participants. The participant was requested to lie quietly in supine position with their eyes closed. The skin was cleaned with NuPrep prepping scrub prior to electrode placement, in order to reduce electrode impedance. Reusable gold cup electrodes filled with Ten20 electrode paste were held in place with micropore tape. A two-channel electrode configuration was used. The non-inverting electrode was placed on the high forehead, with the inverting electrode on the ipsilateral mastoid and the ground electrode on the low forehead. Electrode impedance was measured before testing began to ensure electrode impedance is below 5 kΩ. The test protocol was

set up as recommended by Interacoustics for ABR thresholds determination. The stimulus rate, filters and artefact rejection level was kept the same for the purpose of comparison. Click and LS CE-Chirp stimuli were presented through EarTone ABR insert headphones at a rate of 45.1/s. ABRs were recorded monaurally. The order of completion of click compared to CE chirp threshold determination was randomized for each participant.

The EEG was band pass filtered from 33 to 1500 Hz using filter slopes of 6 dB/octave with an artifact rejection level of ±40 µV. Bayesian weighted averaging was used to obtain ABRs and averaging stopped after residual noise levels were 40nV or lower. Rarefaction- and alternating stimulus polarities were used to obtain threshold information for the click and LS CE-Chirp respectively. The stimulus intensity started at 20 dB nHL above the behavioral threshold at 1000 Hz and was decreased in steps of 10 dB until a no response trace was obtained. If wave V could not be observed the stimulus intensity was increased by 10 dB nHL until a response was obtained. The threshold response was defined as the lowest intensity at which a repeatable wave V could be identified by two independent audiologists experienced in AEP testing. At least two traces, with a minimum of 2000 sweeps, were obtained at each threshold intensity to confirm waveform repeatability.

2.7 Reliability and validity

The validity of a measurement procedure refers to how well a test measures what it is intended to measure (Leedy & Ormrod, 2010). Reliability refers to the consistency with which a measuring procedure produces a certain result (Heale & Twycross, 2015). It is important to keep variables as stable and constant as possible. Thus, it is important to establish validity, to ensure that the findings can be effectively used to answer the research question (Leedy & Ormrod, 2010).

Reliability and validity were established by employing the following:

- The same test equipment was used for all participants.
- All participants were assessed in the same test environment.
- All assessments were performed on the same day.
- The within-subject design of the study allowed the direct comparison of click-, LS CE-Chirp- and behavioural pure tone- thresholds within each participant.
- Objective measures were used.

- Cross-check of behavioral results with SRT results.
- Two independent audiologists, experienced in AEP testing, evaluated the thresholds of ABR responses.

2.8 Data analysis procedures

Collected data was captured on a Microsoft Excel (2010) spreadsheet. SPSS (IBM Corp. Released 2017. IBM SPSS Statistics for Windows, Version 25) was utilized to perform statistical data analyses and to graphically represent data. The left and right ear thresholds for both click and LS CE-Chirp were normally distributed ($W=0.949$-0.974, $p>0.05$). A t-test indicated that left and right thresholds for each AEP were not significantly different ($t<0.001$ and $t=0.043$ for click and LS CE-Chirp respectively, $p>0.05$). Further assessment and analysis therefore took place with left and right data pooled. Descriptive statistical measures were used to analyze the quantitative data collected in the study (Irwin, Pannbacker & Lass, 2008). This included determining the mean and standard deviation for ABR thresholds (click and LS CE-Chirp) and each pure tone threshold (125-8000 Hz). Average audiometric thresholds were also calculated for low frequency average at 250, 500, 1000 Hz (LFA), pure tone average at 500, 1000, 2000 Hz (PTA), and high frequency average at 2000, 4000, 8000 Hz (HFA). The difference values between click- and LS CE-Chirp-evoked thresholds and PTA, LFA and LFA mean thresholds were normally distributed ($W=0.962$-0.9690; $p>0.05$) while the absolute difference values were not normally distributed ($W=0.850$-0.939; $p<0.05$). The Wilcoxon signed rank test (for non-parametric data) and Pearson's rank test of correlation (for parametric data) and paired samples t-test (for parametric data) were employed for between group comparisons. As a measure of significance, $p < 0.05$ (95% confidence level) was regarded as significant (*) and $p < 0.001$ as highly significant (***).

3. RESEARCH ARTICLE

Diagnostic accuracy of CE Chirp

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3.1 Abstract

Objective: There has been an increase in the use of the CE-Chirp stimulus in AABR equipment for neonatal hearing screening. The purpose of this study is to evaluate the diagnostic accuracy of the LS CE-Chirp-evoked ABR compared to the click-evoked ABR for the identification of different degrees and configurations of sensorineural (SNHL) hearing loss.

Method: 49 ears with mild to moderate SNHL were assessed: 16 ears with reverse sloping SNHL and 33 ears with sloping high frequency SNHL. Audiometric pure tone thresholds were obtained at 125-8000 Hz and ABR thresholds were measured using the click and LS CE-Chirp stimuli respectively. Click- and LS CE-Chirp-evoked thresholds were compared with each other and with behavioural pure tone average (PTA), high frequency average (HFA) and low frequency average (LFA). Diagnostic accuracy of the two ABR stimuli was also compared by using ROC curves.

Results: Differences between click- and LS CE Chirp-evoked ABR, and behavioural thresholds were not statistically significant ($p>0.05$). The highest significant correlations for ABR using clicks to behavioural thresholds was found at 2000 and 4000 Hz, whereas, the highest correlation for LS CE-Chirp ABRs to behavioural thresholds was found at 1000, 2000 and 4000 Hz ($r>0.7$, $p<0.001$). A very strong, positive correlation was found between both click ($r=0.805$) and LS CE-Chirp ($r=0.825$) and the behavioural PTA ($p<0.001$). The mean differences for LS CE-Chirp were smaller than those of the click for PTA and low frequency range. ROC curves

indicated better AUC values for the LS CE-Chirp at LFA and HFA compared to the click, also showing a narrower confidence interval and less variance than the click.

Conclusion: The predictive accuracy of the LS CE Chirp-evoked ABR was slightly better than that of the click with reference to PTA, HFA and LFA thresholds; furthermore, it is less variable and more accurate than the click-evoked ABR with reference to HFA. Thus, the LS CE-Chirp is an accurate stimulus for estimation of hearing sensitivity using ABR when compared to the gold standard click stimulus for the purpose of identification of different configurations of SNHL.

Keywords: Auditory brainstem response, LS CE-Chirp, click, behavioral hearing threshold, sensorineural hearing loss

3.2 Introduction

The auditory brainstem response (ABR) is an auditory evoked potential that can be clinically used for estimation of hearing sensitivity (Bargen, 2015) and for identifying central and peripheral auditory nervous system pathology (Maloff & Hood, 2014; Mühler et al., 2013). The click stimulus is typically used for obtaining ABRs (Cobb & Stuart, 2014; Gorga et al., 2008; Maloff & Hood, 2014; Zirn et al., 2014), as it has a rapid onset and is a broadband stimulus (Petoe et al., 2010; Spankovich et al., 2008). Because of this broad frequency spectrum, the click stimulus is thought to activate a broader area of the basilar membrane (BM) and elicit large amplitude responses. The click stimulus is therefore especially appropriate for the purpose of hearing screening as it elicits large amplitude responses which can be detected at low sensation levels (Hyvärinen, 2012; K. Johnson, 2002; Young Futures, 2014).

However, the click stimulus does not stimulate the entire cochlea at the exact same time, as the traveling wave takes some time to travel from the high-frequency region to the low-frequency region of the cochlea (Elberling et al., 2007; Petoe et al., 2010; Xu et al., 2014; Zirn et al., 2014). Because the basal region is stimulated before the apical region, the neural activity of the low-frequency is phase-cancelled (Cebulla et al., 2012). Therefore, the click ABR response is mainly a reflection of more basal, high-frequency activity (Chertoff et al., 2010a; Cobb & Stuart, 2014; Maloff & Hood, 2014). Additionally, at lower intensity levels (near threshold); the waveform is likely to represent neural activity closer to the 1000-4000 Hz region. Hence, ABRs elicited by clicks do not provide information about the overall BM activity, which may result in a low-frequency or a mild to minimal hearing loss being missed (Maloff & Hood, 2014).

A way of compensating for the lack of lower frequency contribution with a click-evoked ABR is to use a CE-Chirp stimulus (Dau et al., 2000; Elberling & Don, 2010). The CE-Chirp stimulus was designed to compensate for the cochlear traveling wave delay by timing the stimulus so that lower frequency components of the stimulus are generated first, delaying mid and high frequency components (Cobb & Stuart, 2014; Ferm et al., 2013; Young Futures, 2014; Zirn et al., 2014). Thus low-, mid-, and high-frequency regions of the cochlea are stimulated simultaneously, ensuring enhanced neural synchrony and therefore larger amplitude responses (Cargnelutti, Cóser, & Biaggio, 2017; Cobb & Stuart, 2014; Elberling & Don, 2010; Elberling et al., 2007; Petoe et al., 2010; Young Futures, 2014). The use of such a “rising frequency” chirp

allows activity from lower-frequency regions to be included in the response (Dau et al., 2000).

