Air- and Bone-conducted Brainstem Evoked Response Audiometry

Collection of normative data for the new-developed level-specific CE-chirp stimulus in normal-hearing adults

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Abstract

Background

Between 2010 and 2012, a new ABR stimulus has been developed: the level-specific (LS) CE-chirp. This stimulus attempts to compensate for the cochlear travelling wave delay and the change in latency with frequency per intensity, resulting in better neural synchrony and improving clinical interpretation. By aligning the arrival time of the frequencies in the LS CE-chirp at their location along the basilar membrane, a higher temporal synchronization of excitation for the broadband version of the LS CE-chirp (350 – 11.300 Hz) and similar latencies for the narrowband versions (NB 0.5k, 1k, 2k and 4k LS CE-chirp) should be attained.

Purpose

The aim of this study is to evaluate the suitability of the LS CE-chirp for air-conduction (AC) and bone-conduction (BC) ABR measurements. This study focuses on the latency for the AC and BC broadband and four different narrowband LS CE-chirp evoked ABRs. Latencies between the five chirps within one intensity are compared as well as latencies of the five chirps between AC and BC ABR and between 40, 70 and 90 dB nHL stimulus intensity level for AC ABR.

Methods

Broadband and narrowband LS CE-chirp evoked AC and BC ABRs are recorded in 50 normal-hearing young adults (25 females, 25 males). AC ABR measurements are performed at 40, 70 and 90 dB nHL and BC ABR at 40 dB nHL only. For BC ABR, a click stimulus is also used and compared to BC BB LS CE-chirp evoked ABR. Furthermore, BC ABR hearing threshold is established using the BB LS CE-chirp and compared to the subjective PTA and BB LS CE-chirp threshold. Stimuli are presented in both condensation and rarefaction polarity. Stimulus rates are based on recommendations of the Newborn Hearing Screening Programme (NHSP). EEG filter settings of 30 – 3000 Hz, a residual noise target line of 40 nV, artefact rejection level of 40 µV and Bayesian weighting are applied.

Results

BB and NB LS CE-chirps show similar latencies within one transduction method and one intensity. Between transduction methods, significant differences in latency are found. For the BB, NB 0.5k and NB 2k LS CE-chirp, significantly longer latencies for BC ABR compared to AC ABR are found. For the NB 4k LS CE-chirp, however, shorter latencies are found. Furthermore, significant differences in latency are found between the 40, 70 and 90 dB nHL conditions for each chirp except the NB 2k LS CE-chirp. Additionally, the results of the present study show a significant relationship between ABR latency and gender of the subject. Moreover, the objective BC BB LS CE-chirp hearing threshold is compared to two subjective hearing threshold measures. Results show relatively good agreement between the objective and subjective measures of BC hearing threshold.

Conclusions

Experiment 1 show BB and NB LS CE-chirp latencies are similar within one intensity. This indicates that the latency changes with frequency defined per intensity in the model of the LS CE-chirp are an adequate compensation for the cochlear travelling wave delay. The significant differences in latency for AC and BC ABR and between stimulus intensities for AC ABR are in agreement with what has been found for click-, toneburst- and CE-chirp evoked ABR. Also, the significant differences between click- and BB LS CE-chirp evoked BC ABR are in agreement with earlier research concerning LS CE-chirp evoked AC ABR. Furthermore, experiment 3 shows LS CE-chirp evoked ABRs at 70 dB nHL are a feasible measure to assess otoneurological pathologies, using a TDH-39 supra-aural earphone. Finally, experiment 4 shows that it is possible to perform threshold measurements using BB LS CE-chirp evoked BC ABR and reach fairly good agreement with subjective measures of hearing threshold.

Keywords

Auditory Brainstem Response; LS CE-chirp; narrowband chirps; bone-conduction; latency; otoneurological assessment; BC hearing threshold

Summary in Dutch

Achtergrond

Tussen 2010 en 2012 is er een nieuwe stimulus ontwikkeld voor ABR-metingen: de *level-specific (LS) CE-chirp*. Met deze stimulus wordt getracht de vertraging die ontstaat door de looptijd van auditieve stimuli in de cochlea te compenseren. Daarnaast houdt de LS CE-chirp rekening met de latentieverschillen tussen frequenties per intensiteit. Dit resulteert in betere neurale synchroniteit en verbetering in de klinische interpretatie. Door het oplijnen van de aankomsttijd van de verschillende frequenties in de LS CE-chirp op hun plek langs het basilaire membraan, zou een grotere temporele synchroniciteit in het vuren van de zenuwvezels voor de diverse frequenties en relatief gelijke latentietijden moeten worden bereikt.

Doel

Het doel van deze studie is het evalueren van de geschiktheid van de LS CE-chirp voor lucht- (AC) en beengeleiding (BC) ABR-metingen. Dit onderzoek focust op de latentie van hersenstampotentialen die worden gegenereerd met de breedband (BB) en vier octaafband (NB) LS CE-chirps. Latentieverschillen tussen de vijf LS CE-chirps binnen één intensiteit worden vergeleken, evenals de latentieverschillen per chirp tussen lucht- en beengeleiding en tussen stimulusintensiteiten.

Methode

De hersenstampotentialen (ABRs) zijn geregistreerd in 50 normaalhorende jongvolwassenen (25 vrouwen, 25 mannen). Luchtgeleiding ABR-metingen zijn uitgevoerd op 40, 70 en 90 dB nHL en de beengeleidings-metingen op 40 dB nHL. Bovendien is voor de beengeleiding de respons op een clickstimulus geregistreerd en vergeleken met de BB LS CE-chirpresponsen. Verder is een gehoordrempel vastgesteld voor de BB LS CE-chirp en vergeleken met een subjectief vastgestelde BB LS CE-chirpdrempel en de gemiddelde toonaudiometriegehoordrempel. De stimuli zijn gepresenteerd in *condensation* en *rarefaction* polariteit. De *stimulus rates* zijn gebaseerd op de aanbevelingen van de NHSP. Een EEG-filter van 30 – 3000 Hz, een *residual noise target line* van 40 nV, een artefact-verwerpingsniveau 40 µV en Bayesian weging zijn toegepast.

Resultaten

BB en NB LS CE-chirps laten soortgelijke latenties zien binnen één transductiemethode en stimulus-intensiteit (experiment 1). Tussen de transductiemethoden zijn significante latentieverschillen gevonden. Voor de BB, NB 0.5k en NB 2k LS CE-chirp zijn significant langere latenties gevonden voor BC ABR vergeleken met AC ABR. Voor de NB 4k LS CE-chirp daarentegen zijn significant kortere latentietijden gevonden voor BC ABR. Daarnaast zijn significante latentieverschillen vastgesteld tussen de verschillende intensiteiten binnen de chirps, met uitzondering van de NB 2k LS CE-chirp. Bovendien tonen de resultaten van dit onderzoek een significant verband aan tussen ABR-latentie en het geslacht van de participant. Verder laten de resultaten van het BC-gehoordrempelexperiment een relatief goede overeenkomst zien tussen de objectieve en subjectieve gehoordrempelmetingen.

Conclusies

In experiment 1 is vastgesteld dat de BB en NB LS CE-chirps vergelijkbare latenties hebben binnen een stimulusintensiteit. Dit suggereert dat de latentieveranderingen tussen frequenties die per intensiteit zijn gedefinieerd in het model van de LS CE-chirp een adequate compensatie vormen voor de cochleaire looptijd. De significante latentieverschillen tussen lucht- en beengeleiding en tussen de verschillende intensiteiten binnen de luchtgeleiding zijn in overeenstemming met eerder onderzoek naar click-, toneburst- en CE-chirp-ABR. Daarnaast sluiten de significante verschillen tussen BC click en BB LS CE-chirp aan bij eerder onderzoek naar de AC click vs. LS CE-chirp. Verder laat experiment 3 zien dat op basis van de LS CE-chirp gegenereerde ABR's op 70 dB nHL een bruikbare maat zijn voor otoneurologisch onderzoek. Tot slot is in experiment 4 aangetoond dat het mogelijk is om BC-drempelmetingen uit te voeren met de BB LS CE-chirp en relatief goede overeenstemming met subjectieve maten te bereiken.

Kernwoorden

Auditory Brainstem Response; hersenstampotentialen; LS CE-chirp; octaafband chirps; beengeleiding; latentie; otoneurologie; gehoordrempel beengeleiding

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Abbreviations

ABG	air-bone gap
ABR	auditory brainstem response
AEP	auditory evoked potential
AC	air conduction
BB	broadband
BC	bone conduction
BERA	brainstem evoked response audiometry
CA	chronological age
CHL	conductive hearing loss
CTWD	cochlear travelling wave delay
dBeHL	estimated true hearing level in decibels
dBnHL	normal hearing level in decibels
EEG	electroencephalography
Fmp	F statistic at multiple points
ISI	interstimulus interval
IWI	interwave interval
LS	level specific
NB	narrowband
NH	normal-hearing
PTA	pure tone average
SHL	sensorineural hearing loss
TBABR	toneburst ABR
TWD	total wave delay

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1. Introduction

The past decades, technology has progressed fast. Part of those developments are the quick changes in the field of audiology and particularly the technology concerning hearing aids. Those aids, including cochlear implants, have become more and more advanced, and as a result the optimal conveyance of the auditory signal to the auditory system comes closer at every step. These advances have a strong positive influence on the processing of auditory signals by individuals with a limited auditory function. The auditory information is better processed, which in turn leads to increased perception and, in case of paediatric hearing loss, easier spoken language acquisition. However, to adequately provide the patient with hearing aids, the auditory system has to be assessed in the most effective and efficient manner. One of the available measurement techniques to objectively assess auditory functioning is Brainstem Evoked Response Audiometry (BERA). In BERA-measurements neural activity related to the perception of an auditory stimulus, i.e. auditory evoked potentials, is measured. The upcoming sections provide a brief introduction into the auditory system, the different types of hearing loss and auditory evoked potentials.

1.1. The auditory system

The perception of an auditory signal depends on a chain of anatomical structures. The processing of the auditory signal starts at the peripheral hearing organ, which consists of the outer ear, the middle ear and the inner ear (see Figure 1).

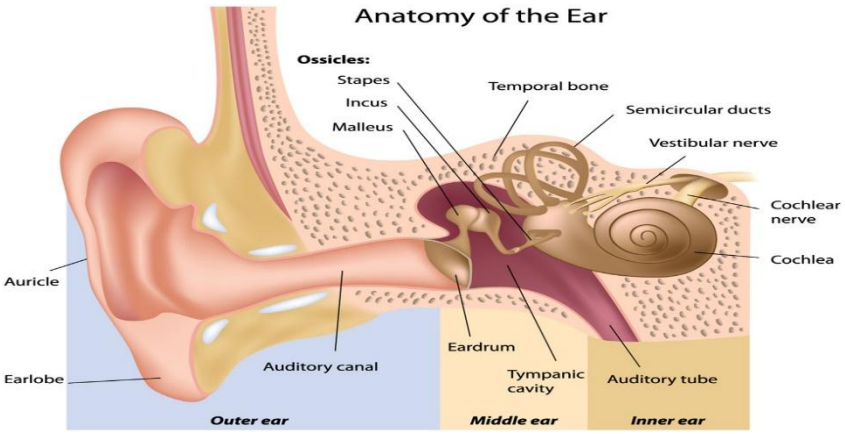


Figure 1 Anatomy of the human ear, retrieved from http://www.nzuaa.org/human-ear-anatomy/anatomy-of-the-human-ear/

The auditory signal enters the middle ear when reaching the tympanic membrane. The wave signal reaching the middle ear travels through air, which has a relatively low impedance. However, in the inner air the sound waves have to travel to liquid, which has a much higher impedance. For the ear to be able to convey the sound waves from outside the ear to the auditory nerve, the signal is mechanically amplified in the middle ear. This increase in energy is provided by the lever function of the ossicles (Hall, 2014), that connect the tympanic membrane to the inner ear, and is essential for the conveyance of sound.

The amplified signal is subsequently transferred to the cochlea. The cochlea is situated in the inner ear and consists of three canals: the scala vestibuli, scala media and scala tympani. The basilar membrane forms the partition between the scala media and scala tympani (Hyvärinen, 2012). The cochlea is tonotopically organised, from the highest frequencies at the basal end of the basilar membrane to the lowest frequencies close to the apex. The basilar membrane is relatively wide and flexible at the apex, but narrow and stiff at the base (Hall, 2014; Hyvärinen, 2012). The gradient of

mass and stiffness along the membrane enables the pressure fluctuations in the fluid (the sound wave) to be transferred into a traveling wave on the basilar membrane and contributes to the tonotopic organisation of the cochlea (Hall, 2014). The traveling wave along the basilar membrane takes time. As a consequence, the hair cells and fibres of the auditory nerve related to the response areas of the various frequencies will not be stimulated synchronously and a compound neural response evoked by a signal containing both high and low frequency information will be temporally smeared (Elberling et al., 2007).

The hair cells of the inner ear, approximately 15.500 cells (Lonsbury-Martin et al., 2009; Hall, 2014), transfer the sound waves into nerve pulses. The auditory nerve leaves the cochlea and carries the electrical sound signal to the brainstem. The first nucleus is the cochlear nucleus. From this nucleus, the auditory information splits into two streams: one continues its path to the ventral cochlear nucleus and the other to the dorsal cochlear nucleus. As the signal leaves these nuclei, the streams split again: into an ipsilateral and a contralateral stream. Subsequently, the auditory information is conveyed to the cortex. The tonotopic organisation of the inner ear is preserved through the central auditory pathway (Hyvärinen, 2012).

1.1.1. Hearing loss

The human auditory system is a complex system. When a patient describes a loss of hearing function, the lack of perception can be caused by a range of components along the peripheral and central auditory pathway. Broadly, clinicians distinguish two types of hearing loss: conductive and sensorineural hearing loss. The distinction between these two types is crucial to the assessment and adequate rehabilitation of hearing function.

Conductive hearing loss is a loss of auditory function due to an impairment in the middle ear, such as an infection or mechanical problems regarding the ossicular chain. Patients with conductive hearing loss can still process auditory signals, but the amplification of the signal by the middle ear is impaired or even absent. As a result, sounds need to be louder to be heard by the patient, i.e. the soundwaves need to be stronger. Only then the waves will be able to set the basilar membrane in motion and convey the signal to the auditory nerve.

Sensorineural hearing loss is the consequence of damage in the inner ear (cochlear hearing loss) or the central pathway from the auditory nerve (N VIII) to the cortex (retrocochlear hearing loss). Cochlear hearing losses can have several causes, including aging, i.e. presbyacusis, hereditary genetics (congenital hearing loss) or (excessive) exposure to noise (>85 dB(A), Hyvärinen, 2012). An example of a retrocochlear hearing loss is loss of hearing function as a cause of a vestibular schwannoma (or acoustic neuroma). Vestibular schwannoma's can often be surgically removed without damaging the central auditory pathway (Lunsford et al., 2005).

Patients with a sensorineural hearing loss have an impairment in the frequencies and intensities they can perceive. Unlike conductive hearing loss, louder stimulation of the system does not help resolve the problem. To the contrary, whereas the soft sounds are not perceived, loud sounds are still perceived as loud. This phenomenon is called recruitment and is a hallmark of cochlear hearing loss: low-intensity sounds are inaudible, but once sound is above threshold, loudness quickly increases. This leads to a compression in dynamic range. (Hamill & Price, 2013).

2. Auditory Evoked Potentials

The human brain is a complex centre of neurons generating electrical activity while in action. This electrical activity can be measured by placing electrodes on the scalp. The resulting recording is called an electroencephalogram (EEG; Hall, 1992). When stimulating a sensory organ, fluctuations in the EEG waveform related to the stimulus will manifest themselves. This series of fluctuations is called an evoked potential (EP; Hall, 1992). When studying hearing, one is interested in the evoked potentials related to auditory stimuli, i.e. auditory evoked potentials. The peaks in the AEP waveform are formed by different functional parts of the auditory pathway. The AEP is subdivided into three parts. The part up to approximately 10 ms after stimulus presentation is called the auditory brainstem response (ABR), the second part, which starts right after the ABR and continues approximately 40 ms, is the middle latency response (MLR) and the third part the long latency response (LLR), with a latency between approximately 100 and 500 ms (Melcher, 2009; Møller, 1994).

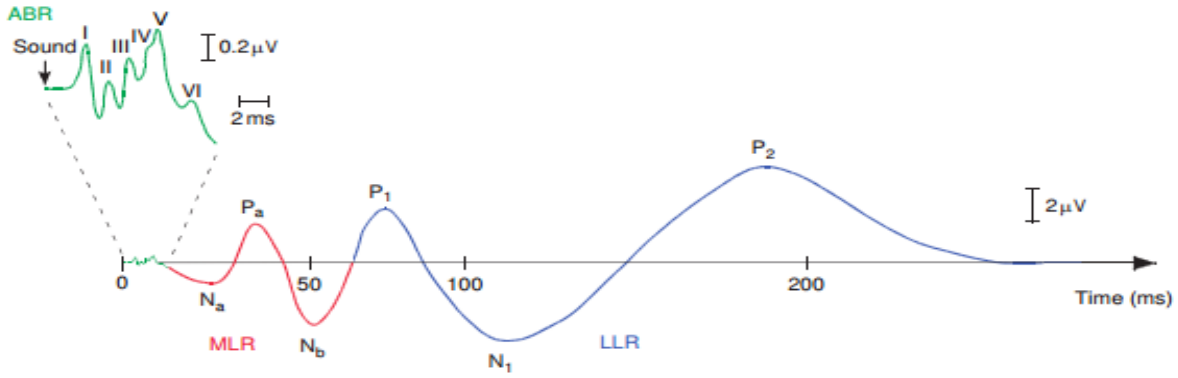


Figure 2 Auditory Evoked Potentials in humans (Hyvärinen, 2012), adapted from Melcher (2009).

Auditory evoked potentials are broadly characterized by means of two elements: amplitude and latency of the peaks in the AEP-waveform. Both these elements are influenced by a range of factors, including for example stimulus intensity. A high intensity stimulus has a shorter latency and increased amplitude in comparison to the same stimulus at a lower intensity (Melcher, 2009). In the upcoming chapters, these elements influencing the AEP-waveform morphology will be discussed.

2.1. The auditory brainstem response

This study focuses on the fastest AEP: the auditory brainstem response (ABR). This response mirrors the activity in the brainstem during the first approximately 10 ms after stimulus presentation, and does not include activity from higher levels in the brain (Hyvärinen, 2012). The ABR is a popular mean in clinical audiology. First, because the ABR waveform is quite similar between individuals, thus relatively straightforward to identify. Second, the level of awareness of the patient does not influence the ABR. For ABR measurements, in order to generate a clear signal patients are asked to relax or preferably sleep (Melcher, 2009). The measurements have also shown to be applicable in sedation and in general anaesthesia (Schmidt et al., 2007; Mühler, Rahne & Verhey, 2013).

The ABR consists of seven waves, each numbered with a Roman numeral (I – VII). Each wave in the waveform corresponds to a processing station in the auditory pathway (see Appendix I). There are III major ABR components: waves I, III and V. Wave I is generated by the auditory nerve, wave III represents the signal entering the cochlear nucleus, and wave V, the most prominent wave that remains visible even nearing hearing threshold, is generated from the lateral lemniscus as it terminates in the inferior colliculus (Hall, 2014). In clinical practice, the focus is on those three most prominent waves (Schwartz, Morris & Jacobson, 1994). Since wave V remains visible even near

hearing threshold, the latency and amplitude of wave V is often used for audiological assessments (Hyvärinen, 2012).

2.1.1. Maturation of the ABR after birth

The first recognizable ABR waves appear as soon as thirty weeks post conception, although amplitudes are still small and latencies prolonged. At that time, the ABR consists of wave I, III and V. Wave IV and wave II appear shortly after; wave IV emerges at 35 weeks and wave II at 51 weeks post conception (Lamoré, 2011). As the child grows, the amplitude of the waves increases and latency decreases. The first wave reaching the normative latency value for an adult listener (± 1.5 ms) at 6 to 24 weeks chronological age (CA). Maturation of the other waves takes more time. Due to neurological immaturity, ABR latencies of the other waves are prolonged for infants from birth to approximately 18 months (Hall, 2014). The maturation of the ABR waveform amplitudes takes even longer, in particular wave V undergoes a large transformation. In adults, the amplitude ratio between wave I and V (V/I ratio) is approximately three, whereas in infants it is only one. However, where the amplitude of wave I increases until about six months CA, wave V amplitude augments until 24 to 60 months CA (Hecox et al., 1981; Hecox & Burkhard, 1982; Stockard et al., 1979).

In the last decade, several studies concerning the maturation of the brainstem have been published. These studies focus on the changes in amplitude and latency of the ABR waves in infants and compare maturation patterns for ABR evoked by different kinds of stimuli. Two recent studies concerning maturation of the brainstem assess the changes in amplitude, latency and waveform morphology for the ABR evoked by a chirp stimulus (Mühler et al., 2013; Cebulla, Lurz & Shehata-Dieler, 2014). Furthermore, the study of Mühler et al. (2013) addresses the influence of state of arousal of the infant on the amplitude and waveform morphology of the ABR.

In Mühler et al. (2013) data of 46 infants (divided in the age groups 0-18 and 18-48 months) who underwent chirp-evoked ABR for the evaluation of hearing loss are analysed retrospectively. ABR was performed while the child was under either chloral hydrate sedation or general anaesthesia with Propofol. These data are compared to the data from Sininger et al. (2000) of 7179 newborns who underwent click-evoked ABR. Results show a significantly better visible wave V and larger amplitudes for chirp-evoked ABR than click-evoked ABR. The amplitude of wave V even approximated adult values (retrieved from Elberling, Kristensen and Don, 2012) in de older age group of the Mühler et al. (2013) study. This difference in amplitude for chirp- and click-evoked ABR underlines the need for separate normative data sets for the various kinds of ABR stimuli. It should be noted, however, that the study of Mühler et al. (2013) did not differentiate between children that passed the ABR hearing evaluation and those that turned out to have a hearing loss. These hearing losses could have had an influence on the results found in this study.

Cebulla, Lurz and Shehata-Dieler (2014) did take this variable into account. They evaluated the waveform morphology, latencies and amplitudes of click- and chirp-evoked ABR in 96 normal-hearing newborns under 5 days of age (Cebulla et al., 2014). In accordance with the results found by Mühler et al. (2013), the study of Cebulla et al. (2014) showed clearly larger amplitudes for chirp-evoked ABR compared to click-evoked ABR. ABR was measured at two intensities, 40 and 60 dB HL, and generally the gain in amplitude for chirp-evoked ABR was greater at the lower intensity. In addition to the larger amplitudes, latencies of the various waves and the interwave intervals (IWI) were shorter for chirp-evoked ABR. Concerning the IWI, the difference was slight in the I-III interval and significant in the I-V interval. Consistent with the Mühler et al. (2013) study, the results of Cebulla et al. (2014) thus suggest that chirp- and click-evoked ABR lead to significantly different waveforms within the same infants. As a result, it is crucial for diagnostic purposes to collect separate normative maturation data for these stimuli.

2.1.2. Influencing patient factors

There are various factors related to the patient that influence the waveform morphology, latency and amplitude of the ABR. One of the clearest factors is age. As has been elaborated upon in the previous section, the brainstem is not fully maturated at birth. Therefore, the ABR waveform changes through the first years of a child's life. At the other end of the spectrum, for patients older than 60 years of age, the ABR waveform morphology amplitude and latency often reflects age-related issues, such as medical problems (Maloff & Hood, 2014). Recently, Lotfi and Zamiri Abdollahi (2012) studied the age effects in three age groups: 18-30, 31-50 and 51-70 years old. Each group consisted of 20 males and 20 females and all subjects had normal hearing (behavioural thresholds $\leq$ 30 dB HL). The results of the study show significantly longer latency of wave I, wave V and the I-V IWI in the older age group compared to the other two groups (Lotfi & Zamiri Abdollahi, 2012). Since Lotfi and Zamiri Abdollahi (2012) controlled for presbyacusis, their results suggest that in addition to the influence of presbyacusis on the ABR of the elderly population (Khullar & Babbar, 2011), aging influences the auditory brainstem response.

In addition to age, gender is also a frequently reported factor that influences the ABR. The latency of the ABR in female subjects is shorter and the amplitudes larger than in males (e.g. Don, Ponton, Eggermont & Masuda, 1993; Esteves et al., 2009; Fallah, Tafti, Karimi & Teimuri, 2007; Li et al., 2013; Lotfi & Zamiri Abdollahi, 2012). Also, the interwave intervals are shorter (Hall, 1992; Lotfi & Zamiri Abdollahi, 2012). These gender related differences in the ABR were first explained by a difference in length of the brainstem pathway. However, although there is a positive relationship between head size and ABR wave latencies (Sininger & Hyde, 2009), females still show shorter latencies when compared to males with equal head size (Trune, Mitchell & Phillips, 1988). The shorter latencies and larger amplitudes can, however, be explained by a shorter traveling wave to the auditory nerve in females, due to a shorter length of the cochlea in comparison to the male cochlea. The female cochlea is approximately 13% shorter than the male cochlea (Don et al., 1993). Furthermore, research has shown that the gender difference is reduced during menopause, shows variations with the menstrual cycle in females and is reduced in females who have a male twin. The differences found are suggested to occur under the influence of hormones, especially oestrogen (Dehan & Jerger, 1990; Elkind-Hirsch et al., 1992; Krizman, Skoe & Kraus, 2012).

Whereas age and gender are frequently studied influencing factors concerning the ABR and are accounted for in research, the measured ear is not. Most researchers and clinicians believe that the ABR of right and left ears is identical and research publications and normative data typically do not mention the ear stimulated (Sininger & Hyde, 2009). However, there are in fact subtle differences in ABRs to left and right ears. In a study with pre- and full-term infants, Eldredge and Salamy (1996) found larger wave amplitudes and shorter interwave intervals elicited by clicks presented to the right ear than to the left. This is corroborated by Sininger and Cone-Wesson (2006), who performed a large scale study (2205 subjects; 2003 left ears and 2011 right ears) of ABRs in neonates generated with 30 dB nHL and 70 dB nHL clicks. In this study, wave V amplitude for both low- and high-level stimuli was found to be significantly larger for ABRs elicited by clicks presented to the right ear. Moreover, the latencies of wave III and V were shorter when the ABR was generated in the right ear.

In addition to the differences found in newborns and infants, small differences between ABR elicited in right and left ears also seen in children and adults. Esteves et al. (2009) showed that wave V amplitude was larger and the interval I-V shorter when ABR was elicited with right ear stimulation in males as well as in females. When the ears were compared regardless of sex, the amplitude and latency difference between the ears was not statistically significant (Esteves et al., 2009). This is most likely caused by the gender influence on the ABR leveling out the small difference caused by the ears. Two early studies by Levine and colleagues on the other hand did find a significant difference regardless of sex (Levine & McGaffigan, 1983; Levine, Liederman & Riley, 1988). They found larger wave III

amplitudes in right-handed and 63% of left-handed adults when the right ear was stimulated. Although differences between the stimulated ear are thus repeatedly demonstrated, the differences are sufficiently small to conclude that they have no clinical significance (Sininger & Hyde, 2009).

A fourth factor that has a significant effect on the ABR is the state of arousal of the patient. A restless patient shows more EEG activity, resulting in a worse signal-to-noise ratio (Jacobson, 1994; Schmidt et al.,2007; Mühler et al., 2013). This influences the quality of the recording and the reliability of the ABR measurements (Mühler et al., 2013). Inability (or unwillingness) of the patient, in particular adults, to fully relax limits the precision of the technique (Lightfoot & Stevens, 2013). Therefore, patients are always instructed to relax and, if possible, to sleep. Due to neurological immaturity, resulting in smaller amplitudes and longer latencies, and higher electrical noise in infants and newborns, the generation of a reliable ABR is even more difficult. It is therefore common practise to record ABR whilst the child is asleep or under sedation or general anaesthesia (Loewy et al., 2005; Mühler et al., 2013; Olson et al., 2001). The recent study of Mühler et al. (2013) showed no significant difference in ABR response for children measured under chloral hydrate (50 mg/kg body weight) sedation or general anaesthesia using Propofol.

Finally, body temperature may influence the ABR. Although temperature typically is not a concern for subjects undergoing an ABR recording, it can be a concern in premature infants. Hypothermia may be encountered and it is important to closely monitor core temperature in these children. This is because lower-than-normal body temperature prolongs ABR latency (Jacobson & Hall, 1994). The opposite is also true. A significant increase in core temperature, such as a fever, can shorten the absolute and interval ABR latencies (Kohshi & Konda, 1991; Takahashi et al., 1990).

3. Brainstem Evoked Response Audiometry

The auditory brainstem response is used for the assessment of hearing function, especially in young children and hard-to-test adults. These objective, non-invasive measurements were introduced in the 1970s as a physiologic instrument to study and diagnose disorders affecting the peripheral and central auditory pathways (Hecox & Galambos, 1974; Starr & Archor, 1975). While behavioural, pure tone audiometry still is the gold standard for assessment of hearing function, it requires a developmental state of the patient that allows for reliable responses (Elsayed et al., 2015). For brainstem evoked response audiometry (BERA) an active response of the subject is not required. This makes the measurement particularly applicable for infants and hard-to-test subjects, for example a patient with a severe disorder in the autism spectrum.

Brainstem evoked response audiometry measures the brainstem response to auditory stimulation. These responses have two distinct applications: otoneurological assessment and threshold measurement. These two applications focus on different elements of the ABR. Otoneurological measurements assess the possibility of a tumour along the pathway to the auditory cortex. Therefore, the latency of the different waves and interwave intervals is closely monitored. A tumour along the pathway, prolongs the latency of the wave corresponding to the site of the tumour, the subsequent waves and the interwave intervals. The most common tumour along the auditory pathway is a vestibular schwannoma, situated at the cerebellopontine angle (Don & Kwong, 2009).

Secondly, BERA can be used to objectively measure the auditory thresholds. This method has been highly advocated for the assessment of hearing thresholds in infants by several associations around the globe, such as the Joint Committee on Infant Hearing (2007), the American Speech-Language-Hearing Association (2004), the Dutch *Rijksinstituut voor Volksgezondheid en Milieu* (Van der Ploeg, Van der Pal & Verkerk, 2015) and the Newborn Hearing Screening Protocol (2014a) of the United Kingdom. To assess which intensity still generates a response from the brainstem, clinicians consider the amplitude of wave V. The auditory threshold is the lowest intensity at which wave V is

clearly visible. The ABR thresholds are higher, less ideal, than behavioural thresholds. It is therefore important to apply a correction factor, based on research data (Ferm et al. 2013, Ferm & Lightfoot, 2015).

3.1. The conventional 'click' and tone burst stimuli and the new developed 'chirp'

For BERA measurements, the stimuli are a key element. They are created in such a way that they stimulate a broad area of the cochlea and therefore create the maximal amount of nerve fibres firing synchronously in time. The early latency evoked potentials, such as the ABR, are optimally generated with brief stimuli. In this section, the different stimuli used in ABR measurements will be described. The stimuli will be discussed in chronological order of development.

3.1.1. The click

The click stimulus (see Figure 3) is the most frequently used stimulus in ABR measurements to date. It is the gold standard for otoneurological assessment as well as hearing threshold determination in most clinics around the globe. Clicks are transient stimuli with an abrupt onset, a short duration and a broad spectrum (Durrant & Boston, 2007). The combination of these factors evokes the largest ABR amplitudes. This is because the ABR is an onset response. Suzuki and Horiuchi (1981) showed that the ABR is elicited by the first few cycles of the stimulus at onset.

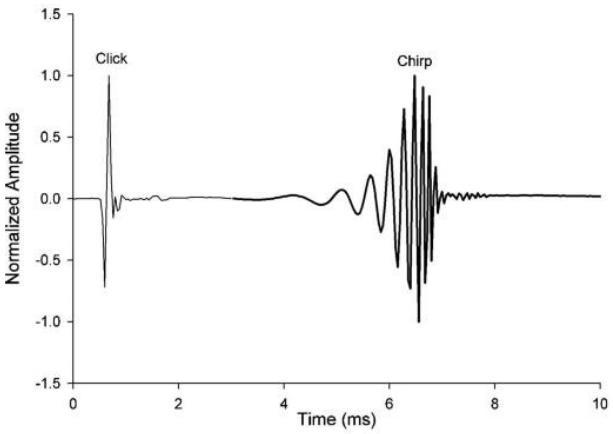


Figure 3 The click and chirp stimulus (Chertoff, Lichtenhan & Willis, 2010).

However, although the click is the gold standard in clinical practice, it has its disadvantages. First and foremost, although the click is considered a broadband (BB) stimulus, the ABR primarily reflects more basal, i.e. high frequency, regions of the cochlea (Maloff & Hood, 2014). The click has a frequency content covering a broad area of the frequencies for which the human cochlea is sensitive, but, as a result of the tonotopic organisation of the cochlea, not all frequencies reach their place on the basilar membrane synchronously. It takes the cochlear wave along the basilar membrane approximately 4 to 5 ms to travel from the basal end to the apex. The neurons of the auditory nerve are thus sequentially activated from high to low frequency (Eggermont, 2007). Therefore, although all frequencies start at the same time, the summed neural response of the various frequency regions is temporally smeared. This reduces the amplitude of the ABR (Elberling & Don, 2010). Moreover, the correlation between click ABR and behavioural pure tone audiometry is restricted to a range of approximately 1-4 kHz (Baldwin & Watkin, 2013; Maloff & Hood, 2014). To conclude, it is possible to pass the ABR hearing test with only high frequency hearing, missing a low-frequency hearing loss.

To overcome this disadvantage of the click stimulus, several stimuli have been developed to enhance the frequency-specificity of the ABR response, such as the toneburst stimuli (section 3.1.2.), and to compensate for the cochlear traveling wave delay (section 3.1.3. – 3.1.5.).

3.1.2. Tone burst stimuli

Toneburst, or tonepips, are the first stimuli developed to elicit a frequency-specific ABR. The goal was to generate stimuli with a sufficiently rapid onset to effectively elicit an ABR, while limiting the frequency content of the stimulus. Tonebursts are defined by their rise, plateau and fall cycles. Most common is a rise and fall time of two cycles and a plateau of one cycle (2-1-2, see Figure 4). The duration, the rise-fall time and the manner in which the stimulus is gated determine the spectral spread in toneburst stimuli (Gorga et al., 2006).

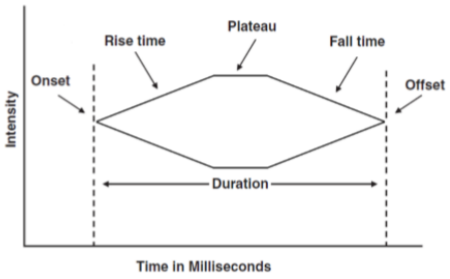


Figure 4 A schematic example of a toneburst. Retrieved from Van Bommel (2014).

Although the frequency-specificity of tone burst stimuli seems a great value for ABR threshold measurements and the use of these stimuli has been recommended by several researchers (e.g. ASHA, 2004; JCIH, 2007; Stapells & Oates, 1997; BCEHP, 2007), tone bursts are still underused in clinical practice. The diagnostic battery of many clinics still primarily consists of ABR threshold testing using the traditional click (Windmill & Windmill, 2006). There are several factors contributing to this. First, the amplitude of toneburst-evoked ABR (TBABR) is on average 70% smaller than the click-evoked ABR amplitude (Ferm et al., 2013). As a result, a longer test time is needed to obtain reliable ABR measurements. Furthermore, clinicians report uncertainty about the accurate protocol and practical difficulty identifying wave V, particularly for the lower frequency range (Windmill & Windmill, 2006). The clinicians additionally doubt the accuracy and stability, within and between subjects, of TBABR (Van der Werff, Prieve & Georgontas, 2009). Therefore, many clinicians resist to use tonebursts for ABR threshold measurements (Rodrigues, Ramos & Lewis, 2013; Van der Werff et al., 2009).

However, research of the past two decades has shown that TBABR can effectively and accurately estimate the hearing threshold of subjects. Stapells (2000) showed that TBABR thresholds at 500, 1000 and 2000 Hz in infants and children with sensorineural hearing loss generally fall within 10 dB of their pure tone audiometry thresholds. More recently, Van der Werff et al. (2009) and Elsayed et al. (2015) studied air-conduction (AC) and bone-conduction (BC) TBABR as an estimation of behavioural hearing thresholds in infants and young adults. Van der Werff et al. (2009) found strong correlations (> r=.85) for objective and subjective thresholds at 0.5, 2 and 4 kHz. Similar results were found by Elsayed et al. (2015). The thresholds found were even slightly lower than the data reported by Van der Werff et al. (2009). The difference is contributed to methodological differences, most importantly the use of Kalman weighting software (Elsayed et al., 2015).

Additionally, Van der Werff et al. (2009) studied the possibility to classify the hearing loss type of infants using TBABR. They showed that TBABR accurately separates the children with conductive hearing loss (CHL) from the children with normal hearing or sensorineural hearing loss. The results suggest that the combination of indicators of CHL studied, i.e. the ABR, AC versus BC TBABR latency and wave I and V latency of the high-level click ABR may provide a strong indication for CHL (Van der Werff et al., 2009).

To conclude, research has convincingly shown that there is great value of frequency-specific AC and BC ABR in hearing threshold estimation and assessment of hearing loss type. However, there are several methodological challenges in TBABR, most importantly the long testtime needed as a result of smaller amplitudes. Therefore, recent studies have focussed on the construction of a new type of stimulus that evokes large amplitudes and can be used in both a broadband and a narrowband version: the chirp stimulus.

3.1.3. Broadband chirp stimuli

Section 3.1.1. has shown that the major disadvantage of the traditional click stimulus is the fact that it does not take the cochlear travelling wave delay (CTWD) into account. The past decades, researchers have attempted to compensate for this delay in order to improve the ABR. In 1994, Don and colleagues developed a technique called Stacked ABR (Don et al., 1994). This technique presents a click stimulus in combination with high-pass masking, which composes the click into smaller frequency bands. The obtained responses are time shifted so that wave V of each response lines up. After time shifting, a summed response is calculated: the stacked ABR (Don et al., 1994). The amplitude of the stacked ABR is significantly larger than in click-evoked ABR (Don et al., 1994). This stacked ABR technique is a form of output compensation for the CTWD. It is also possible to compensate for the CTWD in the input. This means a change in the type or construction of the ABR stimulus to ensure compensation, such as chirp stimuli. In 2009, Don and colleagues demonstrated that input compensation leads to ABR amplitudes that are approximately 35% smaller than the stacked ABR (Don, Elberling & Malof, 2009). However, output compensation techniques are very time consuming, because it uses the CTWD from the recordings in an individual subject, instead of the average CTWD obtained via a model, as is the case in input compensation (Elberling et al., 2007). Therefore, input compensation is preferred for clinical applications.

In order to compensate for the CTWD in the input, several research groups have proposed a new stimulus, based on various models. This line of research initiated in the 1980s and Fobel and Dau (2004) were the first to compare several of these attempts. They compared the chirps developed by Dau et al. (2000) and Dau and Wegner (2002), Shera and Guinan (2000; 2003) and Neely et al. (1988), see Table 1. Dau et al. (2000) demonstrated the possibility of their flat-spectrum chirp to increase the synchrony of neural discharges. Wegner and Dau (2002) subsequently showed that frequency-specific information, particularly at lower frequencies, could also be obtained. However, Fobel and Dau (2004) expected this chirp to be the least efficient, since it is based on high-level data and a linear model of the cochlea. It had already been shown that a linear model of the cochlea is too simplistic and that the response of the basilar membrane is in fact nonlinear (e.g. Rhode, 1971; Ruggero et al., 1997; Rhode & Recio, 2000). This compression of the basilar membrane is associated with level-dependent frequency selectivity (e.g. Moore et al., 1999) and it is therefore suggested that the model of De Boer (1980) underestimates the actual delay at low and moderate stimulus intensities (Fobel & Dau, 2004). The second and third chirp, developed by Shera and Guinan (2000; 2003) and Neely et al. (1988) respectively, were expected to be more efficient. The O-chirp of Shera and Guinan (2000; 2003) is based on an OAE-model and, more than compensation for the CTWD as a whole, this chirp is designed to compensate for frequency dependent traveling time differences. The A-chirp, developed by Neely et al. (1988), is even more complex. This chirp does not only compensate for frequency-specific traveling times, but also for intensity specificity of the cochlear traveling wave.