For this reason, and due to the large response amplitude, the CE-Chirp is used in automated auditory brainstem response (AABR) equipment for the purpose of neonatal hearing screening (Young Futures, 2014). The use of the CE-Chirp stimulus for various clinical applications has increased recently, likely due to following reasons. Firstly, the chirp stimulus enables the representation of overall basilar membrane activity in the ABR waveform, leading to more precise estimates of auditory thresholds, especially lower-frequency thresholds (Cobb & Stuart, 2014; Hall, 2016; Junius & Dau, 2005; Maloff & Hood, 2014). Another presumed advantage, due to the fact that all frequency regions are included in the response, is the ability to identify pathology in any part of the cochlea. Thus, it does not matter what region (low-, mid- or high-) is affected by the pathology, it will likely result in affected amplitudes and latencies of the CE-Chirp evoked ABR (Cebulla et al., 2012). In contrast, pathology in the mid- or low-frequency regions may not alter the amplitude and latency of a click-evoked ABR significantly. Fobel and Dau (2004) also suggested that compared to the click, the chirp stimulus may be a more sensitive stimulus to use for screening purposes.

The CE-Chirp stimulus, however, has some limitations. It is not adequate at higher levels of stimulation (>60 dB nHL) (Xu et al., 2014). The amplitudes of CE-Chirp-evoked ABR responses drop significantly when higher intensity levels are reached (Cho et al., 2015). This is thought to be related to an upward spread of excitation (Dau et al., 2000; Elberling & Don, 2010). At lower levels of stimulation, each frequency component of the CE-Chirp excites an allocated, confined area of the cochlea, but at higher levels of stimulation, the excitation spreads toward the basal end of the cochlea, creating desynchronization, which causes a drop in ABR response amplitude(Cho et al., 2015; Elberling & Don, 2008; Munch et al., 2014). The drop in response amplitude of the CE-Chirp ABR in comparison to the click ABR at higher levels of stimulation suggests there may be a higher level of stimulation at which CE-Chirps are no longer more effective than clicks (Elberling & Don, 2008). Elberling and Don (2010) therefore developed a new delay model; the level-specific CE-Chirps (LS-Chirps), to overcome this. They found that shorter duration CE-Chirps are more effective at higher stimulation levels and longer duration CE-Chirps are

more effective at low stimulation levels (<60 dB nHL). The shorter duration decreases desynchronization and partially compensates for the spread of excitation, generating waves with larger amplitudes and improved resolution (Elberling & Don, 2010; Xu et al., 2014).

Another possible limitation of the CE-Chirp was suggested by Cobb and Stuart (2014). A decrease in sensitivity may take place when using the CE-Chirp for screening. The enhanced synchronization of different parts in the cochlea might lead to false negative results, meaning the overall responses measured from the cochlea might be adequate enough to pass the screening even when a hearing loss is present (Bargen, 2015).

The CE-Chirp was therefore designed and implemented in screening equipment to provide information from the entire cochlea, in contrast to the click's independence of low frequency hearing sensitivity (Cebulla et al., 2012; Chertoff et al., 2010a; Elberling et al., 2007; Petoe et al., 2010; Zirn et al., 2014). However, research on the correlation of CE-Chirp with different degrees and configurations of hearing loss is limited (Cho et al., 2015). Maloff and Hood (2014) brought into question the possibility of generalizing outcomes in normal-hearing individuals to those with hearing loss because CE-Chirp stimuli are based on normal cochlear functioning, and advancements observed in adults with normal hearing may not be observed in adults with hearing loss. Studies looking at the sensitivity and specificity of chirp-evoked ABRs are also limited, and Bargen (2015) suggests that future studies should focus on this, especially in populations with hearing impairments, as most studies only focus on normal-hearing populations. This provides the basis to further explore if advancements, when using the LS CE-Chirp to estimate hearing sensitivity, observed in the normal-hearing population can also be observed in individuals with different degrees and configurations of hearing loss. The same can be said with regard to sensitivity; the comparative accuracy of the click versus LS CE-Chirp in normal-hearing individuals might be different to that of click versus LS CE-Chirp in individuals with hearing loss. This study therefore aimed to evaluate the diagnostic accuracy of the LS CE-Chirp-evoked ABR compared to the click-evoked ABR for the identification of different degrees of hearing loss.

Material and methods

3.3.1 Participants

This study was approved by the institutional research ethics committee (GW20170218HS). Participants were selected from pre-existing clients at the Vestibular Clinic of the University of Pretoria, Department of Speech-Language Pathology and Audiology using non-probability purposive sampling. The study employed an exploratory within-subject comparative research design, yielding quantitative data (Leedy & Ormrod, 2010). Participants were assessed in a single session.

ABRs from 49 ears were analyzed. The study group consisted of 37 participants with different degrees and configurations of SNHL (age range = 18-65 years, mean age = 44.55 years, SD = 16.03): 16 ears with moderate to mild reverse sloping SNHL (mean 44.47 dB HL, SD 14.61) and 33 ears with mild to moderate sloping SNHL (mean 36.61 dB HL, SD 20.47). All participants gave written informed consent prior to testing and were made aware that participation in the study was voluntary and that they may withdraw at any point in time. Participants were assessed in a single session consisting of an otoscopic examination, acoustic immittance measurements, behavioural pure tone assessment, and ABR measurements. Participants did not present with any known history of neurological pathology at the time of testing. All ears presented with normal middle ear functioning as determined by otoscopic examination, Jerger Type A tympanograms, and present ipsilateral acoustic reflexes at 1000 Hz. Air conduction behavioural thresholds were obtained at 125 – 8000 Hz and bone conduction at 250 – 4000 Hz. All ears presented with air-bone gaps of ≤10 dB HL at 250 – 4000 Hz.

3.3.2 Equipment and procedure

Participants were assessed in a single session and all testing took place in a double-walled soundproof booth. Behavioral air conduction thresholds were obtained bilaterally at octave frequencies from 125-8000 Hz using a Grason Stradler GSI 61 clinical audiometer calibrated in accordance with SANS 10154-1 (2012). Pure tones were presented through TDH-39 supra-aural headphones in both ears respectively. Bone conduction thresholds were obtained where the air conduction thresholds

exceeded 10 dB HL by presenting tones through a B71 bone conductor. Masking was applied where needed.

ABRs were performed using the Interacoustics Eclipse EP25 auditory evoked (AEP) response system with V1.3 software (Interacoustics A/S, Assens, Denmark) calibrated in accordance with ISO 389-6 (2007). Calibration was done by measuring the ppeSPL (peak-to-peak equivalent sound pressure level) using a sound level meter and oscilloscope. Testing took place in a sound treated room. The test protocol was set up as recommended by Interacoustics for ABR thresholds determination. The stimulus rate, filters and artefact rejection level was kept the same for the purpose of comparison. Click and LS CE-Chirp stimuli were presented through EarTone ABR insert headphones at a rate of 45.1/s. Rarefaction and alternating stimulus polarities were used to obtain threshold information for the click and LS CE-Chirp respectively.

The EEG was band pass filtered from 33 to 1500 Hz using filter slopes of 6 dB/octave with an artifact rejection level of ±40 µV. Bayesian weighted averaging was used to obtain ABRs and averaging stopped once residual noise levels were 40 nV or lower after a minimum of 2000 responses were averaged. Participants were requested to lie quietly in a supine position with their eyes closed. Electrode placement sites were cleaned with NuPrep prepping scrub prior to electrode placement, in order to reduce electrode impedance. Reusable gold cup electrodes filled with Ten20 electrode paste were held in place with micropore tape. A two channel electrode configuration was used and impedances were kept below 5 kΩ. The non-inverting electrode was placed on the high forehead (Fz), with the inverting electrode on the ipsilateral mastoid (Mi) and the ground electrode on the low forehead (Fpz).

ABRs were recorded monaurally. The order of completion of click compared to CE-chirp threshold determination was randomized for each participant. The stimulus intensity started at 20 dB nHL above the behavioral threshold at 1000 Hz and was decreased in 10 dB steps until a no response trace was obtained. If wave V could not be observed the stimulus intensity was increased by 10 dB nHL until a response was obtained. The threshold response was defined as the lowest intensity at which a

repeatable wave V could be identified by two independent audiologists experienced in AEP testing. Response thresholds were defined in 10 dB steps. At least two traces, with a minimum of 2000 sweeps were obtained at each threshold intensity to confirm waveform repeatability.

3.3.3 Data analysis

Collected data was captured on a Microsoft Excel (2010) spreadsheet. Data was recorded and analyzed using SPSS (IBM Corp. Released 2017. IBM SPSS Statistics for Windows, Version 25). The left and right ear thresholds for both click and LS CE-Chirp were normally distributed ($W=0.949-0.974$, $p>0.05$). A t-test indicated that left and right thresholds for each AEP were not significantly different ($t<0.001$ and $t=0.043$ for click and LS CE-Chirp respectively, $p>0.05$). Further assessment and analysis therefore took place with left and right data pooled. Descriptive statistical measures were used to analyze the quantitative data collected in the study (Irwin et al., 2008). This included determining the mean and standard deviation for ABR thresholds (click and LS CE-Chirp) and each pure tone threshold (125-8000 Hz). Average audiometric thresholds were also calculated for low frequency average at 250, 500, 1000 Hz (LFA), pure tone average at 500, 1000, 2000 Hz (PTA), and high frequency average at 2000, 4000, 8000 Hz (HFA). Raw and absolute difference scores between the respective ABR thresholds and behavioural pure tone averages were calculated. Data was also plotted in scatter plots to investigate the amount of variance between the ABR thresholds and audiometric thresholds using r squared. Pearson correlation coefficient was used to explore correlation between ABR and behavioural pure tone thresholds. The strength of the correlation was determined using the guide that Evans (Evans, 1996) suggests for the absolute value of r=0.00-0.19 “very weak”; r=0.20-0.39 “weak”; r=0.40-0.59 “moderate”; r=0.60-0.79 “strong”; r=0.80-1.0 “very strong”.