Table 1. Chirp stimulus models evaluated by Fobel and Dau (2004).

Developers	**Name of chirp**	**Model**
Dau et al. (2000); Wegner & Dau, 2004)	M-chirp	De Boer (1980), based on experimental observations of Von Békésy (1960) at 120 – 140 dB SPL. The fundamental relationship between stimulus frequency and place of maximum displacement is derived from Greenwood (1990).
Shera & Guinan (2000; 2003)	O-chirp	Otoacoustic emissions for 0.5 – 10 kHz at 40 dB SPL
Neely et al. (1988)	A-chirp	TBABR at 0.25, 0.5, 0.75, 1, 1.5, 2, 3, 4, 6, and 8 kHz at 20 – 100 dB SPL in 10 dB steps.

Fobel and Dau (2004) analysed ABR responses in nine normal-hearing subjects between 28 and 38 years of age evoked by the different chirps and an 80 µs click stimulus. The results show larger wave V amplitudes for all chirps in comparison to the click stimulus. Wave V was the only peak visible in all stimulus conditions. For the O-chirp, earlier waves were not present, even at 60 dB SL. In contrast, wave I and III are present at higher stimulus levels for the M-chirp and A-chirp. For the A-chirp, this even holds down to a level of 20 dB SL. The peak-to-peak amplitude of wave V of the O-chirp was comparable to that of the M-chirp, which was hypothesized to be the least efficient. This suggests the construction method used for the O-chirp is not optimal for creating a stimulus that compensates for the cochlear travelling wave along the basilar membrane. However, the results of the A-chirp were promising. This chirp produced the largest amplitudes, particularly at low intensities. This suggests the chirp successfully managed to compensate for the CTWD. Moreover, the level-specific compensation for different intensity levels seems to have paid off. Fobel and Dau (2004) therefore conclude that the A-chirp might be very useful for clinical applications.

Elberling et al. (2007) follow in the footsteps of Fobel and Dau (2004) and study the models underlying chirp stimuli and their capacity to compensate for the CTWD. The cochlea and peripheral part of the nerve fibres seem to form a nonlinear system, which, as Fobel and Dau (2004) indicated, is not accurately approximated by a linear model. Elberling et al. (2007) examine four models: (1) the data of Eggermont (1979) based on narrowband ACAP recordings, (2) the data of Neely et al. (1988), constructing the A-chirp, (3) the data from Don et al. (2005), based on narrowband click-evoked ABR recordings and (4) the frequency domain data of De Boer (1980), in contrast to the M-chirp of Dau et al. (2000) that is constructed in the temporal domain. The data underlying the different models can be described using a power function:

$$T = k \cdot f^{d} \qquad (1)$$

in which, *T* is the latency in seconds, *f* is the frequency in hertz and *k* and *d* are constants (in the data of Neely et al. (1988) the value of *k* varies with intensity level of the stimulus). An overview of the latency-frequency functions of the different models and the values of the constants is shown in Figure 5.

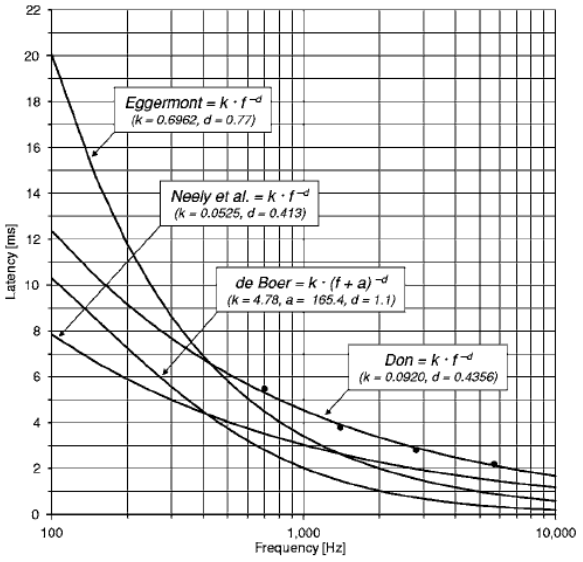


Figure 5 Latency-frequency functions deduced from: (1) narrowband ACAP (Eggermont, 1979), (2) TBABR (Neely et al., 1988), (3) narrowband ABR (Don et al., 2005), and (4) a cochlear model (De Boer, 1980). Figure retrieved from Elberling et al. (2007).

Elberling and colleagues have chosen three of these four latency-frequency functions for the clinical experiments of their study. The Eggermont (1979) data are excluded. They examined the efficiency of the three chirps by comparative ASSR measurements at 50 and 30 dB nHL in 49 normal-hearing young adults (Elberling et al., 2007). Research of Junius and Dau (2005) had suggested that ASSR using high rates of stimulation responds in a comparable way to chirp stimuli as ABR and Elberling et al. (2007) thus assume that their results will also apply to ABR. The results show that all three chirps have shorter detection times and larger SNRs than click-evoked ABR. Significantly different results within the three chirps were also found. At 40 dB nHL, the Don chirp was more efficient than the other two. This significant result was not

found at the lower intensity level. The findings of Fobel and Dau (2004) regarding higher ABR amplitudes for the A-chirp (Neely et al., 1988) at low intensities cannot be confirmed, since the lowest stimulus level used in the study of Elberling et al. (2007) was 30 dB nHL.

The evaluation of the chirp stimuli by Elberling et al. (2007) is used as the foundation for the construction of a new ABR stimulus: the CE-chirp (Elberling & Don, 2008). This chirp is based on the Don chirp (Elberling et al., 2007) and adjusted based on derived-band latency values of the combined datasets from Don et al. (1998) and Don et al. (2005). The resulting broadband chirp follows the same power function as described above, in which the values of constants *k* and *d* are: k = 0.0920 and d = 0,4356. The broadband (BB) CE-chirp is designed electrically to have a flat amplitude spectrum within five octave bands ranging from 350 – 11.300 Hz and is independent of stimulus level. Analysis of the combined dataset of Don et al. (1998, 2005) did reveal small differences in latency for different stimulus levels (ranging from 10-70 dB nHL), but Elberling and Don (2008) concluded these differences to be small enough to consider the latency delay to be constant across stimulus levels. The results of Elberling and Don (2008) do, however, suggest there might be "an upper level of stimulation beyond which the chirp is no longer more effective than the click" (Elberling & Don, 2008, p. 3035). The CE-chirp is implemented in Interacoustics EP25® and GSI Audera AEP system and currently used in a great amount of experimental research considering chirp-evoked ABR. In Table 2, an overview of commercial auditory evoked potential systems and implemented stimuli is given. As can be seen, the Pilot Blankenfelde Corona ABR system uses another type of ABR stimulus. For the sake of brevity, this chirp will not be elaborately discussed in the present study.

Table 2. Overview of commercial ABR systems. * = systems with only click and toneburst ABR.

ABR system	Chirp implemented?	Design chirp
Interacoustics Eclipse	Yes	(LS) CE-chirp
GSI Audera	Yes	(LS) CE-chirp
Pilot Blankenfelde Corona	Yes	Broadband chirp Low-Chirp (100 – 800 Hz) High-Chirp (1000 – 10000 Hz)
Otometrics ICS Chartr EP 200	No*	
Bio-logic (Natus) Navigator Pro	No*	
Intelligent hearing systems SmartEP	No*	

These studies have convincingly shown the effectiveness and efficiency of the BB CE-chirp. The chirp generates significantly larger amplitudes than the traditional click stimulus and this, in turn, results in a substantially reduced test time. These results have been found in adult testing (e.g. Cebulla & Elberling, 2010; Elberling, Callø & Don, 2010; Elberling & Don, 2010; Elberling, Kristensen & Don, 2012; Maloff & Hood, 2014; Petoe, Bradley & Wilson, 2010a,b) as well as ABR testing in infants (Cebulla, Lurz & Shehata-Dieler, 2014; Cebulla & Shehata-Dieler, 2012; Cobb & Stuart, 2016a,b; Mühler et al., 2013; Stuart & Cobb, 2014; Van den Berg, 2010). Moreover, Maloff and Hood (2014) have shown that the BB CE-chirp has its value in testing the hearing impaired population. They examined ABRs of 25 normal-hearing adults and 25 adults with mild to severe sensorineural hearing loss (group 1: mild to moderate, group 2: moderate to severe). The results showed that wave V peak-to-peak amplitudes were larger for the CE-chirp compared to the click, particularly at lower intensities, for all groups (Maloff & Hood, 2014). Furthermore, chirp-evoked ABR thresholds were closer to the behavioural thresholds of the subjects for all groups (Maloff & Hood, 2014).

Additionally, several studies examining newborns reported comparable test sensitivity and specificity in the newborn hearing screening for chirp stimuli compared to the traditional click (Cebulla & Shehata-Dieler, 2012; Cebulla et al., 2014; Van den Berg et al., 2010).

However, the amplitude advantage of the chirp seems to be mainly restricted to wave V amplitude. Petoe et al. (2010a) found reduced presence of waves I and III in chirp-evoked ABR compared to click-evoked ABR. The stimuli were presented at 40 dB HL with alternating polarity. Similar results were found by Kristensen and Elberling (2012). Their study shows reduced presence of waves I and III for the BB CE-chirp at 60 and 80 dB HL with alternating polarity. Both research groups suggest the longer duration of the CE-chirp is the reason for the reduced morphology of early waveform components (Kristensen & Elberling, 2012; Petoe et al., 2010a). Furthermore, Elberling et al. (2010) explain that at higher intensities an upward spread of excitation along the basilar membrane may cause desynchronization of the neural firing. This also affects the waveform morphology of the ABR (Elberling et al., 2010). As Cobb and Stuart (2016a) conclude: "clearly, the chirps were designed to maximize wave V amplitude and not earlier wave components" (Cobb & Stuart, 2016a, p. 4).

3.1.4. Narrowband chirp stimuli

Rather quickly after the implementation of the CE-chirp, the CE-chirp family has been expanded to include four narrowband chirps (NB CE-chirps). The NB chirps are obtained by decomposing the BB CE-chirp and are designed around four centre frequencies: 0.5, 1, 2 and 4 kHz. The octave-band filters used to construct the broadband CE-chirp and the frequency-specific versions have amplitude-frequency characteristics in accordance with the specifications given in IEC 61260 (1995) for octave-band filters (see Figure 6; Elberling & Don, 2010). Since the NB chirps are a decomposition of the BB CE-chirp, these chirps are also level-independent. In Figure 7, the waveform and envelope of the BB CE-chirp and the four NB chirps are shown.

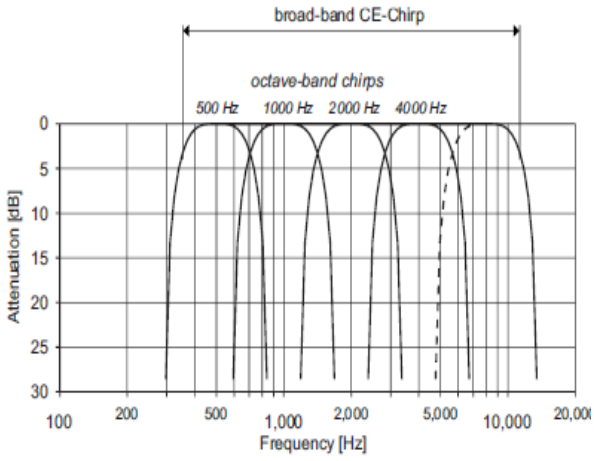


Figure 6 Amplitude-frequency characteristics of the filters used for the design of the BB and NB CE-chirp, following the specification given in IEC 61260 (1995). Retrieved from Elberling & Don (2010).

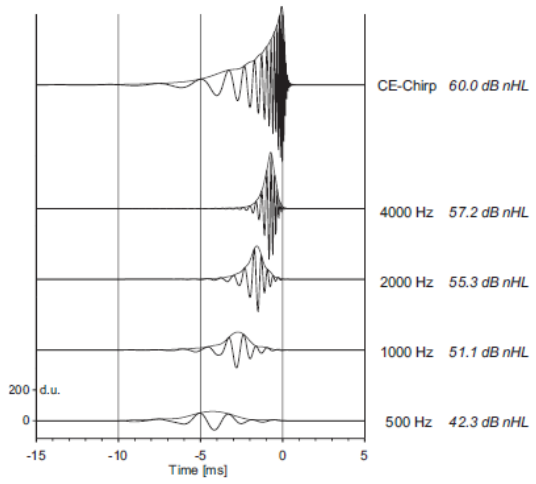


Figure 7 Waveform and envelopes of the broadband and four narrowband CE-chirps. Narrowband chirps are displayed with the amplitudes by which they appear in the CE-chirp. The zero point (0 ms) corresponds to the temporal location of the 10.000 Hz component of the CE-chirp. Retrieved from Elberling & Don, 2010).

The frequency specificity of the NB stimuli allows for the collection of more detailed ABR threshold information. The NB chirps enable assessment of frequency-specific hearing losses that might have been missed using a click or BB chirp, in particular a low frequency hearing loss with intact hearing in the higher frequencies.

The function of NB CE-chirps is thus similar to that of toneburst ABR. The question now is whether NB chirp-evoked ABR can overcome the disadvantages related to TBABR. The past five years, several researchers have compared the effectiveness and efficiency of the NB CE-chirp compared to tonebursts. This research is generally conducted in neonates and infants, since this is the main population for ABR threshold measurements. Threshold measurements in adults mainly consist of behavioural assessment and the use of ABR threshold measurements is restricted to difficult-to-test individuals and medico-legal procedures. To evaluate the NB CE-chirp evoked ABR, Ferm, Lightfoot and Stevens (2013) and Ferm and Lightfoot (2015) assessed the response amplitude, response quality (Fmp) residual noise, test time and estimation of hearing thresholds in NB CE-chirp evoked ABR and TBABR. Ferm et al. (2013) studied the 1 and 4 kHz NB CE-chirp in 30 babies (42 ears) and Ferm and Lightfoot (2015) the 0.5 and 2 kHz NB CE-chirp in 39 babies (42 ears). The results of both studies show a significant improvement in chirp-evoked ABR compared to TBABR (see Table 3). Furthermore, since NB CE-chirps seem to result in lower ABR thresholds compared to tonebursts, Ferm et al. (2013) and Ferm and Lightfoot (2015) suggest the ABR threshold to eHL correction for NB CE-chirps should be 5 dB less than the corrections for tonebursts with the same centre frequency (for correction tables, see NHSP (2014b), p. 14-15).

Table 3. Summary of the results of Ferm et al. (2013) and Ferm & Lightfoot (2015).
* = significant difference ($p < 0.001$).

	Amplitude CE-chirp: toneburst ratio	**Fmp CE-chirp: toneburst ratio**	**Threshold advantage NB CE-chirp evoked ABR vs. TBABR (NB. Chirp-ABR thresholds were never higher than TBABR).**
0.5 kHz	1.31*	3.0*	-6.2 dB nHL
1 kHz	1.70*	2.5*	-6.2 dB nHL
2 kHz	1.52*	2.1*	-5.7 dB nHL
4 kHz	1.60*	1.8*	-5.2 dB nHL

In a similar research design, Rodrigues, Ramos and Lewis (2013) assessed both amplitude and latency of ABRs evoked by NB CE-chirps compared to TBABR in 40 normal-hearing infants. In agreement with Ferm and colleagues, they found significantly larger amplitudes for the NB CE-chirp compared to the toneburst at 0.5, 1, 2 and 4 kHz, with the exception of stimulation at 80 dB nHL. At 80 dB nHL, ABR amplitudes evoked by the 0.5 kHz toneburst were significantly greater than those evoked by the 0.5 kHz NB CE-chirp. At 1, 2 and 4 kHz, there was no significant difference in amplitude at 80 dB nHL (Rodrigues et al., 2013).

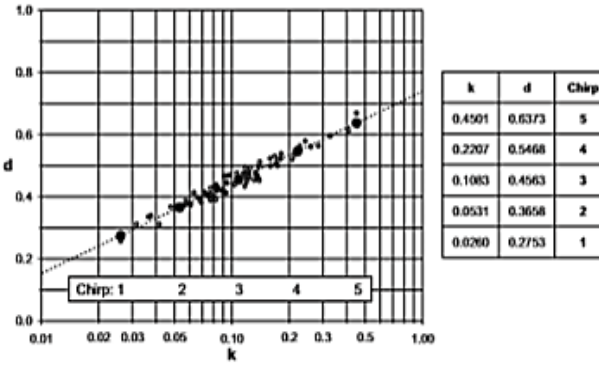
In addition to amplitude, Rodrigues et al. (2013) also assessed ABR latency. Results show significantly shorter latencies at all intensities for the 0.5, 1 and 2 kHz NB CE-chirps. At 4 kHz, the latency difference was not statistically significant. Rodrigues et al. (2013) explain the difference in latency by a difference in response pattern of ABRs evoked by tonebursts or NB CE-chirps. Where TBABRs show the expected pattern, based on general behaviour of ABR latency of decreasing latency with increasing frequency, the opposite occurred for the ABRs evoked by NB CE-chirps (Rodrigues et al., 2013). This difference in latency response pattern was also found very recently by Cobb and Stuart (2016a) in 168 healthy neonates and can be explained by the construction of the NB CE-chirps. The four NB CE-chirps are constructed by decomposing the BB CE-chirp and, consequently, the timing of the octave band chirps corresponds to their temporal location within the broadband chirp. In the BB CE-chirp, the 0-ms point on the time axis of the ABR corresponds to the estimated time of arrival of the 10.000 Hz component of the chirp at the tympanic membrane. Since the four NB chirps have centre frequencies below 10.000 Hz, all stimulus onsets precede the 0-ms point on the time axis (Cobb & Stuart, 2016a; Elberling & Don, 2010; Rodrigues et al., 2013). The 0.5 kHz NB-chirp starts earliest

and the 4 kHz chirp latest (for an overview, see Appendix II). For tonebursts, to the contrary, the stimulus onset is at 0 ms. The paradoxical finding of high frequency NB CE-chirps evoking ABRs with longer latencies than lower frequency NB CE-chirps is thus essentially artefactual (Cobb & Stuart, 2016a).

3.1.5. Level-specific chirp stimuli

In section 3.1.3. is mentioned that Elberling and Don (2008) have re-examined the data of Don et al. (1998; 2005). This re-examination indicated that the change in latency with frequency, determined for derived bands between 1400 and 5700 Hz, varied with stimulus intensity: the lower the stimulus level, the larger the changes in latency with frequency. However, this difference in latency change for high and low intensities was only about 0.55 ms. Elberling and Don (2008) hence concluded stimulus level was not a major influence on the relative cochlear-neural delay and that the final delay model they developed would be valid over a wide range of stimulus levels.

Two years later, Elberling, Callø and Don (2010) revise this statement and join the perspective of Fobel and Dau (2004) that an optimal chirp for ABR measurements should be level-dependent. Elberling et al. (2010) hypothesize that an increasing stimulus levels enlarges the upward spread of excitation. At higher stimulus levels, a broader range of frequency components along the basilar membrane will be excited; resulting in a temporally smeared signal and desynchronization of neural firing. To test this hypothesis, Elberling et al. (2010) examined the ABR recordings evoked by five different chirps of ten normal-hearing subjects between the age of 23 to 64 years old. Each of these five chirps has its own cochlear-neural delay model function, i.e. they changed the values of constants *k* and *d* of the original delay model (eq. 1) of Elberling and Don (2008). The model corresponding to the third chirp uses the mean values of *k* and *d* and therefore approximates the final chirp design of Elberling and Don (2008), see also Figures 8 and 9.



k	d	Chirp
0.4501	0.6373	5
0.2207	0.5468	4
0.1083	0.4563	3
0.0531	0.3658	2
0.0260	0.2753	1

Figure 8 Distribution of the parameter values k *and* d*, which define the latency-frequency function (Eq. 1). Retrieved from Elberling, Callø and Don (2010).*

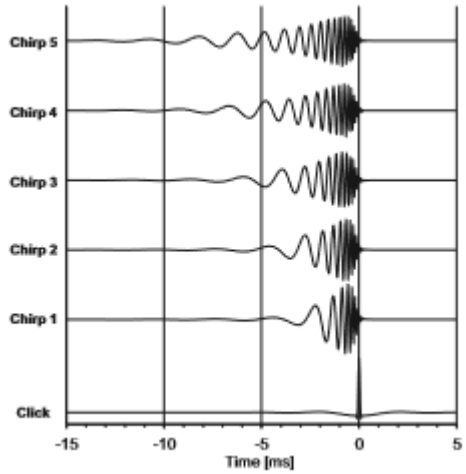


Figure 9 Electrical waveform and temporal location of the stimulus level-dependent chirps in the study of Elberling, Callø and Don (2010).

The results of Elberling et al. (2010) demonstrate that the efficiency of the five different chirps changes with stimulus level. Moreover, they confirm the original findings by Fobel and Dau (2004) that the most efficient chirp is a chirp which becomes progressively longer with decreasing stimulus level. Elberling et al. (2010) suggest this change in efficiency is caused by two different mechanisms, one at lower and one at higher intensities. At 40 dB nHL, the medium intensity level in the study of

Elberling et al. (2010), the largest ABR amplitude was generated with chirp 3. However, at 20 dB nHL chirp 3 was not the most efficient. Chirp 4 and 5, based on a model with a larger change of delay with frequency, generated greater amplitudes (Elberling et al., 2010). These results agree with the original finding from Don et al. (1998) that the latency difference between the 5700 and 1400 Hz derived bands was approximately 0.55 ms longer at 10 – 20 dB nHL compared to 60 dB nHL. However, where Elberling and Don (2008) concluded that, although the difference was statistically significant, the change was small enough to have no practical significance and could therefore be ignored, Elberling et al. (2010) reach a different conclusion. Since the small change in delay results in a shift from chirp 3 to chirp 4 and 5 being the most efficient, Elberling et al. (2010) argue that the cochlear-neural delay model of the CE-chirp should have progressively larger changes of latency delay with frequency the lower the stimulus intensity.

In addition to this mechanism affecting the latency of the chirp at the lower intensities, upward spread of excitation seems to influence the efficiency of the chirp at higher stimulus levels (Elberling et al., 2010; Fobel & Dau, 2004). At lower stimulus levels, the chirps stimulate a restricted part of the basilar membrane, but for higher levels, the excitation broadens. This will cause desynchronization, or temporal smoothing, of the resulting compound excitation of the different excited locations and this, in turn, distorts the waveform morphology of the ABR (Elberling et al., 2010). Since this temporal smoothing is greater the longer the chirp, a short chirp stimulus will limit the desynchronization at higher stimulus levels. The chirps studied in Elberling et al. (2010) are all variants of the same latency-frequency model. Therefore, the results cannot be generalised to other stimulus levels or latency-frequency models. However, the results reported by other research groups using different types of models (Fobel and Dau, 2004; Elberling et al., 2007) do not contradict the results found by Elberling et al. (2010). This indicates that a chirp that compensates for the change in latency delay with intensity for each frequency, would be optimal for the recording of auditory brainstem responses.

To adequately implement this compensation in the design of the chirp, Elberling and Don (2010) introduce a new approach to formulate the latency delay compensation for chirp stimuli: the direct approach. They used the ABR latency to the NB CE-chirps for a range of stimulus levels to construct a new level-specific delay model for the various octave-bands (Elberling & Don, 2010; Kristensen & Elberling, 2012), see Figures 10 and 11. This new level-specific delay model can be described using the following equation:

$$T = k_1 \cdot e^{k2 \cdot L} \cdot f^{-(d_1 \cdot L + d_2)} \qquad (2)$$

in which T is the delay in seconds, f is the frequency in Hertz, L is the stimulus level in dB nHL, k_1 = 1.65, k_2 = -0.0625, d_1 = -0.00755 and d_2 = 0.788. This model should ensure that all the octave-band chirps within the broadband chirp produce frequency-specific ABRs with similar latencies at each stimulus level (Kristensen & Elberling, 2012).

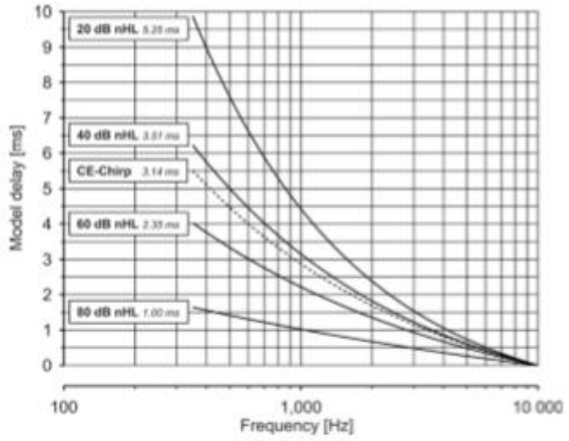


Figure 10 Final delay models corresponding to the broadband chirp levels 20, 40, 60 and 80 dB nHL. The delay with frequency becomes increasingly larger for decreasing stimulus level. The model corresponding to the level-independent broadband CE-chirp is shown for comparison. Retrieved from Elberling & Don (2010).

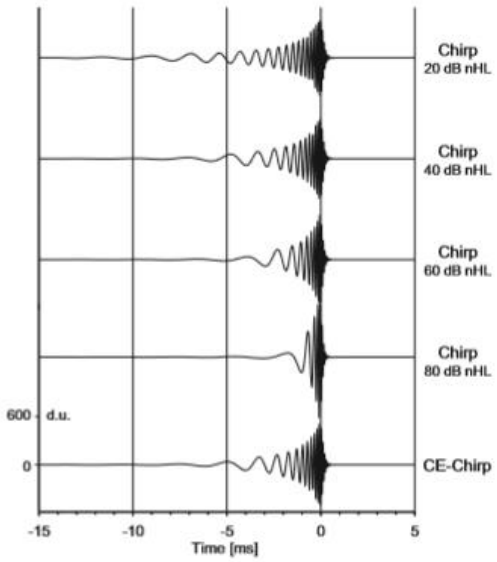


Figure 11 Waveforms of the broadband chirps corresponding to the final delay models of Elberling and Don (2010).

Kristensen and Elberling (2012) tested the adequacy and efficiency of the BB chirp resulting from this new level-specific delay model. They compared the new BB level-specific chirp (LS-chirp) to the level-independent BB CE-chirp in ten normal-hearing adults and hypothesized that the efficiency of the LS-chirp compared to the CE-chirp would be better at higher stimulus levels. The results indeed showed that at 80 dB nHL, the amplitude and waveform resolution of the LS-chirp evoked ABR were significantly better than in the CE-chirp evoked ABR. At 20, 40 and 60 dB nHL, no significant differences were found, although the waveform resolution at 60 dB nHL was better for the LS-chirp (Kristensen & Elberling, 2012). Furthermore, the results of both chirps were compared to the traditional 100 µs click. The ABR amplitudes evoked by the two chirps were significantly greater than in click-evoked ABR, except for the CE-chirp at 80 dB nHL, where the ABR gets distorted and is low in amplitude (Kristensen & Elberling,2012).

These results regarding amplitude clearly show the advantage of the LS-chirp over the CE-chirp and click and higher levels of stimulation. However, when latency is concerned, the results are somewhat more complex. Where latency differences between the LS-chirp, CE-chirp and click are very small to almost zero at 20 and 40 dB nHL, the latency difference increases to a statistically significant difference of approximately 0.5 ms at 60 dB nHL. At 80 dB nHL, the latency difference is even much larger: the CE-chirp generates the shortest response latency (M = 4.29, SD = 0.51 ms), followed by the click (M = 5.29, SD = 0.27 ms) and the LS-chirp (M = 6.31, SD = 0.27 ms). This latency difference can be explained by two phenomena: the design of the LS CE-chirp, i.e. a shorter stimulus at higher stimulus intensity levels, and the temporal location of the LS-chirp (Kristensen & Elberling, 2012).

In Kristensen and Elberling (2012), the temporal location of both the LS CE-chirp and the CE-chirp corresponds to an onset delay of 1.5 ms (see Figure 12). Kristensen and Elberling (2012) chose this delay in an attempt to ensure the chirp-ABR latencies would approximate the click-ABR latencies at lower levels of stimulation, since it has been shown that the level-independent CE-chirp evokes significantly shorter latencies than the click (Cebulla & Elberling, 2010; Elberling et al., 2010; Elberling, Kristensen & Don, 2012). For stimulus levels of 20, 40 and 60 dB nHL, the results show latencies for all three stimuli are approximately the same. Thus, for lower stimulation levels, the temporal forward shifting of the chirps by 1.5 ms seems adequate.

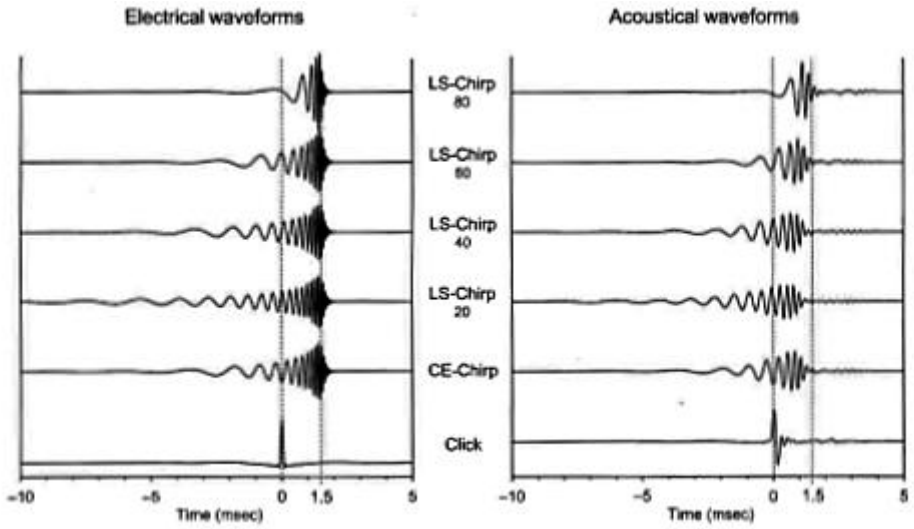


Figure 12 Electrical and acoustical waveforms of the LS-chirp (20, 40, 60 and 80 dB nHL), CE-chirp and click. The 1 ms delay between the electrical (left) and acoustical (right) input is ignored in this figure. The zero ms- point on the time axis for the acoustical waveform indicate the estimated time of arrival of the click at the tympanic membrane. The temporal location of the 10.000 Hz-component of the chirps is delayed 1.5 ms in an attempt to align the latencies for the chirps and click in normal-hearing adults, especially at lower intensity levels. Figure retrieved from Kristensen and Elberling (2012).

However, at 80 dB nHL latencies for the LS CE-chirp are significantly longer than for the CE-chirp and click. Where the temporal forward shifting explains the latency difference concerning the LS CE-chirp and CE-chirp versus the click, it does not explain the latency difference within the chirps, since both stimuli have been temporally shifted. This difference can, however, be explained by the difference in design of these two chirps. As can be seen in Figure 12, the duration of the 80 dB nHL LS CE-chirp is much shorter than the duration of the CE-chirp and, since the 10.000 Hz components in the chirps are temporally aligned at 1.5 ms, all frequency components of the LS CE-chirp below 10 kHz will reach the cochlea later than the corresponding components in the CE-chirp. This results in longer latencies for the LS CE-chirp (Kristensen & Elberling, 2012).

In a small study in our laboratory, Van Bommel (2014) also compared the amplitude and latency of the ABR evoked by the BB and NB LS- and CE-chirps. Unfortunately, this research did not include measurements at 80 dB nHL. The comparison included a moderate intensity stimulus corresponding to the default level for threshold measurement by the NHSP (NHSP, 2014a, see Table 4) and measurements at 25 dB nHL. The results show almost no significant difference in ABR amplitude for the LS-chirp in comparison to the CE-chirp, except for a larger amplitude evoked by the NB 0.5 kHz LS-chirp at the moderate intensity in males and the NB 1 kHz LS-chirp at 25 dB nHL in females. The results at moderate intensities do show a tendency for the LS-chirp to have slightly higher amplitudes than the CE-chirp. The lack of statistical significance might be due to two limitations. First, the study only measured 11 subjects, which were also separated by gender (5 male and 6 female subjects). Secondly, the high intensity measurements used in this research are considerably lower than the highest intensity used by Kristensen and Elberling (2012). Despite these limitations, the findings of Van Bommel (2014) concerning latency do reach statistical significance. Latencies for the LS CE-chirps were significantly longer compared to the CE-chirps at moderate intensities, in spite of using lower intensities than Kristensen and Elberling (2012).

Table 4. Default stimulus levels for threshold measurement according to NHSP (2014a).

Stimulus	**BB chirp**	**0.5 kHz chirp**	**1 kHz chirp**	**2 kHz chirp**	**4 kHz chirp**
Default intensity	45 dB nHL	60 dB nHL	55 dB nHL	50 dB nHL	50 dB nHL

3.1.6. Air-conduction and bone-conduction ABR

Most research concerning ABR has focussed on the adequacy and efficiency of air-conduction ABR (AC ABR) (e.g. Cebulla et al., 2014; Cho et al., 2015; Cobb & Stuart, 2014; Elberling et al., 2007; Elberling & Don, 2008, 2010; Kristensen & Elberling, 2012, Maloff & Hood, 2014; Xu, Cheng & Yao, 2014). However, as with pure tone audiometry, there is a significant role for bone conduction ABR (BC ABR), in particular for the assessment of hearing loss in infants (JCIH, 2007). By using BC ABR, the presence of a conduction component in the potential hearing loss can be assessed (Hall, 2014) in children and adults in which pure tone audiometry is not feasible. An unrecognized conductive component hinders appropriate management, because rehabilitation is dependent on the aetiology of the hearing loss. Moreover, a conductive hearing loss component complicates the detection of retrocochlear pathology for both retrocochlear pathology and conductive hearing loss significantly prolong ABR latencies and a clinician cannot unravel the influence of conductive hearing loss and retrocochlear pathology when only AC ABR is available. To correctly detect retrocochlear pathology the clinician must determine whether the latencies are prolonged independent of a conductive hearing loss component. When there is a retrocochlear pathology at play, the BC ABR recording will show a waveform morphology in which wave I is found at a normal temporal position and subsequent waves, and as a result the interval between wave I and the subsequent waves, are prolonged.

To detect a conductive hearing loss, BC ABR can be used. The clinician examines the ABR air-bone gap, i.e. a difference in latency (temporal approach) and ABR hearing threshold between AC and BC ABR (intensity approach). In order to adequately detect conductive hearing loss, it is very important that the ABR indeed is generated by the tested ear. Therefore, the first goal in BC ABR is to record wave I from the stimulus side (Hall, 2013). A two-channel recording eases this task, because both ipsi- and contralateral ABR curves are obtained. The presence of wave I on the stimulus side in absence of wave I in the second channel, confirms that you have an ear-specific result (Hall, 2013).

In addition to wave I, wave V is an important ABR characteristic to assess the air-bone gap (ABG). It is the crucial factor in both the temporal and the intensity approach of ABG assessment. Conductive hearing loss leads to a higher hearing threshold and prolonged latencies of all five waves in the presence of normal IWIs, i.e. a Total Wave Delay (TWD), in AC ABR. To adequately determine the ABG, both the temporal and the intensity approach should be used subsequently. First the presence of an ABG is determined by comparing wave I and Wave V latencies in both AC and BC ABR. Secondly, AC and BC ABR hearing threshold is determined to establish the magnitude of the ABG in dB (Beattie, 1998; Hall, 2013).

It thus seems clear that there is a clinical advantage of BC ABR measurements. Nevertheless, in most clinics around the globe, BC ABR is hardly used. This is because BC ABR still faces several methodological and technical challenges, which leads to scepticism among clinicians regarding BC ABR and reluctance to use the technique (e.g. Campbell et al., 2004; Elsayed et al, 2015; Hatton, Janssen & Stapells, 2012). Furthermore, normative data for BC ABR measurements are lacking. This renders implementation in clinical practice invalid, since recordings cannot be compared to recordings of normal-hearing subjects. However, several recent studies, including the present study, have examined BC ABR and this has led to an emerging normative database concerning BC ABR (Cobb & Stuart 2016a,b; Elsayed et al., 2015; Hatton et al., 2012). Furthermore, as will be elaborated upon in section 3.1.7.5., several of the mechanical challenges that most clinicians still assume applicable to BC ABR have in fact been worked out in the past decade (e.g. Ginter & Margolis, 2013; Håkansson, 2003; Hall, 2007; Jansson et al., 2014; Small, Hatton & Stapells, 2007; Small & Hu, 2011; Stenfelt & Goode, 2005b).

3.1.7. Stimulus parameters

There are several variables regarding the stimulus that influence the ABR, such as stimulus rate, polarity and intensity level.

3.1.7.1. Stimulus level

The auditory system reacts differently to low or high intensity auditory signals and this is reflected in the ABR waveform, i.e. latencies prolong and amplitudes decrease with decreasing stimulus level (e.g. Beattie, 1998; Cobb & Stuart, 2016a,b; Elberling et al., 2010; Elberling & Don, 2010; Neely et al. 1988; Sininger & Hyde, 2009). This influence of stimulus level seems to be largest within 10 dB of ABR threshold. The latencies tend to prolong faster and amplitudes diminish, in particular at lower frequencies where the peak-to-trough wave V (V-V') complex is often the only wave present and earlier waveform components disappear completely (Sininger & Hyde, 2009).

Moreover, the effect of stimulus level on the ABR is dependent on the applied transduction method, because the maximum output level of the transducers is limited. A supra-aural earphone or insert earphone can deliver stimuli up to 140 dB SPL, but bone transducers can only deliver stimuli up to 50 (500 Hz stimuli) or 60 dB nHL. Furthermore, care must be taken when using insert earphones in infants. Due to a significantly smaller ear canal compared to older children and adults, the stimulus level reaching the cochlea of the newborn will be 10 to 20 dB HL louder (NHSP, 2014a,b). To avoid damage to the cochlea, the NHSP has established maximum stimulus levels for the use of insert earphones in early audiological assessment (NHSP, 2014b, p.13).

3.1.7.2. Stimulus rate

Furthermore, the ABR waveform is also influenced by the stimulus rate. The appropriate stimulus rate for AEP measurements is dependent on the latency of the response. Since the ABR occurs within approximately 10 ms, a fast stimulus rate is permitted (Hall, 2007; Van Bommel, 2014). Furthermore, the stimulus rate should not be faster than the refractory time of the hair cells, i.e. the time the neural units need to recover from firing and after which they can be activated again. When the interstimulus interval (ISI) does not permit for this recovery, the resulting ABR may be altered (Hall, 2007). The refractory time of the onset neurons underlying the ABR is sufficiently rapid to allow for ISIs shorter than 10 ms (Hall, 2007). The same influence on stimulus rate applies to the duration on the stimulus. The shorter the stimulus, the faster the rate can be. This influences in particular the stimulus rate for the various stimuli within the CE-chirp family. As discussed in section 3.1, the duration of the CE-chirps depends on frequency, i.e. the NB 0.5 kHz CE-chirp is the longest and the 4 kHz the shortest. Therefore, the NSHP (2014a) recommends different stimulus rates for the members of the CE-chirp stimuli. For the BB CE-chirp and the NB 1 kHz CE-chirp, a rate of 39.1/sis recommended, 37.1/s for the NB 0.5 kHz CE-chirp, 45.1/s for the NB 2 kHz CE-chirp and 49.1/s for the NB 4 kHz CE-chirp.