In order to determine the sensitivity and specificity of click- and LS CE-Chirp-evoked ABR to identify the presence of a hearing loss, a behavioral pure tone level of $\geq$30 dB HL was used to indicate the presence of a hearing loss (Joint Committee on Infant Hearing, 2007). Receiver operating characteristic (ROC) curves were employed to determine the sensitivity and specificity of the click and LS CE-Chirp-evoked ABRs for identification of hearing loss. The diagnostic accuracy is measured

by the area under curve (AUC). A guide based on the traditional academic point system was used to classify the accuracy of LS CE-Chirp- and click-evoked ABRs (Pines, Carpenter, Raja, & Schuur, 2012). AUC values of 0.90-1.00 were indicative of excellent accuracy, 0.80-0.90 good accuracy, 0.70-0.80 fair accuracy and 0.60-0.70 poor accuracy. The difference values between click- and LS CE-Chirp-evoked ABR thresholds and PTA, LFA and LFA mean thresholds were normally distributed ($W=0.962-0.9690$; $p>0.05$) while the absolute difference values were not normally distributed ($W=0.850-0.939$; $p<0.05$). The Wilcoxon signed rank test (for non-parametric data) and paired samples t-test (for parametric data) were employed for between group comparisons. As a measure of significance, $p<0.05$ (95% confidence level) was regarded as significant (*) and $p<0.001$ as highly significant (***).

3.4 Results

A total of 49 ears with mild to moderate SNHL with both sloping and reverse sloping configurations were assessed (mean PTA 38.27 dB HL, SD 17.92; mean HFA 49.93 dB HL, SD 18.87; mean LFA 34.93 dB HL, SD 19.86) using three different measures (behavioural pure tone assessment, click ABR and LS CE-Chirp ABR). The mean, standard deviation and 25th, 50th and 75th percentiles for behavioural pure tone thresholds, LS CE-Chirp-evoked ABR and click-evoked ABR thresholds are presented in Table 1.

Table 1 Mean, standard deviations, median and 25th and 75th percentiles for low frequency (250, 500, 1000 Hz), pure tone (500, 1000, 2000 Hz), and high frequency (2000, 4000, 8000 Hz) thresholds in decibels (dB) for behavioural pure tone thresholds, click-evoked ABR and LS CE-chirp-evoked ABR thresholds (n=49 ears)

		LFA	PTA	HFA	LS CE-Chirp Threshold	Click Threshold
Mean		34.93	38.27	49.93	39.69	40.61
SE		2.837	2.560	2.695	2.954	2.703
SD		19.86	17.91	18.86	20.676	18.920
Percentiles	**25th**	24.17	24.17	36.67	27.50	27.50
	50th	33.33	33.33	46.67	40.00	40.00
	75th	52.50	52.50	63.33	55.00	60.00

SE = standard error; SD = standard deviation; PTA = pure tone average; LFA = low frequency average; HFA = high frequency average

In the current participant sample, behavioural thresholds showed lower mean values in the low frequency range with higher mean values in the high frequency range, indicating a mean audiogram with a mild to moderate degree of hearing loss. A

paired t-test was run for click-evoked ABR thresholds and for LS CE-Chirp-evoked ABR thresholds (t(48)=0.689; p>0.05). No significant difference was found between the ABR threshold levels for either click- or LS CE Chirp-evoked ABR.

Raw and absolute difference scores between behavioural PTA, LFA and HFA and respective ABR thresholds are presented in Table 2.

Table 2 Mean and standard deviation of raw and absolute differences between behavioural low frequency (250, 500, 1000 Hz), pure tone (500, 1000, 2000 Hz), and high frequency (2000, 4000, 8000 Hz) average thresholds, and click and LS CE-Chirp- evoked ABR thresholds (dB; n=49)

	Difference		**Absolute difference**	
	Mean	*SD*	*Mean*	*SD*
PTA and click	2.35	11.55	9.25	7.49
PTA and LS CE-chirp	1.43	11.87	9.01	7.46
LFA and click	5.68	17.84	14.39	11.83
LFA and LS CE-chirp	4.76	17.15	13.54	11.41
HFA and click	9.31	15.61	13.95	11.50
HFA and LS CE-chirp	10.24	15.46	15.27	10.39

SD = standard deviation; PTA = pure tone average; LFA = low frequency average; HFA = high frequency average

For prediction of PTA, absolute differences of about 9 dB were found for both ABR stimuli. Standard deviations are also similar for both techniques. Mean raw and absolute difference values are smaller between LS CE-Chirp-evoked ABR threshold and LFA than for click-evoked ABR threshold and LFA. For prediction of HFA smaller mean raw and absolute difference values were observed for the click compared to the LS CE-Chirp-evoked ABR threshold. A Wilcoxon sign rank test was used to compare both the absolute and raw difference between the click- and LS CE Chirp-evoked ABR thresholds and LFA, PTA and HFA (W=-1.056 to 1.367, p>0.05), while a paired samples t-test was run to compare the difference scores between click- and LS CE Chirp ABR thresholds and the LFA (t(48)=0.689, p>0.05). There was no significant difference between difference or absolute difference between LFA, PTA and HFA, and the ABR thresholds measured by the two different broadband stimuli.

3.4.1 ABR versus behavioural pure tone average (PTA=500, 1000, 2000 Hz)

A PTA was calculated for behavioural pure tones at 500, 1000 and 2000 Hz. Data was plotted in scatter plots to present the amount of variance between ABR thresholds and PTA threshold (Figure 1).

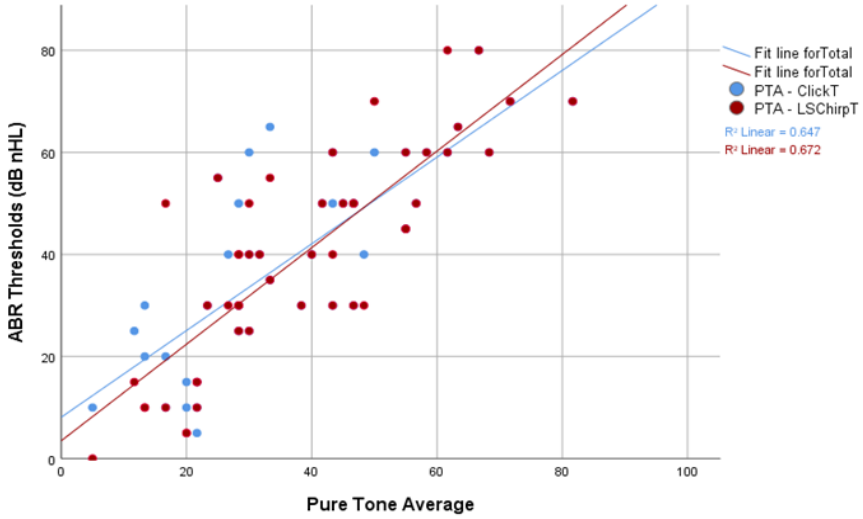

Figure 1 Scatterplot comparing click- and LS CE-Chirp ABR thresholds to pure tone average (PTA)

The r squared value for the LS CE-Chirp evoked ABR was slightly better than for the click (R^2 click=0.647; R^2 LS CE-Chirp=0.672). The determination coefficient (R^2) as shown in Figure 1 suggests that the LS CE-Chirp ABR accurately predicted 67.2% of the PTA threshold compared to the 64.7% for click ABR. Identical sensitivity and specificity values were obtained for click and LS CE-Chirp for prediction of PTA showing a very high sensitivity (96.7%) but low specificity (57.9%).

Figure 2 shows the diagnostic accuracy of click- and LS CE-Chirp-evoked ABRs for the estimation of behavioural PTA as calculated using receiver operating characteristic (ROC) curves.

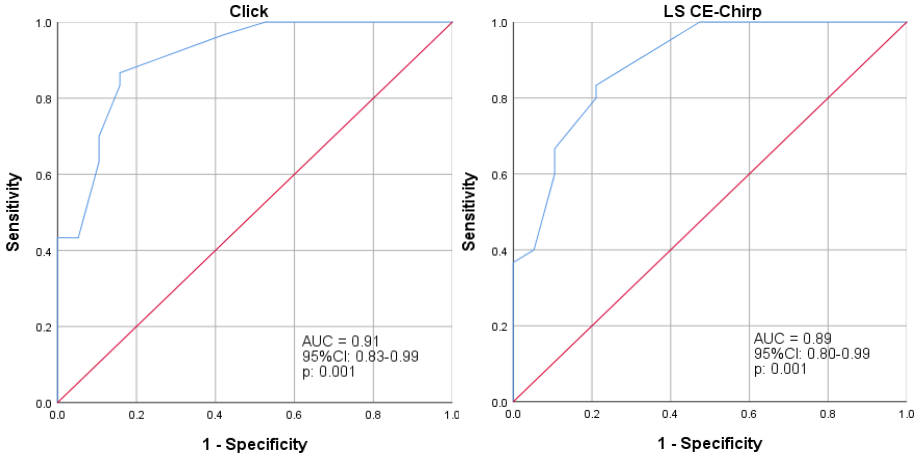

Figure 2 ROC curves illustrating the diagnostic accuracy of the click and LS CE-Chirp for the estimation of pure tone average (PTA; AUC = area under the curve; CI = confidence interval)

The AUC values were similar for both ABR stimuli (AUC^{click}=0.91; $AUC^{LS\ CE\text{-}Chirp}$=0.89), but is slightly better for the click with regard to identification of a hearing loss in the PTA range.

A very strong, positive, statistically significant correlation was found between both click and LS CE-Chirp thresholds, and PTA (r^{click}=0.805, p<0.05 and $r^{LS\ CE\text{-}Chirp}$=0.820, p<0.05). This shows a slightly better r value and less variance for the LS CE-Chirp compared to the click with reference to correlation with PTA.

3.4.2 ABR versus low frequency average (LFA = 250, 500, 1000 Hz)

Figure 3 shows the amount of variance between the audiometric LFA and the ABR thresholds.

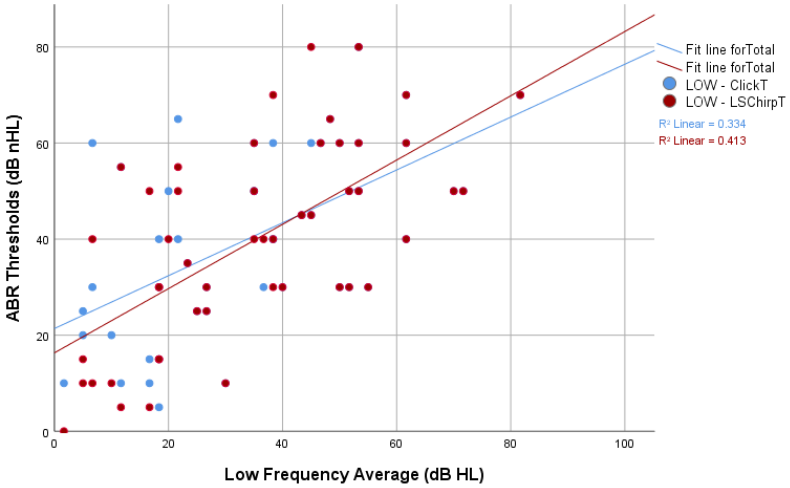

Figure 3 Scatterplot comparing click- and LS CE-Chirp thresholds to low frequency average (250, 500, 1000 Hz)

The r squared value was again found to be slightly better for the LS CE-Chirp (R^2 click=0.334; R^2 LS CE-Chirp=0.413). With regard to sensitivity and specificity, scores were identical for both ABR stimuli with a high sensitivity (96.4%) but low specificity (52.4%). The ROC curves in Figure 4 illustrate the diagnostic performance of the click compared to the LS CE-Chirp when predicting LFA.

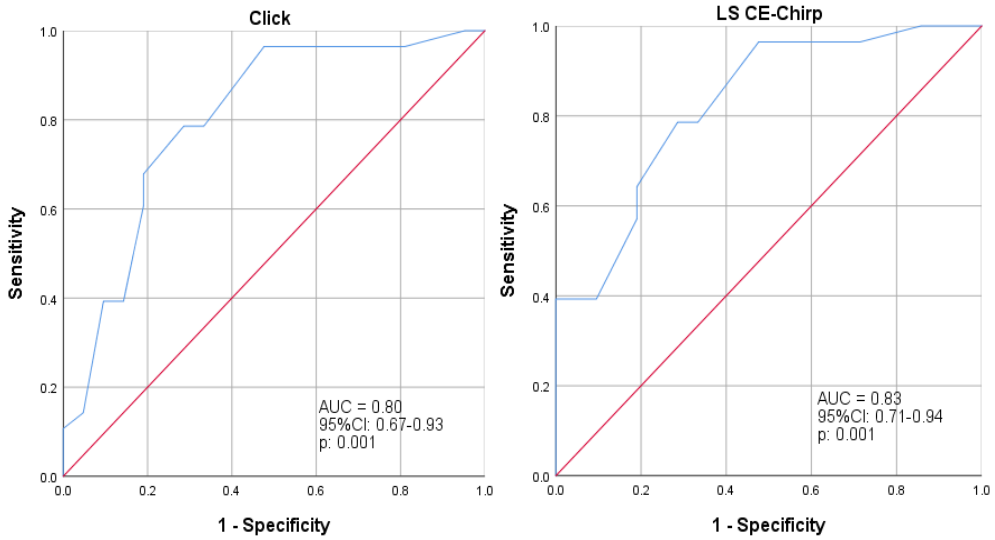

Figure 4 ROC curves illustrating the diagnostic accuracy of the click and LS CE-Chirp for the estimation of low frequency average (LFA; AUC = area under the curve; CI = confidence interval)

Both techniques showed good AUC values (AUC^{click}=0.80; $AUC^{LS\ CE\text{-}Chirp}$=0.83), with the LS CE-Chirp performing marginally better. A Pearson product-moment correlation indicated a moderate, positive, statistically significant correlation between audiometric LFA and the click- evoked ABR thresholds (r^{click}=0.578, $p<0.05$), and a strong, positive, statistically significant correlation between audiometric LFA and LS CE-Chirp-evoked thresholds ($r^{LS\ CE\text{-}Chirp}$=0.643, $p<0.05$).

3.4.3 ABR versus high frequency average (HFA = 2000, 4000, 8000 Hz)

The amount of variance between ABR thresholds and HFA is illustrated in Figure 5.

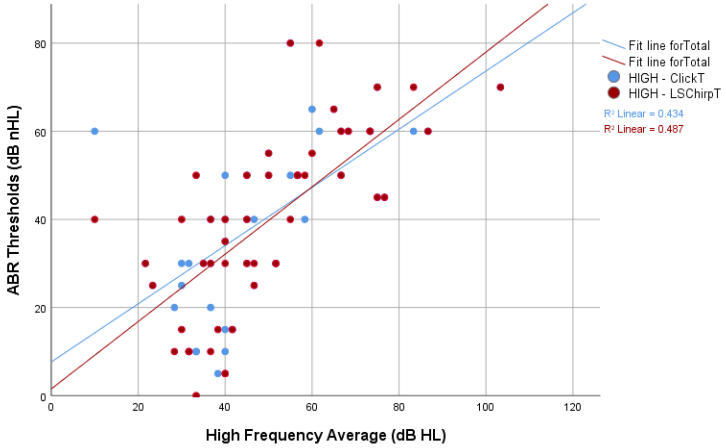

Figure 5 Scatterplot comparing click- and LS CE-Chirp thresholds to high frequency average (2000, 4000, 8000 Hz)

A very similar r squared value was found for click and LS CE-Chirp compared to HFA, with the LS CE-Chirp being slightly better again (R^2 click=0.434; R^2 LS CE-Chirp=0.487).

With regard to diagnostic accuracy when predicting audiometric high frequency average, similar sensitivity (77.8%) and specificity (50%) scores were obtained for both click- and LS CE-Chirp-evoked ABR's. The diagnostic performance of the click versus the LS CE-Chirp is presented in the ROC curves in Figure 6.

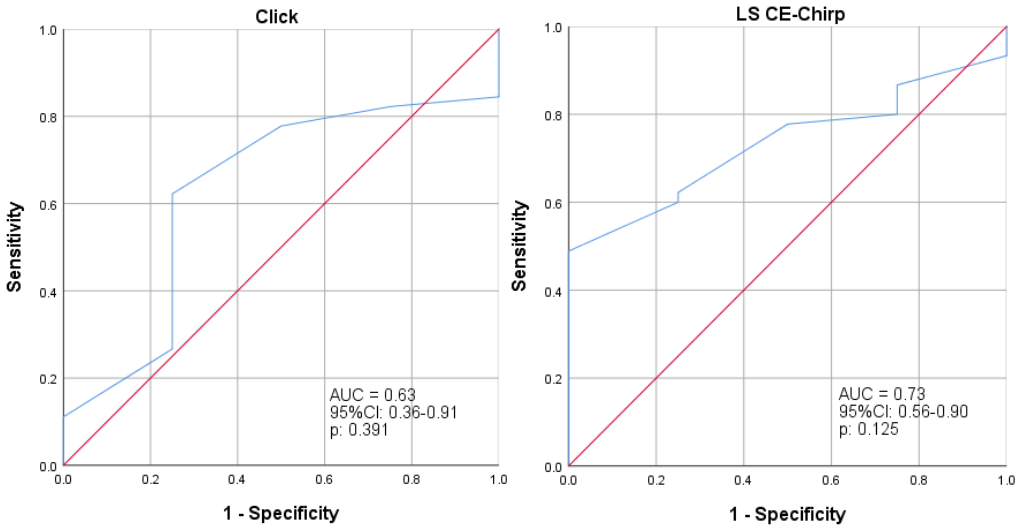

Figure 6 ROC curves illustrating the diagnostic accuracy of the click and LS CE-Chirp stimulus for the estimation of high frequency average (HFA; AUC = area under the curve; CI = confidence interval).

These ROC curves shows a poor AUC value with a broad confidence interval for click (AUC=0.63) and a fair AUC value for LS CE-Chirp (AUC=0.73). The Pearson product-moment correlation showed a strong, statistically significant, positive correlation between audiometric HFA and ABR thresholds (r^{click}=0.659, $p<0.05$; $r^{LS\ CE\text{-}Chirp}$=0.698, $p<0.05$).

3.4.4 Frequency specific correlation

Frequency specific correlations between behavioural pure tone thresholds and click- and LS CE-Chirp-evoked ABR thresholds are presented in Table 3.

Table 3 Correlation between individual behavioural pure tone thresholds, behavioural low frequency (250, 500, 1000 Hz), pure tone (500, 1000, 2000 Hz), and high frequency (2000, 4000, 8000 Hz) average thresholds, and click and LS CE-Chirp-evoked ABR thresholds.