In addition to these practical restrictions concerning the stimulus rate, there seems to be no substantial influence of stimulus rate on the ABR. A study of Stevens et al. (2013) on the effect of stimulus rate on the ABR shows that there is no significant effect on test efficiency between 39.1/s and 59.1/s. Test efficiency was measured by confidence in the ABR for a given test time. Also, Gøtsche-Rasmussen, Poulsen and Elberling (2012) showed that ABR threshold differed only 3.8 dB between 20/s and 90/s stimulus rate across the five chirp stimuli. This finding is corroborated by Burkhard and McNerney (2009) citing diverse studies (Burkhard & Hecox, 1983, 1987; Burkhard, Shi & Hecox, 1990) comparing stimulus rates for click-evoked threshold measurements. There is only a moderate influence of stimulus rate on wave V amplitude and Burkhard and McNerney (2009) therefore advocate the use of a relatively fast stimulus rate, that way reducing test time.

However, the recommendations mentioned thus far are strictly applicable to threshold measurements. For otoneurological assessment, a fast stimulus rate is not permitted. Otoneurological assessment requires clear visibility of all ABR waveform components and this can only be obtained by using relatively low stimulus rates. The NHSP (2014a) recommends a stimulus rate of 17.1/s in this context, since a stimulus rate between 10 and 20 Hz enhances the probability of observing wave I. In addition to otoneurological assessment, a low stimulus rate is also recommended for bone-conduction measurements. Because of the lack of interaural attenuation in bone conduction, the signal will reach both cochlea's. Since a low stimulus rate enhances the probability of observing wave I, it provides an opportunity the cochlea that generates the ABR, i.e. the cochlea corresponding to the EEG channel that shows wave I in the ABR waveform (NHSP, 2014c). In this context, the NHSP (2014a,c) recommends a stimulus rate of 19.1/s for bone-conduction measurements.

Finally, the stimulus rate must be chosen wisely in relation to powerline interference, i.e. the 50- or 60-Hz artefact (Ferree et al., 2001; Hall, 2007; Sininger & Hyde, 2009). A stimulus rate that can be evenly divided into 50/60 or harmonics of this frequency should be avoided, since the powerline interference will then be locked in phase to the averaging of the ABR signal and linearly summated. Therefore, the stimulation frequency must lead to the waveform of the powerline interference being out of phase from one sweep to the next (Sininger & Hyde, 2009), such as a rate of 29.1/s (Hatton et al., 2012; NHSP, 2014a), 27.1/s (Elberling et al., 2012; Kristensen & Elberling, 2012) or 57.7/s (Cobb & Stuart 2016a, b, 2014; Stuart & Cobb, 2014).

3.1.7.3. Polarity of the stimulus

A third stimulus variable influencing the ABR is the polarity of the stimulus. Auditory brainstem responses can be measured using three categories of stimulus polarity: condensation, rarefaction, or alternating. Polarity is related to the polarity of the electrical pulse and the subsequent movement of the transducer diaphragm. If a positive electrical pulse and movement of the transducer diaphragm towards the tympanic membrane is generated, a stimulus with a positive pressure wave originates. This movement in a positive direction is called condensation polarity (Hall, 2007). On the contrary, a stimulus can also be presented in negative direction, i.e. rarefaction polarity. Thirdly, alternating polarity is a switching between condensation and rarefaction polarity at subsequent stimulus presentations. The manner in which the switching takes place can differ, i.e. the polarity can change each time a stimulus is presented or it can be switched after a fixed period of time, for example 1 second (e.g. Gøtsche-Rasmussen, Poulsen & Elberling, 2012).

The polarity of click stimuli in ABR measurements has been investigated by a number of studies. Since the hair cells in the cochlea are only excited by a deflection of the stereocilia in the direction of the basal body, i.e. when the basilar membrane moves upwards in the direction of the scala vestibuli, the hair cells and eighth-nerve fibres perform a half-wave rectification of the input signal. This suggest that the rarefaction phase of a stimulus should be most effective (Hall, 1992; Burkhard & McNersey, 2009), because rarefaction polarity theoretically produces an outward movement of the tympanic membrane and in turn the stapes footplate and the oval window (Hall, 1992; 2007). Research of Stockard and colleagues has indeed shown that stimulation with rarefaction clicks leads to shorter latencies and larger amplitudes in comparison to condensation clicks (Stockard et al., 1979). However, other studies have shown that these trends are irregular and that polarity effects are (at best) small and variable (Schwartz, Morris & Jacobson, 1994; Borg & Lofqvist, 1981). Moreover, research of the effects of polarity on auditory brainstem responses is complicated by the fact that the polarity of the stimulus may be reversed by ringing of transducers, ear-canal acoustics and/or middle ear and inner ear mechanics (Borg & Lofqvist, 1982; Dallos, 1975; Gerull et al., 1985). Therefore, it is difficult to ensure that the polarity presented to the cochlea is indeed the stimulus polarity reaching the hair cells (Hall, 2007).

3.1.8. Acquisition parameters

There are various factors related to data acquisition that influence the ABR waveform morphology, amplitudes and latencies. These factors will be discussed in the following sections.

3.1.8.1. The EEG

The ABR recording is obtained using electroencephalography (EEG). The EEG is recorded using four electrodes defined according to the International 10-20 system (Jasper, 1958), i.e. an inverting electrode on the ipsi- and contralateral mastoid, a noninverting electrode on the vertex (Cz) or high on the forehead (Fz) and an electrode on the lateral forehead serves as a ground (BCEHP, 2012; Beattie et al., 1986). There is a univocal relationship between the auditory evoked response and the electrode site: the closer the electrode is to the anatomic generator, the larger the response (Hall, 2007). However, in recording far-field responses with electrodes placed far from the anatomic generator, such as ABR, the exact location of the non-inverting electrode is not critical. The ABR is essentially comparable when the non-inverting electrode is placed along the midline from Cz to Fz (Hall, 2007). The placement of electrodes on both the ipsi- and the contralateral mastoid allows for two-channel recordings: forehead/vertex to right mastoid and forehead/vertex to left mastoid (BCEHP, 2012). Furthermore, the pathway of the electrode wires is of significance. The wires should be led away from the transducers to reduce stimulus artefact. Moreover, considering decrease of the 60- or 50-Hz artefact, electrode wires should be kept close together, short and preferably braided (BCEHP, 2012).

In addition to the placement of the electrodes, the quality of the ABR recording depends on electrode impedance, since the induced electrical interference is proportional to the (difference in) electrode impedances. Therefore, electrode impedance should be kept under 5000 ohms and should be as similar as possible between electrodes, preferably within 2000 to 3000 ohms (Hall, 2007; NHSP, 2014a). The British Columbia Early Hearing Program (BCEHP, 2012) recommends even stricter values, i.e. electrode impedances of less than 3000 ohms for all electrodes, and impedance differences of less than 1000 ohms.

When the electrodes are placed correctly, the clinician can start the ABR recording. This is a delicate process since the ABR is imbedded in the general EEG signal of the brain and in comparison to this general signal the ABR is particularly small. To increase the detectability of the ABR signal, the EEG signal is filtered. By filtering the EEG, the unwanted noise in the signal, for example as a result of muscle activity is reduced. That way, the signal-to-noise ratio (SNR) is increased, enlarging the reliability of the ABR (Sininger & Hyde, 2009).

However, choosing accurate filter settings is crucial. The ABR has spectral energy just below 100 Hz to a little above 1000 Hz. Electromyogenic activity shares the spectrum of the ABR in the low frequencies (approximately 100 – 500 Hz) and can therefore not be filtered out entirely. It can, however, be filtered out at the higher end of the filter, since neuromuscular activity contains frequencies up to 5000 Hz. Furthermore, research in adults has shown that including energy below 100 Hz in the recording by setting the cut-off frequency of the high-pas filter to 30 Hz increased the ABR amplitude, in particular for low-frequency stimuli (Boston & Ainslie, 1980; Domico & Kavanagh, 1986; Kavanagh, Harker & Tyler, 1983), and this effect is even greater in infants (Hyde, 1985; Stapells, 1989; Stuart & Yang, 1994). Consequently, a band-pass filter setting of 30 to 1500/3000 Hz will effectively minimize general EEG activity (Hall, 2007).

This increase in low-frequency information on the other hand also has its disadvantages. It increases the risk of including unwanted noise, including electromyogenic activity and 50- or 60-Hz electrical interference from electrical power sources, in the recording. Lowering the high-pass filter from 100 to 30 Hz should thus be restricted to clean recording conditions with low electrode impedances, little electrical interference and a quite subject. Only in these situations, the increase in

ABR amplitude can be reliably attributed to a better quality of the ABR recording (Sininger & Hyde, 2009).

To conclude, filter settings should be carefully determined, in order to adequately filter the EEG, without filtering out crucial information concerning the ABR itself. The safest clinical policy is to filter as little as is strictly necessary, that way reducing the possibility of filter settings contributing to distortion in the latency of ABR waves and the probability of waveform components actually being EEG artefacts (Hall, 2007). Therefore, wider filter settings (within reasonable limits) are preferred during data collection. Even more so when the evoked response system permits digital filtering after data collection (Hall, 2007).

3.1.8.2. Averaging and artefact rejection

"Signal averaging is the heart of evoked response systems" (Hall, 2007, p.94). By averaging the recording of brain activity following multiple presentations of the stimulus, the AEP can be extracted from the EEG noise (Sininger & Hyde, 2009). Since the ABR has small amplitudes compared to later AEPs, it requires more stimulus presentations. Typically, most clinicians record 1000 – 4000 sweeps per stimulus for ABR, dependent on stimulus level and the quality of the recording. When the EEG signal is clean, the number of sweeps can be lower (Hall, 2007). To ensure a sufficient number of sweeps is obtained, without wasting clinical time on excessive recording of responses, a stop criterion can be set in most ABR systems (Hall, 2007). There are generally two stop criteria used in ABR measurements, i.e. Fmp or an estimation of residual noise level (RNL). Most common is a value of 99% Fmp or 30 to 40 nV_{RMS} estimated residual noise (e.g. Cho et al., 2015; Elberling & Don, 2010; Kristensen & Elberling, 2012; Mühler, Rahne & Verhey, 2013; Rodrigues, Ramos & Lewis, 2013).

The RNL is an ongoing calculation as the average accumulates that measures the variability of the noise remaining in the average record, ideally as a standard deviation (Sininger & Hyde, 2009). A 99% Fmp, to the contrary, is a statistical measure. This response detection statistic calculates the variance of the EEG noise at on forehand determined data points and all points in a time region of interest around it, for example 10 ms (signal + noise). Subsequently, the ratio of variance of the data points versus variance in the time region is calculated. The larger this ratio is, the greater the probability that an actual response is present. Since Fmp is an F statistic and the calculated ratio can be looked up in the statistical table of the F distribution to determine the likelihood of obtaining a value as large or larger (Sininger & Hyde, 2009). The most important F-values are 2.25 ($\alpha = 0.05$, 95% likelihood of response), 2.65 ($\alpha = 0.025$, 97,5% likelihood of response) and 3.1 ($\alpha = 0.01$, 99% likelihood of response) (Elberling & Don, 1984).

Recently, Stuart & Cobb (2014) evaluated the influence of number of sweeps on the wave V amplitude in 23 neonates, using 100 µs click and CE-chirp stimuli. The stimulus level used was low, i.e. 30 dB nHL, as typically used in newborn hearing screenings (Stuart & Cobb, 2014). Response were obtained using an exponentially increasing number of sweeps, i.e. 116, 232, 464, 928 and 1856. For all neonates to have a response, 1856 sweeps were necessary in click ABR, compared to 464 in CE-chirp ABR. The amplitude of CE-chirp measurements was significantly larger than the amplitude of the click measurements, that way improving the response detection and reducing test time. Stuart & Cobb (2014) explain the smaller number of sweeps necessary and larger amplitudes for CE-chirps with the notion that chirp stimuli compensate for the traveling wave delay along the cochlea and increase temporal synchrony of firing. This is in accordance with findings in studies concerning ABR measurements using CE-chirp stimuli in adults (Cebulla & Elberling, 2010; Elberling & Don, 2008; Elberling, Callø & Don, 2010; Fobel & Dau, 2004; Kristensen & Elberling, 2012; Petoe, Bradley & Wilson, 2010a,b).

An ABR waveform thus consists of the average of a significant number of stimulus presentation. However, there may be stimulus presentations in which an exceptional amount of noise is present.

There are two techniques to minimize the influence of these presentations on the resulting ABR waveform: weighted averaging and artefact rejection. First, the average can be weighted. In 1985, Elberling and Wahlgreen developed a technique in which the various sweeps receive more or less weight in the final average based on the amount of EEG noise. This technique is called Bayesian weighting and the essence of this technique is that the change of variance in the amplitude of sweeps contributing to the average is taken into account and a more reliable ABR signal is obtained. Bayesian weighting is not the only weighted averaging technique, but it is the most common used in ABR recordings. It is important to realise, however, that weighted averaging does not resolve the problem of a noisy EEG. Weighting a generally noise EEG still leads to inefficient measurements, as the weighting technique will just give more weight to sweep subsets containing a little less noise compared to other subsets, thus generating a final average that contains a relatively high amount of EEG noise. The golden rule for ABR recordings still applies: 'Get the quietest possible EEG from the subject's head by whatever means available' (Sininger & Hyde, 2009, p. 296).

In complementation with Bayesian weighting, the artefact rejection technique ensures that sweeps containing an excessive amount of EEG noise will not be included in the averaging process. By rejecting these high-amplitude EEG noise artefacts, the final average is protected against electrical activity resulting in high noise, such as waking up of the subject (Sininger & Hyde, 2009). The artefact rejection criterion is a predetermined value in µV, typically 40 µV in adults. In infants, this value can be lower since noise levels in a sleeping baby can decrease to as little as 2 µV (NHSP, 2014a). Therefore, artefact rejection levels in infant ABR often range from 20 µV (e.g. Cobb & Stuart, 2014) to 5 µV (Ferm & Lightfoot, 2015; Ferm, Lightfoot & Stevens, 2013; Stevens et al., 2013). The recent study of Stevens et al. (2013) has examined the test efficiency of 5 and 10 µV artefact rejection in infant ABR. The 5 µV artefact rejection level resulted in a 25% shorter test time to obtain the same SNR. This result suggest that clinicians should always strive for the lowest artefact rejection criterion possible. A useful rule of thumb is that the rejection rate should be maximally 5 – 10% of the accepted sweep count. Then, EEG noise artefacts will be successfully eliminated from the average and the final average will not be corrupt (Sininger & Hyde, 2009).

3.1.8.3. Cross hearing and contralateral masking

Contralateral masking is noise presented to the non-test ear in an attempt to ensure the non-test ear does not contribute to the ABR. By presenting the noise, the experimental stimulus cannot reach the cochlea of the non-test ear and cross hearing is prevented. The most common type of noise used for this purpose is 'white noise'. The exact frequency content of this broadband noise is determined by the frequency response of the transducer, for example supra-aural earphones have a frequency response that falls off for frequencies above 5000 - 6000 Hz. As a consequence, so does the masking noise energy (Hall, 2007).

Contralateral masking should be applied as soon as the interaural attenuation (IA) threshold is surpassed (Campbell et al., 2004; Hall, 2007; Yang, Rupert & Moushegian, 1987). This threshold differs between transducers. Supra-aural headphones and insert earphones have an IA threshold of 40 and 60 dB nHL, respectively (Interacoustics, 2016). To the contrary, an early study on bone conduction by Yang et al. (1987) suggests that in clinical testing with BC ABR, clinicians should assume the IA for adults to be 0 dB nHL. This is corroborated by various researchers (e.g. Hood, 1960; Studebaker, 1967; Sanders and Ritelman, 1964; see Yacullo (2009) for a review). Thus, for BC ABR in adults contralateral masking is always necessary. Furthermore, it is highly recommended to use two-channel recordings of the ABR, as it permits the recording of a contralateral response and aids the determination of which cochlea is stimulated (Campbell et al., 2004; Stapells & Ruben, 1989; Valeriote, 2015). For one-year-olds, Yang et al. (1987) estimate the IA to be approximately 10 dB and for infants roughly 25 dB nHL.

Recently, two handbooks have suggested that contralateral masking is not strictly necessary when a subject has unequivocally normal auditory evoked responses in both ears (Hall, 2007; Yacullo, 2009). Although two unmistakably normal ears within the same subject should lead to essentially the same ABR, research has shown that binaural presentation of stimuli leads to small changes in the ABR, in particular larger amplitudes, as a result of the interaction between the left and right peripheral auditory system (Dobie & Berlin, 1979; Fowler & Horn, 2012; Van Yper et al., 2015). The safest clinical procedure is thus to always use contralateral masking in BC ABR.

3.1.8.4. Challenges of bone-conduction ABR

In the previous sections, the most important factors related to ABR data acquisition have been discussed. Although the auditory route for air- and bone conduction is considerably different, these factors apply to AC as well as BC ABR. However, the deviant auditory route for bone conduction in which the sound waves enter the cochlea through the surrounding bone instead of the outer ear and the middle ear, leads to several challenges in BC ABR that do not hinder AC ABR. Furthermore, regarding the transduction method for BC ABR, a few obstacles need to be faced.

The occlusion effect

The occlusion effect refers to an improvement of bone-conduction hearing for sounds below 1000 Hz when the outer ear of the subject is covered with supra-aural or insert earphones (Hall, 2014; John, Dimitrijevic & Picton, 2001; Picton et al., 2001; Stenfelt & Goode, 2005a,b; Tonndorf, 1966). This effect is most likely caused by two factors. First, there is an enhancement of osseotympanic bone conduction. Because the outer ear is covered, the energy generated by osseotympanic vibration deep in the ear canal, cannot escape via the ear canal. Therefore, in covered conditions this energy is added to energy that vibrates the tympanic membrane, resulting in a higher energy level reaching the inner ear (Hall, 2014). Secondly, the earphones block some ambient sound from entering the ear canal, which, as a result, cannot mask the bone-conducted sound (Hall, 2014).

Due to this occlusion effect, it is very important that the test ear in bone conduction measurements is not covered by a transducer, since the resulting occlusion effect would render the bone conduction thresholds inaccurate (Elpern & Naunton, 1963; Hall, 2014; Herdman & Stapells, 2003). After all, the calibration of bone vibrators and determination of reference levels for bone conduction testing is based on the assumption that the test ear is uncovered (Hall, 2014). However, the occlusion effect is age dependent. For infants under 10 – 22 months of age, the effect is negligible (John & Picton, 2000; Small, Hatton & Stapells, 2007; Small & Hu, 2011).

To conclude, using supra-aural or insert earphones for contralateral masking in BC ABR is possible, but the clinician should ensure that only the non-test ear is occluded by the earphone.

Sensitivity to vibrator placement

Bone-conduction stimulation can be presented anywhere on the head, but the most common vibrator placements for clinical purposes are the mastoid bone and the frontal bone. In 2007, researchers Small, Hatton and Stapells demonstrated that forehead placement, although it is commonly used, is less efficient than placement on the mastoid when conducting ABR and ASSR measurements in infants. The measurements with the bone transducer placed on the forehead led to significantly higher thresholds (Small et al., 2007). Similar results were found in research involving adult subjects (ANSI S3.43, 1992, cited in Schlauch & Nelson, 2009; Hall, 2007).

This decrease in efficiency can be explained by an attenuation effect. Due to a larger distance from the transducer to the ear, the intensity of the sound reaching the cochlea will be lower. This expected decrease is influenced by the age of the subject, stimulus frequency and stimulus type and lies between approximately 5 and 15 dB nHL in adults (Studebaker, 1967; Durrant & Boston, 2007;

Stenfelt & Goode, 2005b; Hall, 2007). For infants, the effect is even larger, most likely due to the membranous sutures surrounding the temporal bone in infants (Yang et al., 1987; Small et al., 2007). The attenuation factor can increase to as high as 30 dB nHL in infants (Small et al., 2007). To conclude, placement on the mastoid bone is preferred for BC ABR.

A second factor related to the sensitivity to vibrator placement applies to both mastoid and forehead placement and concerns the proximity to the recording electrodes, respectively the electrode on the ipsilateral mastoid or the Cz/Fz. This proximity, in combination with a substantially higher driving signal needed for BC stimulation to reach equal sensation levels compared to AC stimulation, creates a substantial electromagnetic artefact (Fowler & Durrant, 1994; Durrant & Boston, 2007; Van der Heijdt, 2016).