	Correlation between pure tone thresholds and click-evoked ABR	***Correlation between pure tone thresholds and LS CE-Chirp-evoked ABR***
Frequency (Hz)	*Pearson*	*Pearson*
250	0.472***	0.526***
500	0.526***	0.597***
1000	0.641***	0.701***
2000	0.781***	0.768***
4000	0.726***	0.715***
8000	0.357**	0.472**
PTA	0.805***	0.820***
LFA	0.578***	0.643***
HFA	0.659***	0.698***

ABR=auditory brainstem response; PTA=pure tone average; LFA=low frequency average; HFA=high frequency average; *=p<0.05; **=p<0.01; ***=p<0.001

For ABR using a click stimulus, statistically significant, strong correlations with behavioural thresholds were found at 2000 Hz (r=0.781) and 4000 Hz (r=0.726). For ABR using LS CE-Chirp, correlations were strong at 1000 Hz (r=0.701), 2000 Hz (r=0.768) and 4000 Hz (r=0.715), with the highest correlation being at 2000 Hz (r=0.768).

3.5 Discussion

The aim of this study was to evaluate the diagnostic accuracy of LS CE-Chirp-evoked ABRs compared to click-evoked ABRs for the identification of different degrees of hearing loss. In contrast to the click stimulus, the CE-Chirp is designed to elicit responses from the entire cochlea, in the hope that this would lead to better predictive performance, especially in the lower frequency range (Cobb & Stuart, 2014; Junius & Dau, 2005; Maloff & Hood, 2014). Therefore the expected outcome of this study was that the LS CE-Chirp stimulus would be able to accurately identify hearing loss greater than 30 dB HL in low-, mid- and high-frequency ranges.

Overall, the results in this study indicated slightly better correlation between LS CE-Chirp-evoked thresholds and behavioural PTA, LFA and HFA thresholds compared to click-evoked ABR thresholds. With reference to difference scores between ABR thresholds and behavioural thresholds (PTA, LFA and HFA), the LS CE-Chirp performed marginally better with closer proximity to PTA and LFA, while the click-

evoked thresholds was in closer proximity to HFA. Both ABR stimuli showed similar sensitivity and specificity for prediction of behavioural thresholds.

Comparative AEP sensation levels

No significant differences were observed between difference scores between behavioural PTA, LFA and HFA and click- and LS CE-Chrip-evoked ABR thresholds (Table 2, $p>0.05$). Although similar difference values were obtained for both ABR stimuli, slightly smaller difference values were observed between LS CE-Chirp-evoked ABR thresholds and behavioural thresholds (LFA and PTA), indicating closer proximity of LS CE-Chirp thresholds to LFA and PTA compared to click-evoked thresholds. Click-evoked thresholds were in closer proximity to HFA with marginally smaller difference values observed between click-evoked thresholds and HFA compared to LS CE-Chirp. When looking at the proximity of ABR thresholds to PTA, absolute difference scores for click (9.25 dB) and LS CE-Chirp (9.01 dB) were similar, showing over- or underestimation of about 9 dB HL. For LFA thresholds, both raw- and absolute difference values (click=14.39 dB; LS CE-Chirp=13.54 dB) were higher than for PTA thresholds, indicating less accuracy for both ABR stimuli in the lower frequency range. However, smaller difference values were observed between LS CE-Chirp-evoked ABR threshold and LFA than between click-evoked ABR threshold and LFA, indicating closer proximity for LS CE-Chirp to LFA. This is consistent with previous literature (Maloff & Hood, 2014; Xu et al., 2014). Maloff and Hood (Maloff & Hood, 2014) reported that although there was no significant difference between click-evoked and CE-Chirp-evoked ABR thresholds, thresholds were closer to overall behavioural threshold for the CE-Chirp stimulus.

The click performed slightly better for prediction of the HFA, with click thresholds being closer to behavioural HFA thresholds than LS CE-Chirp thresholds (click=13.95 dB; LS CE-Chirp=15.27 dB). Xu et al. (Xu et al., 2014) evaluated the difference between LS CE-Chirp-evoked thresholds and VRA thresholds, and also found smaller difference scores in the LFA compared to the HFA.

Correlation of AEP and behavioural thresholds

On inspection of the squared correlation coefficient and scatterplots, a trend was noted. The LS CE-Chirp-evoked ABR showed better correlation to behavioural thresholds than the click-evoked ABR when predicting LFA, PTA and HFA.

The LS CE-Chirp predicted 67.2% of the PTA thresholds accurately compared to the click's 64.7%. However, that leaves 33-35% of variance in audiometric PTA data that was inaccurately predicted by both stimuli. Thus ABR using LS CE-Chirp stimulus predicts the PTA threshold slightly better than using a click stimulus.

Both ABR stimuli showed a greater variability and broader scatter for prediction of LFA- and HFA behavioural thresholds compared to prediction of the PTA threshold. The LS CE-Chirp however, showed slightly better correlation to behavioural LFA- and HFA thresholds than the click. LS CE Chirp- and click-evoked ABR respectively predicted 41.3% and 33.4% of the audiometric LFA thresholds accurately.

For audiometric HFA thresholds 48.7% and 43.4% of the observed variance can be explained for LS CE-Chirp and click respectively. These findings show that the LS CE-Chirp performs better than the click when used for prediction of PTA, LFA and HFA.

The better goodness of fit observed for PTA suggests that the LS CE-Chirp performed better in the mid frequency range (500, 1000 and 2000 Hz) compared to the click. This is similar to the observations made by Xu et al. (Xu et al., 2014), where they explored the clinical efficacy of the LS CE-Chirp stimulus by investigating the relationship between LS CE-Chirp-evoked ABR thresholds and visual reinforcement audiometry (VRA) thresholds in infants presenting with different degrees of sensorineural hearing loss. A clear correlation was observed between LS CE-Chirp ABR thresholds and VRA thresholds especially in the low to middle frequency range (250–1000 Hz) (Xu et al., 2014).

Pearson's correlation co-efficient values were calculated to further investigate the correlation between behavioural pure tone- and LS CE Chirp-evoked ABR thresholds, and between behavioural pure tone- and click-evoked thresholds. A very

strong, positive, statistically significant correlation was found between both click and LS CE-Chirp thresholds, and PTA (r^{click}=0.805; $r^{LS\ CE\text{-}Chirp}$=0.820). A moderate, positive, statistically significant correlation was found between audiometric LFA and click- evoked ABR thresholds (r^{click}=0.578), while, a strong, positive, statistically significant correlation was found between audiometric LFA and LS CE-Chirp-evoked thresholds ($r^{LS\ CE\text{-}Chirp}$=0.643). Strong, positive, statistically significant correlations were observed between both ABR thresholds and HFA (r^{click}=0.659; $r^{LS\ CE\text{-}Chirp}$=0.698). A similar trend was observed here, showing slightly better correlations and less variance for the LS CE-Chirp stimulus at all frequency averages. A study by Cho et al. (Cho et al., 2015) compared the correlation between click- and CE-Chirp-evoked ABR thresholds and behavioural pure tone thresholds in participants with sensorineural hearing loss. They found significant correlations at 500, 1000, 2000 and 3000 Hz for CE-Chirps and at 1000, 2000, 3000 and 4000 Hz for clicks, showing that CE-Chirp responses correlate better with behavioural thresholds at 500 Hz, while clicks correlation was marginally better at 4000Hz (Cho et al., 2015). The same was found in the current study, showing that the LS CE-Chirp does include more information from lower-frequency parts of the cochlea.

On inspection of previous studies it is generally considered that there is a clear correlation between behavioural thresholds at 2000-4000 Hz and click-evoked ABR thresholds (Cho et al., 2015; Gorga et al., 2008). Similar findings were made in the current study with regard to frequency specific correlation, with the click ABR correlating best with 2000 and 4000 Hz (r>0.70), while the LS CE-Chirp ABR correlated best with a broader frequency range, namely 1000, 2000 and 4000 Hz (r>0.70). The strongest correlation for both ABR stimuli was measured at 2000 Hz (r^{click}=0.781, p<0.05; $r^{LS\ CE\text{-}Chirp}$=0.768, p<0.05) with the weakest correlation found at 8000 Hz (r^{click}=0.357, p<0.05; $r^{LS\ CE\text{-}Chirp}$=0.427, p<0.05). These findings are in line with findings and hypothetical predictions in literature and confirm the notion that the LS CE-Chirp provides information about a larger portion of the cochlea than the click (Maloff & Hood, 2014; Xu et al., 2014). Maloff and Hood (Maloff & Hood, 2014) reported a strong correlation between overall behavioural pure tone thresholds and CE-Chirp-evoked ABR thresholds in their mild to moderate sensorineural hearing loss group (SNHL>25 dB HL and <70 dB HL), with no significant difference between behavioural thresholds and thresholds estimated using the CE-Chirp. Additionally,

results from the current study showed that the correlational performance of the LS CE-Chirp is slightly better than that of the gold standard click in the high frequencies. So the LS CE-Chirp does not only include more information from lower-frequency parts of the cochlea, it also shows slightly better correlation to high frequency behavioural thresholds when compared to the gold standard click ABR.