Mechanical challenges

Besides the large electromagnetic artefact that is generated in BC ABR, as has been discussed in the previous section, there are several mechanical issues in BC ABR related to bone transduction and the available transducers. An important factor in this matter is the distortion in commercially available bone transducers, in particular at lower frequencies. This distortion factor limits the maximum output that a bone transducer can produce to 50 to 60 dB HL (Durrant & Hyre, 1993b; Durrant & Boston, 2007).

The most commonly used transducer for BC is the Radioear B71. Until recently, the B71 bone transducer revealed the least distortion compared to other transducers. However, a new transducer became commercially available recently: the Radioear B81. The B81 transducer has been elaborately evaluated and compared to the Radioear B71 by Jansson et al. (2014). They have found that B81 reaches 10.7-22.0 dB HL higher maximum output than B71 for frequencies below 1500 Hz, with a total harmonic distortion (THD) of maximally 6% or an input voltage of maximally 6 V_{RMS} as criteria, and that B81 had significantly lower THD up to 1000 Hz. Even at 250 Hz, BC ABR can be recorded up to 50 dB nHL with B81 (Håkansson, 2003).

Furthermore, Jansson et al. (2014) showed that there was no statistically significant difference in frequency response between the two transducers, except for a deviation at the mid frequencies, for which B81 was more efficient. Also, the electrical impedances of the two transducers were practically the same (Jansson et al., 2014). In general, B81 had an improved electro-acoustic performance compared to B71, including significantly better distortion values. In particular, B81 allows for sensorineural hearing loss to be measured at considerably higher hearing levels than with B71 below 1500 Hz (Ginter & Margolis, 2013; Håkansson, 2003; Jansson et al., 2014).

Variability in bone-conduction ABR

The standardization of normative values in BC ABR is hindered by several variable elements regarding BC ABR. First, the delicacy of vibrator placement that has been discussed earlier. Secondly, the pressure by which the vibrator is held to the skull (using a headband or handheld) is important. The recommended coupling force for audiometric BC measurements in adults is 500 g (Hall, 2007). For infants, the coupling force should not exceed 200 g, since results of Yang et al. (1991) showed that a higher coupling force prolongs wave V latencies. The coupling force of the transducer to the head of the subject should thus be controlled and remained constant during the measurement session (Yang et al., 1991).

Furthermore, the interpretation of BC ABR can be complicated due to uncertainty regarding the actual characteristics of the stimulus reaching the cochlea. These characteristics can be substantially different for various subjects and transducers (Hall, 2007). First, the transmission properties of the skull of the subject may lead to a change in stimulus characteristics. The filter

settings of the skull complicate the determination of the frequency composition of the BC stimulus that reaches the cochlea (Arlinger, 1981; Harder, Arlinger & Kylen, 1983; Weber, 1983; Kramer, 1992; Gorga et al., 1993). Secondly, the degree of acoustic radiation varies between commercially available bone transducers (Hall, 2007). This leakage of sound energy may be heard by the subject via the AC auditory route at high test frequencies (from approximately 4000 Hz onward) and may lead to underestimation of the BC threshold (Frank & Crandell, 1986). This acoustic radiation is relatively high for the Radioear B71. The acoustic radiation of the promising new bone transducer Radioear B81 has not yet been assessed (Jansson et al., 2014).

3.2. Aim of the study

Until now, most ABR research has been conducted using click stimuli. Since approximately ten years, a new stimulus has been implemented in the Interacoustics Eclipse ABR system (Interacoustics A/S, Assens, Denmark): the CE-chirp. The past ten years, this stimulus has proven to lead to significantly better ABR results compared to click-evoked ABR, yielding greater amplitudes and significantly reducing test time, as well for the broadband as the later developed octave-band versions of the chirp. Within the last decade, the CE-chirp has been elaborately evaluated within various populations and these evaluations have repeatedly proven that the CE-chirp results in significantly better ABR responses than the traditional click stimulus.

However, Elberling and Don (2008) have re-evaluated their model of the CE-chirp (Elberling et al., 2007) and concluded that the model of the CE-chirp did not sufficiently consider the influence of stimulus level on the change in latency with frequency and as a result did not provide the optimal chirp for ABR measurements. Therefore, Elberling and Don (2010) developed a new level-specific construction model for the CE-chirp, resulting in a level-specific CE-chirp. The broadband version of this LS-chirp has been evaluated by Elberling et al. (2012) and Kristensen and Elberling (2012). The results of these studies suggest that the broadband LS-chirp generates similar results compared to the level-independent broadband CE-chirp at lower intensities, and significantly better ABRs at high intensities (i.e. 80 dB nHL).

The purpose of the present study is to further evaluate the new LS-chirp for air-conduction as well as bone-conduction measurements. The study is focussed on ABR latency. We evaluate the broadband and narrowband versions of this chirp by measuring LS CE-chirp evoked AC ABRs at 40, 70 and 90 dB nHL and BC ABRs at 40 dB nHL. ABR latencies of the BB and four NB chirps are compared within and between air- and bone-conduction and within and between intensities. Based on the theoretical design of the LS CE-chirp model (Elberling & Don, 2010; Kristensen & Elberling, 2012), we do not expect significant changes in latency between the BB and NB versions of the LS CE-chirp at the same intensity and within the same transduction method. We do hypothesize, based on previous research concerning BC click-evoked ABR latency (Beattie, 1998; Elsayed et al., 2015; Gorga et al., 1993; Sohmer & Freeman, 2002; Stenfelt & Goode, 2005a; Van der Werff et al., 2009), that there will be a latency difference between AC and BC LS-chirp-evoked ABR latencies. This expected latency difference implies longer latencies for all waves in BC measurements compared to AC measurements.

Furthermore, we expect to find differences in latency between the three intensities within the chirps. In addition to this general latency evaluation concerning intensity, we have chosen to measure high-intensity ABRs in order to evaluate the feasibility of LS CE-chirp evoked ABR for otoneurological assessment. The intensities 70 and 90 dB nHL are chosen, because these are the default intensities for otoneurological measurements in the Radboud University Medical Centre (Radboud UMC). ABR measurements at these intensities served a double purpose, i.e. (1) evaluation

of the LS-chirp at high intensities and (2) consideration of the possibility to use the LS-chirp for otoneurological assessment. Several researchers have shown that the waveform morphology of early wave components (i.e. wave I to III) in chirp-evoked ABR is less clear compared to click-evoked ABR (e.g. Kristensen & Elberling, 2012; Petoe et al., 2010a,b). We therefore hypothesize that assessment of the I-V interval will not be possible in chirp-evoked ABR. We expect, however, that assessment of the III-V interval is possible.

For the bone-conduction measurements, a lower intensity, i.e. 40 dB nHL, is chosen. At this intensity, well above hearing threshold for our normal-hearing subjects, a clear response can be generated with a manageable influence of the relatively large and long stimulus artefact generated by the chirp in bone-conduction measurements. In addition to the LS CE-chirps, the BC ABR testing protocol contained a traditional click stimulus. This stimulus was added in order to evaluate the differences in latency for click- and BB LS CE-chirp evoked ABR. For AC ABR, Kristensen and Elberling (2012) evaluated the difference in latency between click- and BB LS CE-chirp evoked ABR. Since they found longer latencies for the BB LS CE-chirp compared to the click, we expect to find the same pattern in BC ABR.

Moreover, BC ABR hearing threshold is established using the broadband LS-chirp. This threshold determination serves to explore the possibilities of reliable threshold measurements using BC ABR. To consider the reliability of the obtained threshold, the BC ABR thresholds are compared to a subjective threshold measurement using the BB LS CE-chirp and to the subjective BC pure tone audiometry thresholds. We hypothesize a general agreement between objective and subjective threshold measurements using BB LS-chirp-evoked BC ABR, i.e. discrepancy between objective and subjective threshold measurements generally within 10 dB nHL (NHSP, 2014b, table 7 p. 15).

By means of these experimental comparisons, this study aims to provide an answer to several research questions. In order to structurally address these questions, the study will be divided into four experiments, each with its own central question:

(1) What are the normative latencies of wave I, III and V for the BB and four NB LS CE-chirps?
    a. What is the difference in latency between the five versions of the LS CE-chirp measured at 90, 70 and 40 dB nHL?
    b. What is the difference in latency for air-conducted (AC) and bone-conducted (BC) ABR measurements using broadband and narrowband level-specific CE-chirps measured at 40 dB nHL?
    c. Is there a relationship between LS CE-chirp evoked ABR latency and gender of the subject?
    d. Is there a relationship between LS CE-chirp evoked ABR latency and age of the subject?
    e. Is there a relationship between LS CE-chirp evoked ABR latency and handedness of the subject?
    f. Is there a relationship between LS CE-chirp evoked ABR latency and the measured ear?
(2) What is the difference in latency for BC BB LS-chirp-evoked and click-evoked ABR measurements?
(3) Is it possible to assess otoneurological pathologies with LS-chirp-evoked AC ABR measured at 70 and 90 dB nHL?
(4) What is the agreement between objective and subjective threshold measurements using BB LS-chirp-evoked BC ABR?

4. Method and Materials

4.1. Participants

The participants were 50 healthy, normal-hearing adults (25 females, 25 males). The participants ranged in age from 18 to 33 years (M = 23.30, SD = 2.97). They presented with normal hearing sensitivity, i.e. threshold ≤ 20 dB HL from 500 to 4000 Hz. The tested ear was the ear that presented with the best bone-conducted hearing. Of all subjects, 82% was right-handed and 18% left-handed. Furthermore, no subjects reported otoneurological pathologies. Three (3%) subjects reported a concussion, but they did not report any persisting symptoms. Additionally, two subjects (4%) had a tympanic membrane perforation (right ear) and one subject (2%) reported a devious tympanic membrane in the right ear. We performed the measurements on the left ear. An overview of subject factors can be found in Appendix III. Prior to testing, participants were informed about the purpose and procedure of the measurement and all signed an informed consent.

4.2. Procedure

For this study, we examined several aspects of air-conducted and bone-conducted LS CE-chirp ABR measurements. For the different measurement conditions, ABRs were recorded within the same participants and the same parameter settings for the ABR system were used. Before ABR measurements were performed, hearing thresholds of the subject were tested using air-conducted and bone-conducted pure tone audiometry in both ears. Pure tone audiometry served to confirm participants had normal hearing, i.e. thresholds ≤ 20 dB HL. After confirmation of normal hearing in both ears, one was selected for ABR measurements. ABR measurements were conducted on the ear with the lowest bone-conduction thresholds at all four centre frequencies.

All measurements were conducted using the Interacoustics Eclipse EP25 system®. This system is equipped with the click stimulus, as well as both the CE-chirp and LS CE-chirp (broadband and narrowband) stimuli. Recordings were performed in an anechoic room and the lights were dimmed during recording. Auditory Brainstem Responses were recorded using four electrodes, placed according to the international 10 – 20 system (Jasper, 1958). An ipsilateral recording montage was used with the noninverting electrode on the vertex (Cz), inverting electrodes on the ipsi- and contralateral mastoid ($M_{1,2}$) and a ground electrode on the forehead (Fp_2). The electrodes were attached to the skin with Ten20 conductive paste, after cleaning the skin with an alcohol containing disinfectant and Nuprep Skin Prep Gel. A maximum impedance level of 5kΩ was maintained during all measurements. EEG samples exceeding ± 40 µV were rejected and EEG was bandpass-filtered from 30 to 3000 Hz. The options ‘minimize interference’ and ‘Bayesian weighting’ were applied during all measurements. The option ‘minimize interference’ is a method to minimize the sensitivity to periodic electrical interferences and the Bayesian Weighting tool increases the SNR by giving sweeps with less noise a higher level of importance in signal averaging. Detailed measurement protocols for the air-conducted and bone-conducted measurements are described in Appendix IV and V. After attachment of the electrodes, participants were asked to lie down on a comfortable bed with their eyes closed. Subjects were instructed to relax and, if possible, to sleep.

Stimulus conditions were presented randomly. Half of the participants first received air-conducted stimulation, for the other half measurements started with the bone-conduction measurements. The measurements within each transducer condition were also randomized. Presented stimulus conditions were air-conducted BB and NB LS-CE chirps at three intensities, i.e. 90, 70 and 40 dB nHL, and bone-conducted BB and NB LS-CE chirps and a click stimulus at 40 dB nHL. Due to time constraints, not all participants received all stimulus conditions. Responses to AC and BC BB LS CE-chirp and BC click were obtained in all participants, but for the NB LS CE-chirp, conditions were shared between subjects. All subjects received all AC NB CE-chirps on the lowest intensity, i.e. 40 dB

nHL, but the two higher intensities were only measured for two of the four NB LS CE-chirps. Conditions were equally assigned to the subjects. Concerning the BC measurements, subjects received three out of four NB LS CE-chirp conditions. The number of subjects receiving each stimulus was balanced per gender. Stimuli were presented using condensation as well as rarefaction polarity. Two traces were collected per polarity in order to confirm reproducibility. After measurement with both polarities, waveforms were summed (Grand Average).

For air-conduction measurements stimuli were presented at diverse stimulus rates, i.e. the BB LS CE-chirp was presented at 39.1/s, the NB LS-CE chirps of 500, 1000, 2000 and 4000 Hz at respectively 37.1/s, 39.1/s, 45.1/s and 49.1/s. These are the recommended stimulus rates for BB and NB CE-chirp stimuli by the NHSP (2014a,c). Contrarily, a slower stimulus rate was used for the bone-conduction measurements, i.e. 19.1/s. The NHSP (2014a,c) recommends this rate to increase the probability of observing wave I.

4.3. Analysis

4.3.1. Experiment 1

Identification of the waveform components based on visual inspection of the waveform. The examiner identified all waveform components and this was verified by an experienced clinical audiologist. Statistical analyses were performed with IBM SPSS Statistics, version 22. Aim of this experiment was to assess the waveform morphology and latencies of waves I, III and V. Therefore, the identifiability of the waveform components was assessed first. The percentage of waveforms in which each component was present and reproducible was calculated using SPSS.

In addition to the identifiability of the waveform components, reproducibility of the waveforms was assessed. Two traces were collected per stimulus polarity in order to confirm reproducibility. To confirm summation of the two collected traces is justified, condensation traces of BB LS CE-chirp evoked ABR were analysed separately, i.e. AC BB 90 dB nHL, AC BB 70 dB nHL, AC BB 40 dB nHL and BC BB. A paired samples T-test served to confirm the similarity between both traces.

Furthermore, the latencies of waves I, III and V were assessed. To reduce the number of variables, it was first examined whether the summation trace properly reflected the latency of the condensation and rarefaction trace. Using a paired samples T-test, comparing the latency of the condensation and the rarefaction trace for each variable, the examiner checked whether the mean latency of the condensation and rarefaction trace were significantly different ($p < .05$). If this was the case, condensation and rarefaction traces were evaluated separately. If the mean latency of the condensation and rarefaction trace did not significantly differ, the summation trace was seen as an accurate reflection of both traces and was used in further statistical analyses.

Means and standard deviations of the AC and BC LS CE-chirp were calculated. Additionally, differences in mean latencies for AC and BC ABR measurements were examined per stimulus, i.e. BB, NB 0.5k, NB 1k, NB 2k and NB 4k LS CE-chirp, with a paired samples T-test, after checking for normality of the distribution of the latency data for each variable. The paired samples T-test was performed if both variables had at least 10 valid cases and data for males and females were analysed separately.

Moreover, wave V latency of the ABRs evoked by the five different LS CE-chirps were tested for similarity, as the construction of the chirp implies. A repeated measures ANOVA of wave V latency of ABRs evoked by the five chirps was performed. If the assumption of sphericity was not met, which was examined using Mauchly's Test of Sphericity, a Huynh Feldt correction factor was applied to the degrees of freedom to adequately interpret the ANOVA. Air-conduction and bone-conduction ABRs were analysed separately.

In addition to the assessment of differences in ABR latency, the correlation of ABR latency with influencing patient factors was also examined. For the latency variables that met the assumption of normality, a Pearson's correlation was calculated to evaluate the relationship between ABR wave V latency and the influencing patient factor. If the assumption was not met, Kendell's Tau was performed.

4.3.2. Experiment 2

The determination procedure for ABR latencies was the same as in Experiment 1. Differences in mean latencies for BC click and BC BB LS CE-chirp evoked ABR measurements were calculated using a paired samples T-test, after checking for normality of the latency data distribution. The data for males and females were analysed separately.

4.3.3. Experiment 3

The determination procedure for ABR latencies was the same as in Experiment 1. First, the percentage present and reproducible of each waveform component was calculated for both males and females. Means and standard deviations of waves I, III and V and interwave intervals I-III, I-V and III-V were calculated for males and females separately as well. A repeated measures ANOVA served to assess whether AC ABR wave V latencies for the 40, 70 and 90 dB nHL intensity level differed significantly. If the assumption of sphericity was not met, which was examined using the Mauchly's Test of Sphericity, a Huynh Feldt correction factor was applied to adequately assess the differences.

4.3.4. Experiment 4

The agreement between bone-conduction objective and subjective hearing threshold was examined using the ABR BC BB LS CE-chirp hearing threshold, the mean threshold of the screening audiogram and a subjectively determined BC BB LS CE-chirp hearing threshold. Objective and subjective thresholds were determined in 48 participants (25 females, 23 males). First, the assumption of normality was checked for these three variables. When the assumption was met, a Pearson's correlation was performed to evaluate the agreement between objective and subjective (PTA and BB LS-CE chirp) hearing thresholds. If the assumption was not met, Kendell's Tau was performed. Furthermore, correlation with gender, handedness, ear measured and age was checked.

5. Results

In Table 5 (females) and Table 6 (males), an overview is given of the identifiable and reproducible waves per stimulus. As can be seen from the tables, identifiability percentages do not always reach 100%. This can be explained by the chosen identification procedure. In case of an inconclusive response, we have opted to not identify the waves in order to avoid contamination of the latency data. Furthermore, condensation traces of BB LS CE-chirp evoked ABRs have been analysed separately to confirm that merging 2 traces of the same polarity is justified. The paired samples T-test showed no significant differences in wave I, III or V for all four BB LS CE-chirp evoked ABR conditions. We therefore assume that the reproducibility of waveform components within polarity is ensured.

Table 5. Percentage of identifiable and reproducible waveform components per stimulus for the female subjects.

		I			**III**			**V**		
		Con	Rar	Sum	Con	Rar	Sum	Con	Rar	Sum
Air-conduction										
BB 90	25	92	92	96	100	100	100	100	100	100
0.5k 90	14	-	-	-	7	7	0	100	100	93
1k 90	14	-	-	-	100	100	79	100	100	93
2k 90	15	-	-	-	80	80	87	93	93	93
4k 90	15	20	20	20	100	100	100	100	100	100
BB 70	25	92	88	88	100	100	100	100	100	100
0.5k 70	14	-	-	-	29	21	21	93	93	93
1k 70	14	36	21	29	79	71	71	93	100	100
2k 70	15	67	53	73	100	93	100	100	100	100
4k 70	15	80	93	93	100	100	100	100	100	100
BB 40	25	28	40	44	80	80	88	100	100	100
0.5k 40	25	12	12	12	40	32	20	80	80	76
1k 40	25	24	20	24	44	52	52	88	92	96
2k 40	25	36	40	48	76	76	76	100	100	100
4k 40	25	44	52	60	84	88	92	96	96	96
Bone-conduction										
Click	25	68	68	84	80	80	92	100	100	100
BB	25	52	60	60	64	60	64	100	100	96
0.5k	17	18	12	-	82	76	59	88	82	88
1k	18	33	33	33	72	61	67	89	94	89
2k	18	50	44	44	72	83	89	94	94	94
4k	17	65	53	65	82	82	88	100	100	100

Table 6. Percentage of identifiable and reproducible waveform components per stimulus for the male subjects.

		I			**III**			**V**		
		Con	Rar	Sum	Con	Rar	Sum	Con	Rar	Sum
Air-conduction										
BB 90	25	84	80	84	100	96	100	100	100	100
0.5k 90	13	-	-	-	8	-	8	100	100	100
1k 90	13	-	-	-	69	69	62	92	100	100
2k 90	13	-	-	-	85	85	85	92	92	92
4k 90	14	29	21	29	93	93	93	100	100	100
BB 70	25	92	100	100	100	100	100	100	100	100
0.5k 70	13	-	-	-	62	62	31	100	100	100
1k 70	13	15	31	31	100	100	92	100	100	100
2k 70	13	77	85	77	100	92	100	100	100	100
4k 70	14	93	93	93	93	100	100	100	100	100
BB 40	25	36	36	44	84	80	88	100	100	100
0.5k 40	25	16	8	4	44	36	24	80	88	88
1k 40	25	12	20	12	40	52	32	84	88	84
2k 40	25	40	36	40	80	68	76	100	100	100
4k 40	25	44	44	52	80	68	72	100	100	100

Bone-conduction										
Click	25	76	72	72	80	88	84	96	96	96
BB	25	56	52	56	60	52	56	100	100	100
0.5k	19	16	11	5	74	63	47	95	89	84
1k	19	53	47	16	68	53	58	89	84	95
2k	19	32	47	42	79	74	84	100	100	100
4k	19	58	47	58	79	63	84	100	100	100

In addition to identifiability of the waveform components, the differences in latency between condensation and rarefaction traces have been assessed to ensure the summation curve reflects both traces evenly and can be used for the statistical analyses. For every waveform component per stimulus and at each intensity, a paired samples T-test was performed to check for significant differences in mean latency for the condensation and rarefaction traces. The distribution of the data was assumed to be normally distributed, because the number of participants was larger than 30 (N=50). In general, condensation and rarefaction traces per stimulus and per intensity did not differ significantly from one another. However, Table 7 provides a list of the small number of stimulus conditions in which a significant difference in latency for the condensation and rarefaction traces did occur, organised per gender. For these conditions, the condensation and rarefaction trace were analysed separately in the following statistical analyses and the summation curve was not taken into account.

Table 7. Stimulus conditions with a significant difference in latency between the condensation and rarefaction trace, organised per gender. Latencies may vary from Appendices VII, VIII and IX due to missing values in the paired samples T-test analysis.

Stimulus conditions	**Gender**	**Latency (ms)**				**Latency difference (ms)**	**Value of T**	**Significance level (two-tailed)**
		Con		Rar				
		mean	SD	mean	SD			
AC BB 90 wave III	Males	3.86	0.16	3.76	0.10	0.10	3.982	p = .001
	Females	3.74	0.19	3.66	0.15	0.08	3.425	p < .01
AC BB 90 wave V	Males	5.80	0.22	5.66	0.24	0.14	4.894	p < .001
	Females	5.59	0.17	5.46	0.19	0.13	3.941	p = .001
AC BB 70 wave III	Males	4.03	0.17	4.09	0.21	0.06	-2.960	p < .01
	Females	3.91	0.17	3.97	0.16	0.06	2.830	p < .01
AC 0.5k 90 wave V	Males	5.97	0.55	5.58	0.30	0.39	2.903	p < .05
	Females	5.97	0.47	5.72	0.65	0.25	1.083	p = .298
AC 0.5k 40 wave III	Males	5.04	0.32	5.31	0.82	0.27	-0.998	p = .352
	Females	5.23	0.32	5.80	0.16	0.57	-3.832	p < .01
AC 1k 70 wave III	Males	4.24	0.20	4.48	0.30	0.24	-2.841	p < .05
	Females	4.30	0.19	4.16	0.28	0.14	1.211	p = .257
AC 2k 70 wave I	Males	2.31	0.23	2.39	0.18	0.08	-2.338	p < .05
	Females	2.37	0.19	2.35	0.16	0.02	0.475	p = .650
AC 2k 70 wave III	Males	4.30	0.34	4.31	0.29	0.01	-0.340	p = .740
	Females	4.28	0.19	4.39	0.14	0.11	-2.646	p < .05
BC 2k wave V	Males	7.47	0.53	7.51	0.53	0.04	-2.285	p < .05
	Females	6.95	0.49	6.93	0.49	0.02	0.891	p = .386
BC 4k wave III	Males	5.30	0.40	5.30	0.39	-	-0.302	p = .769
	Females	5.11	0.42	5.07	0.42	0.04	3.680	p < .01
BC 4k wave V	Males	7.20	0.37	7.20	0.35	-	0.128	p = .899
	Females	6.80	0.35	6.75	0.36	0.05	2.324	p < .05

5.1. Experiment 1

The aim of experiment 1 was to examine the (differences in) ABR latencies of wave V evoked by AC and BC LS CE-chirp. First, the mean latency and standard deviation of the condensation, rarefaction and summation trace are calculated. Data for the male and female subjects are separated. An overview of the data can be found in Appendices VII, VIII and IX.

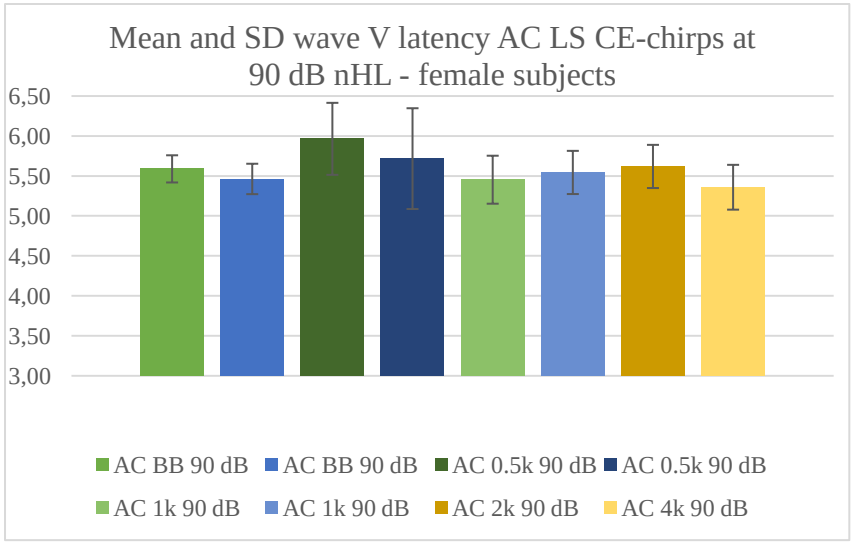
5.1.1. Assessment of differences in wave V latency

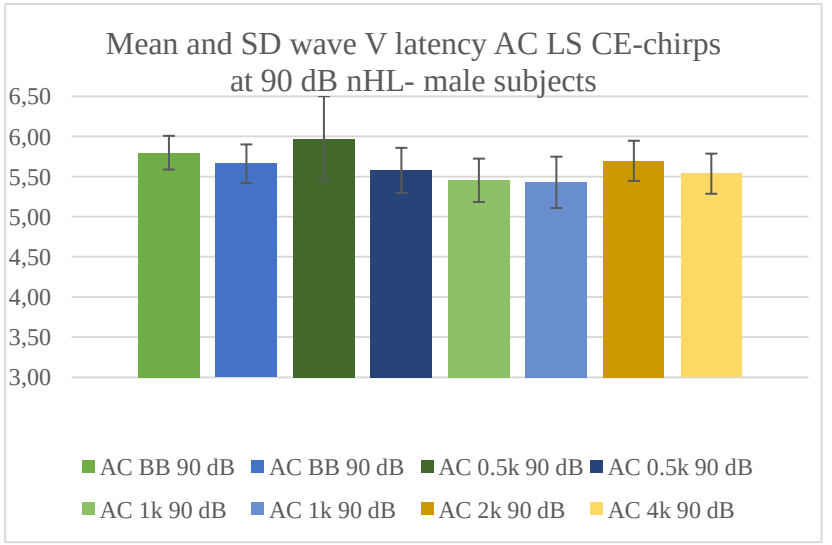
Broadband vs narrowband chirp

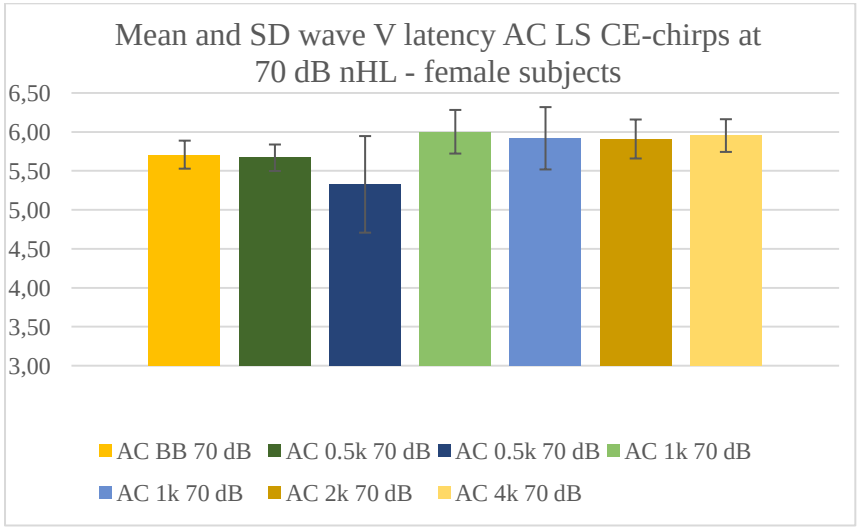
In experiment 1, the broadband and narrowband versions of the LS CE-chirp were compared based on obtained latency. Separate analyses were performed for the AC and BC conditions. The AC BB LS-CE chirp was measured in all 50 participants at 40, 70 and 90 dB nHL. The AC narrowband chirps were measured in all participants at 40 dB nHL. ABRs at 70 and 90 dB nHL were recorded in 27 (14 females, 13 males) participants for NB 0.5k and 1k LS CE-chirp, 28 (15 females, 13 males) participants for the NB 2k LS CE-chirp and 29 (15 females, 14 males) participants for the NB 4k LS CE-chirp. For bone conduction, the click and BB LS CE-chirp were measured in all participants. The 0.5k, 1k, 2k and 4k NB LS CE-chirps were measured in 36, 37, 37 and 36 participants, respectively (19 males and 17 or 18 females).

To examine the differences in latency between the various stimulus types, a repeated measures ANOVA was performed for each transduction type. A repeated measures ANOVA was found suitable since only 5 out of 39 latency variables presented with non-normally distributed data: AC BB 90 V rarefaction, AC BB 70 V summation, AC 4k 90 V summation and AC 4k 70 V rarefaction and summation. To correctly interpret the ANOVA, Mauchly's Test of Sphericity was performed first. If the assumption of sphericity was not met, a Huynh Feldt correction factor was applied to the results of the ANOVA in order to correctly assess the difference.

Results of the air-conduction repeated measures ANOVA show no significant difference between stimulus types at 90 dB nHL (females: $F(2.203, 144) = 0.680$, $p = .525$ and males: $F(1.259, 144) = 1.325$, $p = .268$) or 70 dB nHL (females: $F(1.298, 144) = 0.840$, $p = .395$ and males: $F(1.348, 144) = 2.883$, $p = .088$). This is in accordance with the design of the LS CE-chirp (Elberling et al., 2010; Elberling et al., 2012; Kristensen & Elberling, 2012). However, at 40 dB nHL a significant difference between BB and NB LS CE-chirp latencies is found in the female subjects ($F(1.658, 120) = 5.856$, $p < .01$). Post hoc testing reveals a significant difference between BB and NB 2k LS CE-chirp wave V latency ($p < .001$). For the male subjects, the difference between wave V latency for the five stimuli at 40 dB nHL was not significant ($p = .054$), but the results do show a similar trend in the latency difference between the BB and NB 2k LS CE-chirp. Results of the bone-conduction repeated measures ANOVA show no significant difference in latency between the chirp stimuli (females: $F(2.677, 96) = 1.023$, $p = .382$ and males: $F(1.769, 96) = 1.892$, $p = .167$).







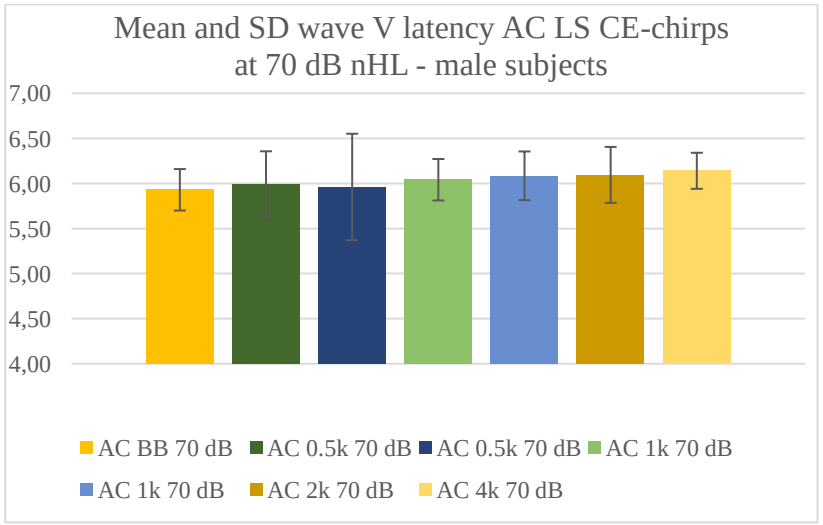
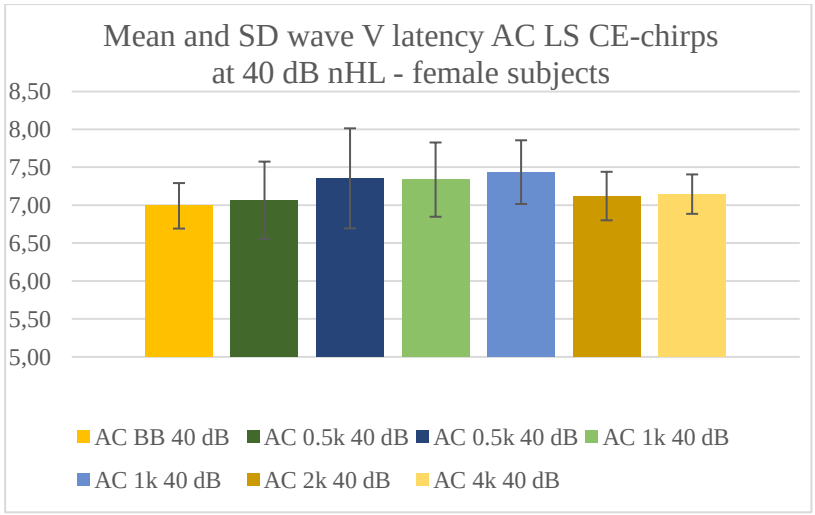
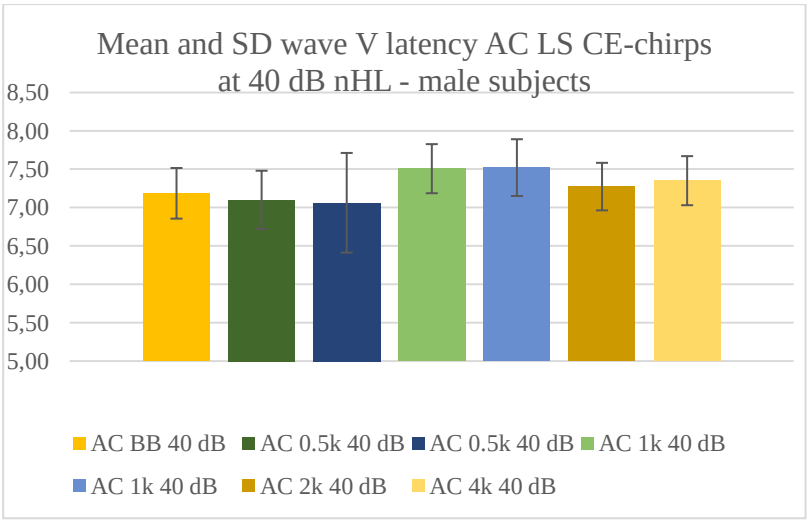
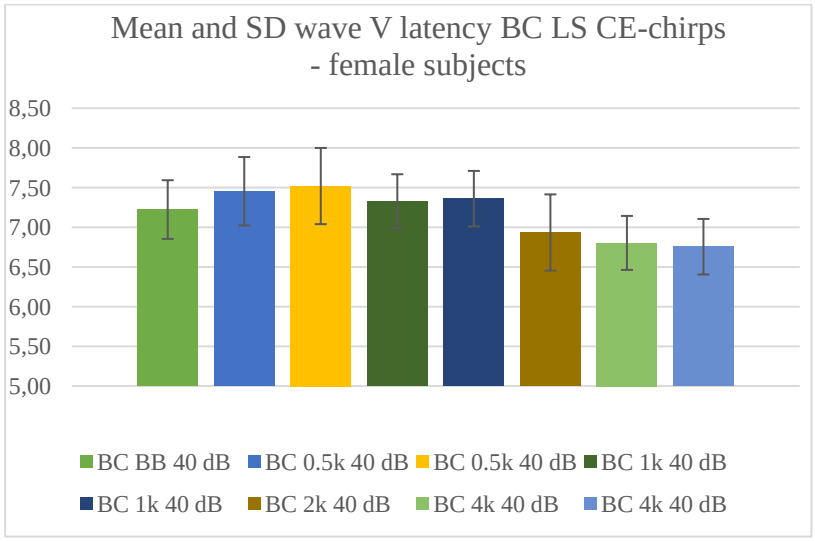


Figure 13 Differences in mean latency between the LS CE-chirps for the AC 70 and 90 dB nHL conditions. Error bars reflect the standard deviation of the mean.







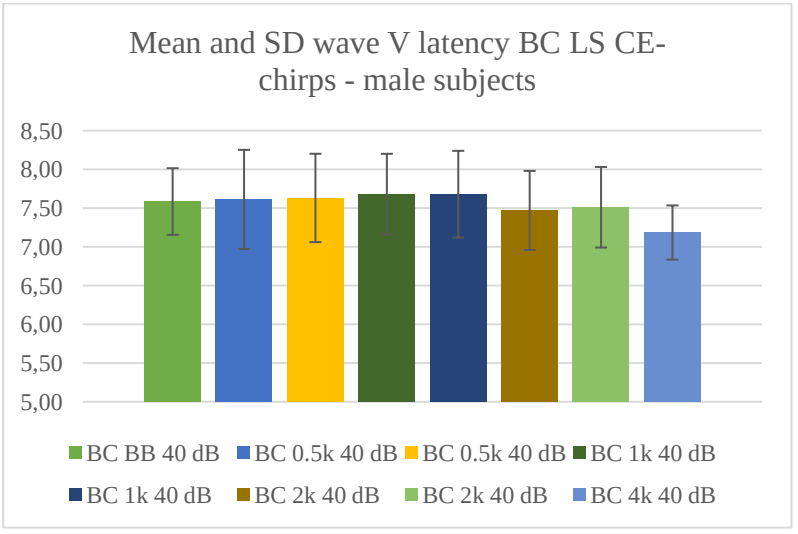


Figure 14 Differences in mean latency between the LS CE-chirps for 40 dB nHL AC and BC conditions. Error bars reflect the standard deviation of the mean.

Air-conducted vs Bone-conducted ABR

Differences in ABR latency for AC and BC ABR were analysed per stimulus type. The data were analysed separately for male and female subjects. As can be seen above, the latency data were, overall, normally distributed. Considering the small number of variables deviating from a normal distribution, a paired samples T-test was found suitable for this dataset. Using the paired samples T-test, differences in mean latency of AC and BC ABR at 40 dB nHL were examined per stimulus type. The results of these test can be found in Table 8 (females) and Table 9 (males).

Table 8. Difference in mean latency for AC and BC ABR at 40 dB nHL for the female subjects. *Standard deviation in parentheses.

Comparison	**Wave V latency in ms***		**N**	**Value of T**	**Statistical significance**
	AC	**BC**			
AC BB vs BC BB	6.99 (0.31)	7.22 (0.39)	24	-4.592	p < .001
AC 0.5k vs BC 0.5k	7.29 (0.58)	7.47 (0.49)	14	-0.872	p = .399
AC 1k vs BC 1k	7.39 (0.40)	7.33 (0.34)	17	0.675	p = .509
AC 2k vs BC 2k	7.13 (0.32)	6.93 (0.49)	17	1.971	p = .066
AC 4k vs BC 4k con	7.17 (0.28)	6.82 (0.36)	16	4.791	p < .001
AC 4k vs BC 4k rar	7.17 (0.28)	6.76 (0.37)	16	5.334	p < .001

Table 9. Difference in mean latency for AC and BC ABR at 40 dB nHL for the male subjects. *Standard deviation in parentheses.