Prediction of presence of hearing loss

In terms of sensitivity and specificity, similar values were obtained for clicks and LS CE-Chirps when using the ABR as a screening tool for predicting hearing loss greater or less than 30 dB HL. Both ABR stimuli showed a very high sensitivity but low specificity for the prediction of behavioural PTA (96.7%; 57.9%) and LFA (96.4%; 52.4%). A drop in sensitivity (to 77.8%) was however noted for the prediction of the behavioural HFA in comparison with PTA and LFA, with specificity remaining approximately the same (50%) for both click and LS CE-Chirp. This shows that both ABR stimuli are better able to identify individual with hearings loss than they are able to identify those with normal hearing sensitivity (of better than 30 dB HL) in the current research sample. This means that 22.2% of individuals with hearing loss in the high frequency range were not identified (false negative). A study by Johnson et al. (J. L. Johnson et al., 2005) explored the accuracy of the two-stage otoacoustic emission (OAE) and AABR protocol that is widely used for identifying hearing loss in newborns. In this study all study sites used AABR systems that use the click stimulus and most study sites used TEOAE except for one. They raised the concern about newborns that the fail OAE screening but then pass AABR screening because AABRs may miss a mild hearing loss (J. L. Johnson et al., 2005). When compared to the current study, it is possible that the number of false negatives may be lower when employing AABR systems that use the LS CE-Chirp instead of the click. Thus there may be less missed newborns when using LS CE-Chirp-evoked ABRs, however, further research on the number of infants that pass with AABR using LS CE-Chirp is needed.

ROC curves were employed to further investigate the sensitivity and specificity of the click and LS CE-Chirp. The AUC value relates to diagnostic accuracy. For identification of hearing loss in the PTA range an excellent AUC value was obtained for click (AUC=0.91) and a good AUC value for LS CE-Chirp (AUC=0.89). However,

a poor AUC value of only 0.63 was measured for the click's ability to identify a hearing loss in the HFA range, whereas, the LS CE-Chirp was able to identify a high frequency hearing loss fairly accurately (AUC=0.73). Despite the poor AUC, the LS CE-Chirp showed marginally better correlation to HFA than the click and is also more sensitive for identification of a hearing loss greater than 30 dB HL in the high frequency range than the click-evoked ABR. This may be due to the variety of hearing loss configurations in the mean sample. The participant sample consisted of individuals (33 ears) with mild to moderate sloping SNHL but also included individuals (16 ears) with moderate to mild reverse sloping SNHL. Research on the diagnostic accuracy of these stimuli is limited, especially in populations with hearing loss and should therefore be explored in future studies.

Good AUC values were recorded for both ABR stimuli in the LFA range (AUC^{click}=0.80; $AUC^{LS\ CE\text{-}Chirp}$=0.83). This was unexpected for the click, as the click ABR is known to be independent of low frequency information (Cebulla et al., 2012; Chertoff, Lichtenhan, & Willis, 2010b; Elberling et al., 2007; Petoe et al., 2010; Zirn et al., 2014). These findings may be due to the presence of a mean mild degree of hearing loss in the high frequencies in the ears with reverse sloping hearing losses. Nevertheless, when it is compared to the chirp's ability to identify the presence of a hearing loss in this sample, the chirp did marginally better, also showing a narrower confidence interval than the click (CI^{click}=0.67-0.93; $CI^{LS\ CE\text{-}Chirp}$=0.71-0.94).

To conclude, the predictive accuracy of the LS CE Chirp-evoked ABR is slightly better than that of the click with reference LFA thresholds(r^{click}=0.578, $r^{LS\ CE\text{-}Chirp}$=0.643; AUC^{click}=0.80; $AUC^{LS\ CE\text{-}Chirp}$=0.83; CI^{click}=0.67-0.93, $CI^{LS\ CE\text{-}Chirp}$=0.71-0.94); furthermore, it is less variable and more accurate than the click-evoked ABR with reference to HFA thresholds(r^{click}=0.659, $r^{LS\ CE\text{-}Chirp}$=0.698; AUC^{click}=0.63; $AUC^{LS\ CE\text{-}Chirp}$=0.73; CI^{click}=0.36-0.91, $CI^{LS\ CE\text{-}Chirp}$=0.56-0.90). When looking at AUC for prediction of PTA the click performed slightly better (r^{click}=0.805, $r^{LS\ CE\text{-}Chirp}$=0.820; AUC^{click}=0.91, $AUC^{LS\ CE\text{-}Chirp}$=0.89; CI^{click}=0.83-0.99, $CI^{LS\ CE\text{-}Chirp}$=0.80-0.99).

The mean audiogram of the total participant sample showed a mild hearing loss in the low frequencies with a greater degree of loss in the mid- and high frequency range. As mentioned before the participant sample included 33 ears with mild to

moderate sloping SNHL but it also included 16 ears with reverse sloping SNHL. With a greater degree of hearing loss in the low frequencies, or with low frequency hearing loss and normal high frequency sensitivity, these results may well be different. Therefore it would be ideal for future studies to focus on participants with purely low frequency hearing losses and normal high frequency hearing thresholds, to evaluate if advancements observed with regard to threshold estimation and diagnostic accuracy in the normal hearing population when using the LS CE-Chirp stimulus can be generalized to this type of hearing impairment, however, such losses are difficult to find.

3.6 Conclusion

The results from this study demonstrated that threshold estimates elicited by LS CE-Chirps and the gold standard click are well correlated without significant differences in results when comparing the two ABR stimuli. However, the predictive performance of the LS CE Chirp-evoked ABR was slightly better than that of the click with reference to PTA, LFA and HFA. For the prediction of HFA the LS CE-Chirp performed better than the click-evoked ABR and showed less variability. Thus, the LS CE-Chirp is an effective, accurate ABR stimulus for the identification of different degrees of hearing loss hearing when compared to the gold standard click stimulus.

4 DISCUSSION AND CONCLUSION

4.1 Summary of results

In recent years the CE-Chirp stimulus has been designed and implemented in AABR equipment for the purpose of newborn hearing screening (Young Futures, 2014) However, research on the correlation of CE-Chirp with different degrees and configurations of hearing loss is limited (Cho et al., 2015). The purpose of this study was to evaluate the diagnostic accuracy of LS CE Chirp-evoked ABRs compared to click-evoked ABRs for the identification of different degrees and configurations of hearing loss. In contrast to the click stimulus, the CE-Chirp is designed to elicit responses from the entire cochlea, in the hope that this would lead to better predictive performance, especially in the lower frequency range (Cobb & Stuart, 2014; Junius & Dau, 2005; Maloff & Hood, 2014). Therefore the expected outcome

of this study was that the LS CE-Chirp stimulus would be able to accurately identify hearing loss greater than 30 dB HL in low-, mid- and high-frequency ranges.

Data from 49 ears with a mean mild to moderate SNHL was analyzed. No significant differences were observed between difference scores between behavioural PTA, LFA and HFA and click- and LS CE-Chrip-evoked ABR thresholds (Table 2). Although similar difference values were obtained for both ABR stimuli, slightly smaller difference values were observed between LS CE-Chirp-evoked ABR thresholds and behavioural thresholds (LFA and PTA), indicating closer proximity of LS CE-Chirp thresholds to LFA (click=14.39 dB, LS CE-Chirp=13.54 dB) and PTA (click=9.25 dB; LS CE-Chirp=9.01 dB) compared to click-evoked thresholds. The click performed slightly better for prediction of the HFA, with click- evoked thresholds being in closer proximity to HFA compared to LS CE-Chirp thresholds (click=13.95 dB; LS CE-Chirp=15.27 dB). This is in line with findings made by Maloff and Hood (2014) who reported that although there was no significant difference between click-evoked and CE-Chirp-evoked ABR thresholds; thresholds were closer to overall behavioural threshold for the CE-Chirp stimulus.

A trend was noted, on inspection of the squared correlation coefficient and scatterplots. The LS CE-Chirp-evoked ABR showed better correlation to behavioural thresholds than the click-evoked ABR when predicting LFA, PTA and HFA. The LS CE-Chirp predicted 67.2% of the PTA thresholds accurately compared to the click's 64.7%. The LS CE-Chirp also showed slightly better correlation to behavioural LFA- and HFA thresholds compared to the click. LS CE Chirp- and click-evoked ABR respectively predicted 41.3% and 33.4% of the audiometric LFA thresholds accurately. For audiometric HFA thresholds 48.7% and 43.4% of the observed variance can be explained for LS CE-Chirp and click respectively. The better goodness of fit observed for PTA suggests that the LS CE-Chirp performs better in the mid frequency range (500, 1000 and 2000 Hz) compared to the click. This is similar to findings obtained by Xu et al. (2014) where they observed a clear correlation between LS CE-Chirp ABR thresholds and VRA thresholds especially in the low- to middle frequency range (250-1000 Hz).

Furthermore, Pearson's correlation co-efficient values were calculated and showed statistically significant correlations between both ABR stimuli and all behavioural pure tone average groups A very strong, positive, statistically significant correlation was found between both click and LS CE-Chirp thresholds, and PTA (r^{click}=0.805; $r^{LS\ CE\text{-}Chirp}$=0.820). A moderate, positive, statistically significant correlation was found between audiometric LFA and click- evoked ABR thresholds (r^{click}=0.578), while, a strong, positive, statistically significant correlation was found between audiometric LFA and LS CE-Chirp-evoked thresholds ($r^{LS\ CE\text{-}Chirp}$=0.643). Strong, positive, statistically significant correlations were observed between both ABR thresholds and HFA (r^{click}=0.659; $r^{LS\ CE\text{-}Chirp}$=0.698). A similar trend was observed here, showing slightly better correlations and less variance for the LS CE-Chirp stimulus at all frequency averages. On inspection of previous studies it is generally considered that there is a clear correlation between behavioural thresholds at 2000-4000 Hz and click-evoked ABR thresholds (Cho et al., 2015; Gorga et al., 2008). Similar findings were made in the current study with regard to frequency specific correlation, with the click ABR correlating best with 2000 and 4000 Hz (r>0.70), while the LS CE-Chirp ABR correlated best with 1000, 2000 and 4000 Hz (r>0.70). The strongest correlation for both ABR stimuli was measured at 2000 Hz (r^{click}=0.781, p<0.05; $r^{LS\ CE\text{-}Chirp}$=0.768, p<0.05) with the weakest correlation found at 8000 Hz (r^{click}=0.357, p<0.05; $r^{LS\ CE\text{-}Chirp}$=0.427, p<0.05). These findings are in line with findings and hypothetical predictions in literature and confirm the notion that the LS CE-Chirp provides information about a larger portion of the cochlea than the click (Maloff & Hood, 2014; Xu et al., 2014). Maloff and Hood (2014) reported a strong correlation between overall behavioural pure tone thresholds and CE-Chirp-evoked ABR thresholds in their mild to moderate sensorineural hearing loss group, with no significant difference between behavioural thresholds and the thresholds estimated using CE-Chirp. Results from this study also showed better diagnostic performance for the LS CE-Chirp in the high frequencies compared to the click. So not only does the LS CE-Chirp include more information from lower-frequency parts of the cochlea, it also showed slightly better correlation to high frequency behavioural thresholds when compared to the gold standard click ABR.

Similar sensitivity and specificity values were obtained for clicks and LS CE-Chirps when using the ABR as a screening tool for predicting hearing loss greater or less than 30 dB HL. Both ABR stimuli showed a very high sensitivity but low specificity for the prediction of behavioural PTA (96.7%; 57.9%) and LFA (96.4%; 52.4%). A drop in sensitivity (to 77.8%) was however noted for the prediction of the behavioural HFA with specificity remaining approximately the same (50%) for both click and LS CE-Chirp. This shows that both ABR stimuli are better able to identify individual with hearings loss than they are able to identify those with normal hearing sensitivity (of better than 30 dB HL) in the current research sample.

ROC curves were employed to further investigate the sensitivity and specificity of the click and LS CE-Chirp. For identification of hearing loss in the PTA range good AUC values were obtained for both click (AUC=0.91) and LS CE-Chirp (AUC=0.89). A poor AUC value of only 0.631 was measured for the click's ability to identify a hearing loss in the HFA range, whereas, the LS CE-Chirp was able to identify a high frequency hearing loss fairly accurately (AUC=0.73). Good AUC values were recorded for both ABR stimuli in the LFA (AUC_{click}=0.80; $AUC_{LS\ CE\text{-}Chirp}$=0.83). This was unexpected for the click, as the click ABR is known to be independent of low frequency information (Cebulla et al., 2012; Chertoff et al., 2010; Elberling et al., 2007; Petoe et al., 2010; Zirn et al., 2014). Nevertheless, when it is compared to the chirp's ability to identify the presence of a hearing loss in this sample, the chirp did marginally better, also showing a narrower confidence interval than the click (CI_{click}=0.67-0.93; $CI_{LS\ CE\text{-}Chirp}$=0.71-0.94).

The general observations from results of this study indicated slightly better correlation between LS CE-Chirp-evoked thresholds and behavioural PTA, LFA and HFA thresholds compared to click-evoked ABR thresholds. With reference to difference scores between ABR thresholds and behavioural thresholds (PTA, LFA and HFA), the LS CE-Chirp performed marginally better for prediction of PTA and LFA, while the click performed slightly better for prediction of HFA. Both ABR stimuli showed good diagnostic accuracy when predicting PTA and LFA, however, a drop in sensitivity was noted for prediction of HFA for both click and LS CE-chirp.

4.2 Clinical implications

The findings of this study showed that the LS CE-Chirp is an effective stimulus to use for the purpose of objective estimation of hearing sensitivity for a few reasons. Firstly, the LS CE-Chirp yields responses that are better correlated to behavioural thresholds at all frequency averages compared to the click. Secondly, when compared to click-evoked ABRs, LS CE-Chirp-evoked ABRs provides a more accurate representation of overall BM activity, as it includes information from lower frequency areas in the cochlea. Additionally, in the high frequency regions, the LS CE-Chirp performs similar to the gold standard click stimulus which is generally used in AABR equipment (Cobb & Stuart, 2014; Hyvärinen, 2012; K. Johnson, 2002; Young Futures, 2014). These findings and findings from previous studies suggest that the implementation of the LS CE-Chirp in screening equipment has several advantages. The LS CE-Chirp yields improved reliability, better quality of hearing sensitivity estimations and due to the large response amplitude elicited by CE-Chirps, responses are easier to interpret and test time is reduced (Bargen, 2015; Cebulla, Lurz, & Shehata-Dieler, 2014; Cobb & Stuart, 2014; Elberling & Don, 2008; Maloff & Hood, 2014; Mühler et al., 2013; Young Futures, 2014).

4.3 Critical evaluation and future research

A critical evaluation of this study was conducted to evaluate its strengths and limitations. These are indicated below:

Strengths

This study was one of the first to investigate the diagnostic accuracy of LS CE-Chirp-evoked ABRs in populations with hearing impairments, especially reverse sloping hearing loss configurations, as most previous studies only focus on normal normal-hearing populations (Bargen, 2015). Because the LS CE-Chirp stimulus is based on normal cochlear functioning it is still unclear whether advancements seen in normal-hearing populations can also be seen in different hearing loss groups (Maloff & Hood, 2014). Findings suggested that the LS CE-Chirp is an effective, accurate stimulus to use for estimation of hearing sensitivity and that these advancements can be observed in populations with hearing impairments. In this study, variables were

kept consistent; data was collected in a controlled environment using objective measures leading to results that are relatively independent of the researchers. The study also identified limitations and provided information on which to further build and explore in future research studies.

Limitations of the study

One of the main limitations in this study was the size of the research sample, as low frequency hearing losses are difficult to find. Secondly, assessments for each participant were long and the data collection procedure was very time consuming. Another limitation was the configuration of the mean behavioural audiogram of the study sample. Due to the combination of reverse sloping- and high-frequency sloping sensorineural loss, there was a broad variance between the different thresholds at each frequency. The mean audiogram of the total participant sample showed a mild hearing loss in the low frequencies with a greater degree of loss in the mid- and high frequency range. With a greater degree of hearing loss in the low frequencies these results may be different. Therefore it would be ideal for future studies to focus on participants with purely low frequency hearing losses and normal high frequency hearing thresholds, to evaluate if advancements observed with regard to threshold estimation and diagnostic accuracy in the normal hearing population when using the LS CE-Chirp stimulus can be generalized to this particular type of hearing impairment, however, such losses are difficult to find.

4.4 Conclusion

The results from this study demonstrated that threshold estimates elicited by LS CE-Chirps and the gold standard click are well correlated without significant differences when comparing the two ABR stimuli. However, the predictive performance of the LS CE Chirp-evoked ABR was marginally better than that of the click with reference to PTA and LFA. Additionally, for the prediction of high frequency hearing thresholds the LS CE-Chirp performed better than the click-evoked ABR and showed less variability. Thus, the LS CE-Chirp is an effective, accurate ABR stimulus for the identification of different degrees and configurations of hearing loss when compared to the gold standard click stimulus.

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6 APPENDICES

APPENDIX A: Ethical approval

UNIVERSITEIT VAN PRETORIA
UNIVERSITY OF PRETORIA
YUNIBESITHI YA PRETORIA

Faculty of Humanities
Research Ethics Committee

2 May 2017

Dear Ms van Dyk

Project:	**Frequency correlation of the LS CE-Chirp evoked auditory brainstem response in adults with a sensorineural hearing loss**
Researcher:	**Z van Dyk**
Supervisors:	**Prof B Vinck and Dr L Biagio**
Department:	**Speech-Language Pathology and Audiology**
Reference number:	**13098421 (GW20170218HS)**

Thank you for the response to the Committee's correspondence of 1 March 2017.

I have pleasure in informing you that the Research Ethics Committee formally **approved** the above study at an *ad hoc* meeting held on 2 May 2017. Data collection may therefore commence.

Please note that this approval is based on the assumption that the research will be carried out along the lines laid out in the proposal. Should your actual research depart significantly from the proposed research, it will be necessary to apply for a new research approval and ethical clearance.

We wish you success with the project.

Sincerely

Prof Maxi Schoeman
Deputy Dean: Postgraduate and Research Ethics
Faculty of Humanities
UNIVERSITY OF PRETORIA
e-mail: tracey.andrew@up.ac.za

cc: Prof B Vinck (Supervisor)
Dr L Biagio (Supervisor)

APPENDIX B: Informed consent form

UNIVERSITEIT VAN PRETORIA
UNIVERSITY OF PRETORIA
YUNIBESITHI YA PRETORIA

Faculty of Humanities
Department of Speech-Language Pathology and Audiology

INFORMED CONSENT FORM

Please complete the following:

I_____, hereby confirm that I have read and understood the information form detailing the purpose and procedure of this research study. I have also had an opportunity to ask any questions I had about the study.

I hereby consent to participation in this study. I understand that participation in the research study is voluntary and that I may withdraw from the study at any time without any negative consequences. I also understand that the data will be used for research purposes, in accordance with the information provided in the information letter.

_____
Signature

_____
Date

_____
Contact number(s)

APPENDIX C: Participant information letter

UNIVERSITEIT VAN PRETORIA
UNIVERSITY OF PRETORIA
YUNIBESITHI YA PRETORIA

Faculty of Humanities
Department of Speech-Language Pathology and Audiology

PARTICIPANT INFORMATION LETTER

Dear Participant,

Thank you for considering participating in the research study titled '*Diagnostic accuracy of CE-Chirp'*. Information regarding this study as well as what can be expected to happen during the study is detailed in this letter. Please read the information and complete the consent form should you choose to participate in the research.

Information regarding the research study:
The purpose of the study is to evaluate the diagnostic accuracy of the LS CE-Chirp-evoked ABR compared to the click-evoked ABR for the identification of different degrees of hearing loss. The CE-Chirp stimulus was designed to provide information from the entire cochlea which yields large response amplitudes. For this reason, the CE-Chirp has recently been implemented in auditory brainstem response equipment for the purpose of newborn hearing screening. However, research on the correlation of CE-Chirps with different degrees and configurations of hearing loss is limited. Therefore this study will explore how accurately the level-specific chirp (LS CE-Chirp) is able to identify a hearing loss.

Participant candidacy and selection process
For this study adults with a mild or greater degree of hearing loss in at least the low frequencies are required. During the selection process, we will determine if the participant is a candidate for participation through a brief interview and audiological assessment. The results of the audiological tests must indicate a low frequency sensorineural hearing loss and no evidence of middle ear pathology.

Procedure
Participation in the study will involve a single assessment period lasting about two and a half hours. The assessment will include a quick test to ensure the middle ear is healthy (these tests are conducted by placing an eartip in the participant's ear during which you will hear different sounds, participants are not required to respond in any way), a behavioural hearing assessment (this test will require the participant to indicate when they hear sounds that are presented to them) and an objective hearing assessment (this test will require no co-operation from the participant). Participants willing to partake in the study should have an understanding of conversational English or Afrikaans as it will be required of the participant to follow instructions during the behavioral hearing test.

Test venue
The tests will take place at the University of Pretoria at the Department of Speech-Language Pathology and Audiology (in the Communication Pathology building, main campus).

Possible risks and benefits associated with this study
There are no risks involved in participating in the study. The assessment is quite long and participants might fatigue. It is however recommended that participants relax during the objective hearing test as it is not necessary for them to respond or co-operate during this test. There are no direct benefits of participating in this study and no reimbursements will be given to participants.

Confidentiality and anonymity
All participants' personal information and audiometric results will be kept confidential. Each participant will be allocated an alpha-numeric code to ensure anonymity. This code will be used during data analysis. The code will only be known by the researchers. The results of the research will be stored at the Department of Speech-Language Pathology and Audiology for a minimum period of 15 years as this is policy at the University of Pretoria. During this period data may be used for future research.

Sharing of results
The knowledge obtained from this research will be reported in the form of a scientific article. This dissertation will be available to professionals in the field of audiology. The article will be published in a scientific journal. If you would like a summary of the findings a copy can be sent to you when the project is complete.

Refusal or withdrawal from the research
Participation in this research is completely voluntary. If you wish to withdraw from the study, you may do so at any time.

Contact details
If you have any questions or concerns about any aspect of this study please feel free to contact us.

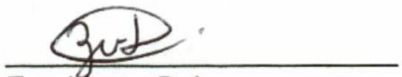
Researcher
Miss Zandri van Dyk
Tel: +27 79 502 6363
Email: vandyk.zandri9@gmail.com

Supervisor
Prof Bart Vinck
Tel: +27 12 420 2355
Email: bart.vinck@up.ac.za

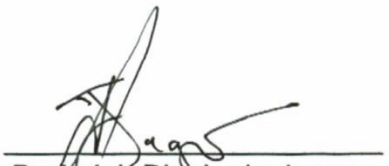
Supervisor
Dr Leigh Biagio de Jager
Tel: +27 12 420 6774
Email: leigh.biagio@up.ac.za

Thank you for considering participating in this study.

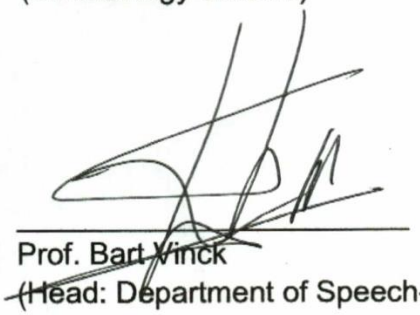
With thanks and kind regards,



Zandri van Dyk
(B.Audiology student)



Dr. Leigh Biagio de Jager
(Supervisor)



Prof. Bart Vinck
(Head: Department of Speech-Language Pathology and Audiology)

APPENDIX D: Case history form

UNIVERSITEIT VAN PRETORIA
UNIVERSITY OF PRETORIA
YUNIBESITHI YA PRETORIA

Case history

Participant Code: _____ Gender: _____

DOB: _____ Age: _____

1. What do you think caused the hearing loss?

_____

2. How long has it been since you noticed a problem?

_____

3. Has your difficulty with hearing been gradual or sudden?

_____

4. How has it evolved/changed since the start?

_____

5. Does your hearing problem affect both ears or just one ear?

_____

6. Do you have a history of ear infections?

_____

7. Have you noticed any pain in your ears or any discharge from your ears?

_____

8. Is there a history of hearing loss in your family?

_____

9. Do you experience dizziness/imbalance?

_____

10. Do you experience tinnitus/ringing in your ears?

_____

11. Are there situations where it is particularly difficult for you to follow a conversation, such as noisy restaurants, group situations, or in the car?

_____

12. Name all the medication that you are currently taking:

_____

13. Have you seen any other specialists (physician, psychologist, neurologist, etc.)? If yes, indicate the type of specialist, when you were seen, and the specialist's conclusions or suggestions.

_____

_____

APPENDIX E: Plagiarism declaration

DECLARATION OF ORIGINALITY

UNIVERSITY OF PRETORIA

The Department of Speech-Language Pathology and Audiology places great emphasis upon integrity and ethical conduct in the preparation of all written work submitted for academic evaluation.

While academic staff teach you about referencing techniques and how to avoid plagiarism, you too have a responsibility in this regard. If you are at any stage uncertain as to what is required, you should speak to your lecturer before any written work is submitted.

You are guilty of plagiarism if you copy something from another author's work (eg a book, an article or a website) without acknowledging the source and pass it off as your own. In effect you are stealing something that belongs to someone else. This is not only the case when you copy work word-for-word (verbatim), but also when you submit someone else's work in a slightly altered form (paraphrase) or use a line of argument without acknowledging it. You are not allowed to use work previously produced by another student. You are also not allowed to let anybody copy your work with the intention of passing if off as his/her work.

Students who commit plagiarism will not be given any credit for plagiarised work. The matter may also be referred to the Disciplinary Committee (Students) for a ruling. Plagiarism is regarded as a serious contravention of the University's rules and can lead to expulsion from the University.

The declaration which follows must accompany all written work submitted while you are a student of the Department of Speech-Language Pathology and Audiology. No written work will be accepted unless the declaration has been completed and attached.

Full names of student: Zandri van Dyk

Student number: 13098421

Topic of work: Diagnostic accuracy of CE-Chirp

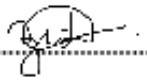
Declaration

1. I understand what plagiarism is and am aware of the University's policy in this regard.

2. I declare that this dissertation (eg essay, report, project, assignment, dissertation, thesis, etc) is my own original work. Where other people's work has been used (either from a printed source, Internet or any other source), this has been properly acknowledged and referenced in accordance with departmental requirements.

3. I have not used work previously produced by another student or any other person to hand in as my own.

4. I have not allowed, and will not allow, anyone to copy my work with the intention of passing it off as his or her own work.

SIGNATURE 

APPENDIX F: Declaration for the storage of research data and/or documents

UNIVERSITEIT VAN PRETORIA
UNIVERSITY OF PRETORIA
YUNIBESITHI YA PRETORIA

FACULTY OF HUMANITIES
RESEARCH ETHICS COMMITTEE

Declaration for the storage of research data and/or documents

I/ We, the principal researcher(s) Zandri van Dyk

and supervisor(s) Dr. Leigh Biagio-de Jager + Prof. Bart Vinck

of the following study, titled Frequency correlation of the LSCE-Chirp evoked auditory brainstem response in adults with a sensorineural hearing loss

will be storing all the research data and/or documents referring to the above-mentioned study in the following

department: Department of Speech-Language Pathology and Audiology

We understand that the storage of the mentioned data and/or documents must be maintained for a minimum of 15 years from the commencement of this study.

Start date of study: 1 January 2017

Anticipated end date of study: December 2017

Year until which data will be stored: 2032

Name of Principal Researcher(s)	Signature	Date
Zandri van Dyk		02/02/2017

Name of Supervisor(s)	Signature	Date
L. BIAGIO DE JAGER		7/2/2017

Name of Head of Department	Signature	Date
VINCK BART		03/02/2017

APPENDIX G: Proof of Submission (Article)

Gmail zandri van dyk <vandyk.zandri9@gmail.com>

Submission Confirmation

1 message

eesserver@eesmail.elsevier.com <eesserver@eesmail.elsevier.com> Mon, Dec 2, 2019 at 3:51 AM
Reply-To: PEDOT@elsevier.com
To: vandyk.zandri9@gmail.com

*** Automated email sent by the system ***

Dear Ms. Zandri van Dyk,

Your submission entitled "Diagnostic accuracy of CE Chirp" (Full Length Article)has been received by International Journal of Pediatric Otorhinolaryngology

You will be able to check on the progress of your paper by logging on to the Elsevier Editorial System as an author. The URL is https://ees.elsevier.com/ijporl/.

Your manuscript will be given a reference number once an Editor has been assigned.

Thank you for submitting your work to this journal.

Kind regards,

Administrative Editor
International Journal of Pediatric Otorhinolaryngology

For further assistance, please visit our customer support site at http://help.elsevier.com/app/answers/list/p/7923. Here you can search for solutions on a range of topics. You will also find our 24/7 support contact details should you need any further assistance from one of our customer support representatives.