Comparison	**Wave V latency in ms***		**N**	**Value of T**	**Statistical significance**
	AC	**BC**			
AC BB vs BC BB	7.18 (0.34)	7.58 (0.44)	24	-5.211	p < .001
AC 0.5k vs BC 0.5k	7.19 (0.45)	7.61 (0.57)	13	-2.593	p < .05
AC 1k vs BC 1k	7.54 (0.28)	7.58 (0.54)	13	-0.396	p = .698
AC 2k vs BC 2k con	7.28 (0.32)	7.47 (0.53)	19	-2.021 -2.525	p = .058 p < .05
AC 2k vs BC 2k rar	7.28 (0.32)	7.51 (0.53)	19		
AC 4k vs BC 4k	7.37 (0.36)	7.18 (0.36)	18	2.127	p < .05

Patient factors influencing wave V latency

In addition to the differences in wave V latency for the various stimulus type, the influence of several patient factors, i.e. gender, age, handedness and ear measured, on wave V latency was also examined. For the five wave V latency variables that significantly deviated from a normal distribution, i.e. AC BB 90 V rarefaction, AC BB 70 V summation, AC 4k 90 V summation and AC 4k 70 V rarefaction and summation, Kendall's tau correlation coefficient was calculated. For all other wave V latency variables, the relationship was examined using a Pearson correlation coefficient.

Results show a significant influence of gender on AC BB (90 dB: $r_\tau = .420$, $p < .001$, 70 dB: $r_\tau = .414$, $p < .001$ and 40 dB: $r_{pb} = .296$, $p < .05$) and 4k NB LS CE-chirp (90 dB: $r_\tau = .328$, $p < .05$, 70 dB: $r_\tau = .383$, $p < .01$ and 40 dB: $r_{pb} = .328$, $p < .05$) wave V latency at all three intensities, AC 2k NB LS CE-chirp wave V latency at 40 dB nHL ($r_{pb} = .238$, $p < .05$) and BC click and BB, 1k NB, 2k NB

and 4k NB LS CE-chirp wave V latency (click: r_{pb} = .588, p < .001, BB: r_{pb} = .401, p = .01, 1k: r_{pb} = .386, p < .01, 2k: r_{pb} = .492, p = .001 and 4k: r_{pb} = .501 p = .001).

Furthermore, results show a significant correlation between handedness and wave V latency for the AC NB 0.5k LS CE-chirp at 40 dB nHL and the BC BB LS CE-chirp in the female subjects (respectively r_{pb} = .554, p < .01 and r_{pb} = .429, p < .05) and the AC NB 0.5k LS CE-chirp at 70 dB nHL and AC NB 4k LS CE-chirp at 40 dB nHL in the male subjects (respectively, r_{pb} = .488, p < .05 and r_{pb} = .420, p < .05). Also, a significant relationship between age and wave V latency was shown for the AC NB 0.5k LS CE-chirp (rarefaction) at 90 dB in the male subjects (respectively, r_{pb} = .534, p < .05). Additionally, the relationship between the measured ear and wave V latency was statistically significant for the AC NB 0.5k (rarefaction) and 2k LS CE-chirp at 90 dB nHL and the BC NB 0.5k LS CE-chirp in the female subjects (respectively, r_{pb} = -.638, p < .01, r_{pb} = -.703, p < .01 and r_{τ} = -.542, p < .05) and NB 0.5k LS CE-chirp at 40 dB nHL in the male subjects (r_{pb} = .371, p < .05).

5.2. Experiment 2

The aim of experiment 2 was to examine the difference in latency for BC click-evoked and broadband LS CE-chirp evoked ABR. First, the normality of de data distribution of both variables was checked using a Kolmogorov-Smirnov test of normality. Results showed only a significant deviation from normality for BC click wave III and wave V in female subjects (respectively, D(23) = .189, p < .05 and D(25) = 0.220, p <.01). All other variables for female and male subjects were normally distributed. A paired samples T-test was therefore performed to examine the differences in mean latency of click- and BB LS CE-chirp evoked BC ABR for male and female subjects separately. Significant differences in mean latency were found for each waveform component in both the male and female subjects, see Table 10.

Table 10. Difference in mean latency for BC Click and BB LS CE-chirp evoked ABR. *Standard deviation in parentheses.

Comparison	**Gender**	**Latency in ms***		**N**	**Value of T**	**Statistical significance**
		Click	**BB LS**			
BC click vs BB LS CE-chirp wave I	Female	3.11 (0.13)	3.40 (0.31)	12	-2.241	P < .05
	Male	3.31 (0.19)	3.86 (0.35)	13	-5.012	P < .001
BC click vs BB LS CE-chirp wave III	Female	5.22 (0.24)	5.52 (0.38)	15	-4.207	P = .001
	Male	5.48 (0.29)	6.05 (0.29)	13	-3.418	P < .01
BC click vs BB LS CE-chirp wave V	Female	6.98 (0.27)	7.22 (0.37)	24	-4.299	P < .001
	Male	7.42 (0.34)	7.58 (0.43)	24	-2.110	P < .05

5.3. Experiment 3

As has been discussed earlier, identifiability of waveform components has been assessed for all LS CE-chirp evoked ABRs. As can be seen from Table 5 and 6, wave I is not present for the 0.5k NB LS CE-chirp at 70 and 90 dB and the 1k and 2k NB LS CE-chirp at 90 dB nHL. This is because wave I is obscured by the stimulus artefact (see figure 15 for an example). For the BB and NB 4k LS CE-chirp, wave I has been identified in most traces.

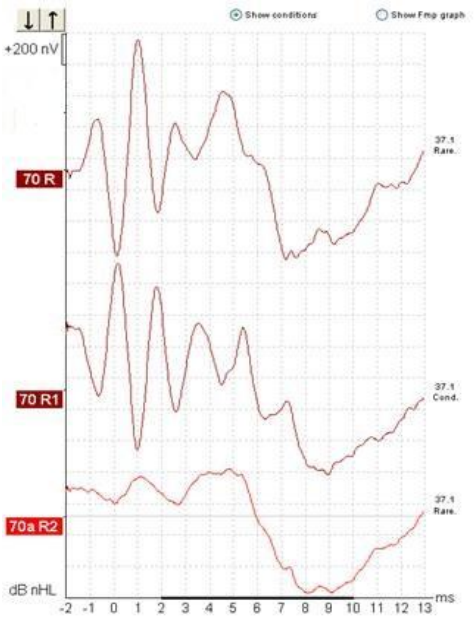


Figure 15 Stimulus artefact of the AC NB 0.5k LS CE-chirp at 70 dB nHL. Respectively, the rarefaction, condensation and summation trace are shown.

5.3.1. Normative data for otoneurological assessment

The Radboudumc normative data pool for otoneurological assessment from a previous study (Van Bommel, 2014) consists of ABR data evoked by a traditional click stimulus. These data can now be complemented by the LS CE-chirp data that have been assembled in the present study. Therefore, means and standard deviations of waves I, III and V and interwave intervals I-III, I-V and III-V have been calculated for males and females separately. The complete normative data pool can be found in Appendices IX and X and representative examples of ABR waveforms evoked by the five different LS CE-chirps in Appendix XI.

Furthermore, a repeated measures ANOVA was carried out to examine the differences in latency between the three intensity levels per stimulus type. A Huynh Feldt correction on the degrees of freedom was performed in each ANOVA. For the BB LS CE-chirp, a significant difference in latency between the intensity levels (females: $F(1.873, 72) = 457.464$, $p < .001$, males: $F(1.683, 72) = 472.634$, $p < .001$) was found. Post hoc analyses showed significant differences in latency between each pair of intensity levels, i.e. 40 vs 70 dB nHL, 40 vs 90 dB nHL and 70 vs 90 dB nHL.

For the 0.5k NB LS CE-chirp, the repeated measures ANOVA also showed a significant difference in latency between the intensity levels (females: $F(1.430, 72) = 9.007$, $p < .01$, males: $F(1, 72) = 6.269$, $p < .05$). Post hoc analyses revealed a significant difference between ABR latency at 40 dB nHL compared to 70 and 90 dB nHL in the female subjects. Latencies of ABRs evoked at 70 and 90 dB nHL did not differ significantly. For the male subjects, only wave V latency of NB 0.5k LS CE-chirp 70 dB nHL at condensation and rarefaction polarity differed significantly.

For the 1k NB LS CE-chirp, a significant difference in latency between the intensity levels has likewise been shown by the repeated measures ANOVA in the male subjects ($F(1, 48) = 8.930$, $p < .01$). Post hoc analyses showed significant differences in latency between each pair of intensity levels, i.e. 40 vs 70 dB nHL, 40 vs 90 dB nHL and 70 vs 90 dB nHL. Concerning the female subjects, no significant differences in latency have been found ($F(1.611, 48) = 1.832$, $p = .179$).

For the 2k NB LS CE-chirp, the significant difference in latency between intensity levels has not been shown by the repeated measures ANOVA (females: $F(1.096, 96) = 1.467$, $p = .239$, males: $F(1.097, 96) = 1.812$, $p = .190$).

For the 4k NB LS CE-chirp, the repeated measures ANOVA showed a significant difference in latency (females: $F(1.096, 72) = 4.595$, $p < .05$, males: $F(1.001, 72) = 42.013$, $p < .001$) and post hoc analyses revealed significant differences in latency for all pairs of intensity levels, i.e. 40 vs 70 dB nHL, 40 vs 90 dB nHL and 70 vs 90 dB nHL, for the male subjects. For the female subjects, only a significant difference in latency for 70 vs 90 dB nHL has been found.

Table 11. Wave V latency measured at 40, 70 and 90 dB nHL for all five LS CE-chirps, organised per gender. The latency values shown are measured at the summation trace.

		BB LS CE-chirp		**NB 0.5k LS CE-chirp**		**NB 1k LS CE-chirp**		**NB 2k LS CE-chirp**		**NB 4k LS CE-chirp**	
		Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
40 dB	Males	7.18	0.33	7.11	0.47	7.51	0.31	7.27	0.31	7.35	0.32
	Females	6.99	0.30	7.31	0.52	7.45	0.46	7.12	0.32	7.14	0.26
70 dB	Males	5.93	0.23	5.89	0.36	6.03	0.20	6.10	0.31	6.14	0.20
	Females	5.71	0.18	5.73	0.40	5.92	0.33	5.91	0.25	5.95	0.21
90 dB	Males	5.72	0.20	5.71	0.33	5.40	0.22	5.70	0.25	5.54	0.25
	Females	5.52	0.15	5.62	0.32	5.47	0.22	5.62	0.27	5.36	0.28

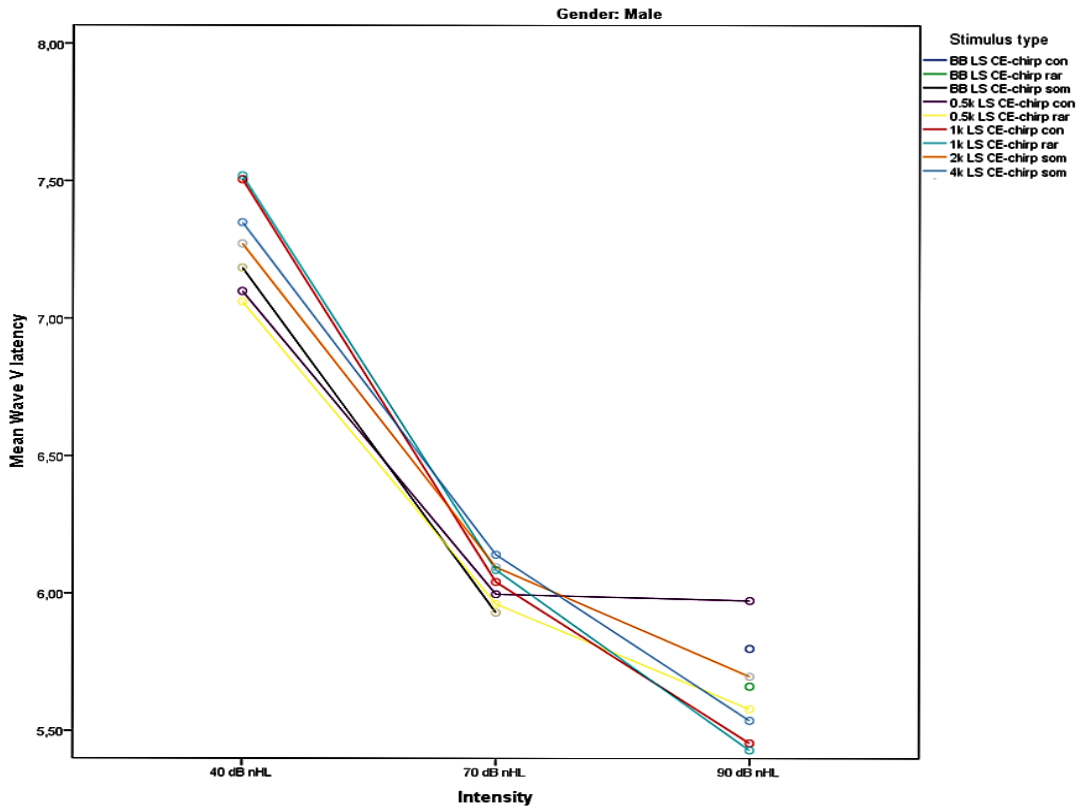


Figure 16 Latency-intensity function of the male subjects. At 90 dB BB, NB 0.5k and NB 1k condensation and rarefaction are shown and NB 2k and 4k summation traces. At 70 and 40 dB, the summation trace of the BB and NB 2k and 4k LS CE-chirp are shown and the condensation and rarefaction trace for the NB 0.5k and 1k LS CE-chirp. Data show similar patterns in latency change with intensity for all chirps, except for the NB 0.5k LS CE-chirp in condensation polarity, for which almost equal latencies were found between 70 and 90 dB nHL.

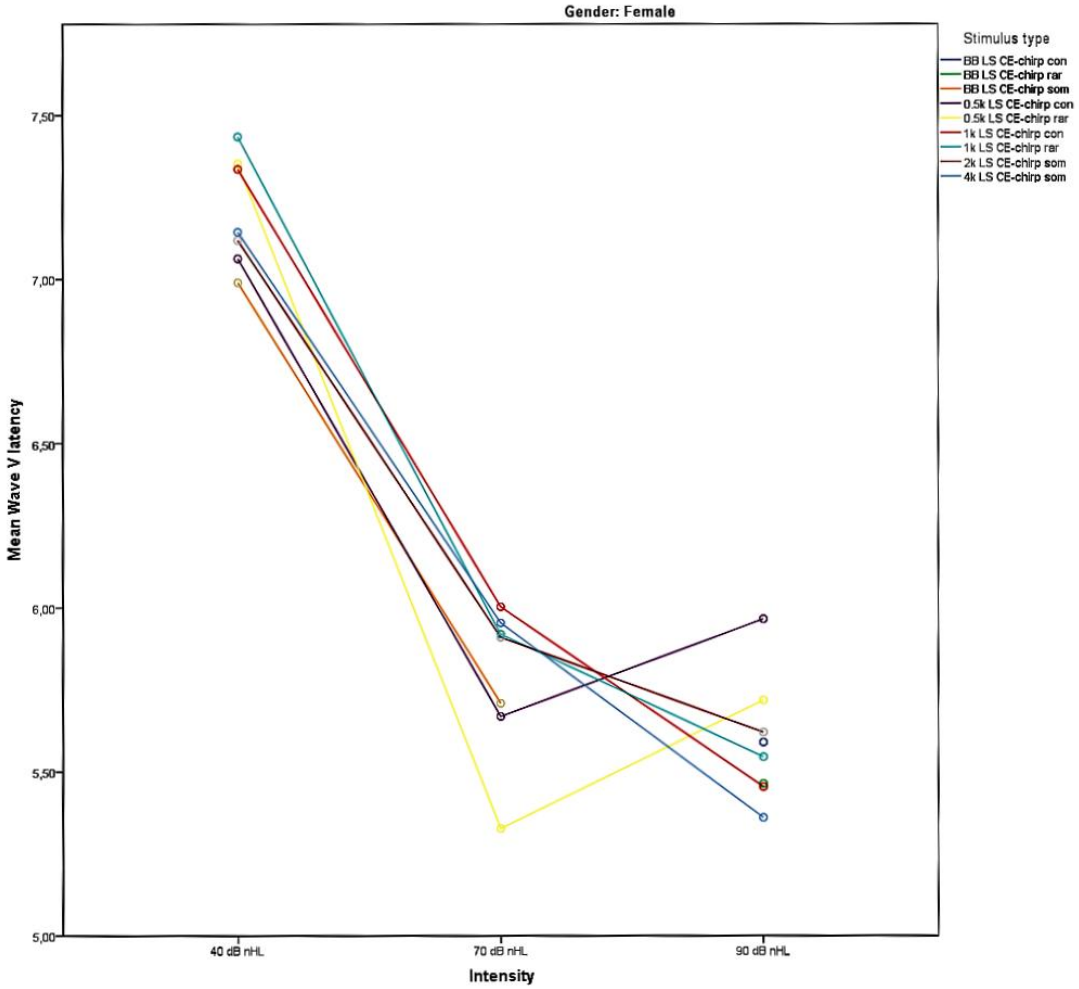
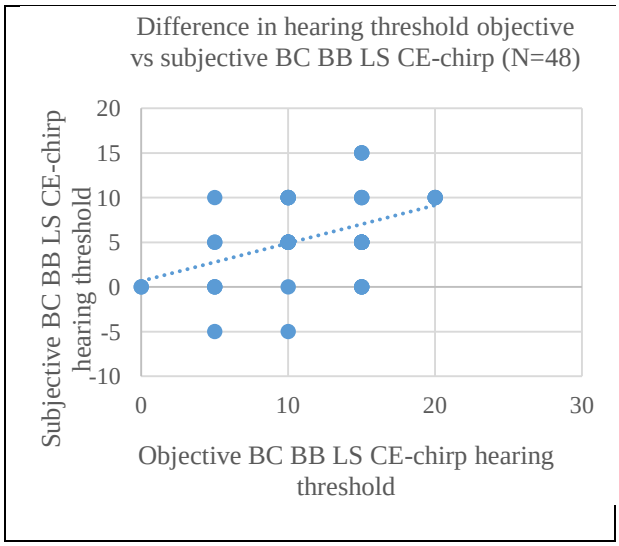


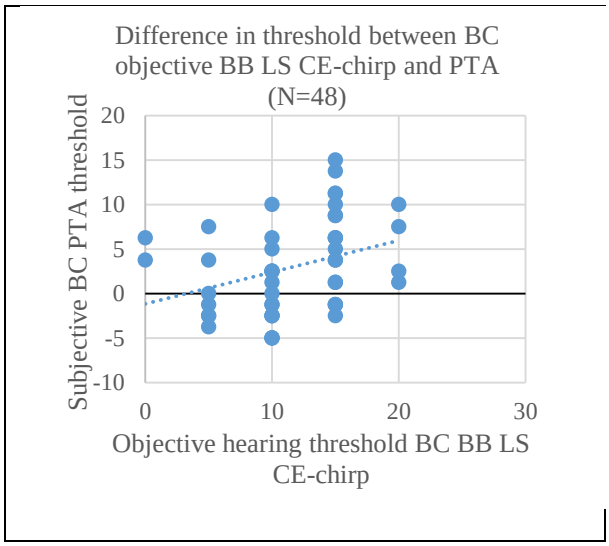
Figure 17 Latency-intensity function for the female subjects. At 90 dB BB, NB 0.5k and NB 1k condensation and rarefaction are shown and NB 2k and 4k summation traces. At 70 and 40 dB, the summation trace of the BB and NB 2k and 4k LS CE-chirp are shown and the condensation and rarefaction trace for the NB 0.5k and 1k LS CE-chirp. Data show similar latency changes with intensity for each chirp, except the NB 0.5k LS CE-chirp in condensation and rarefaction polarity. For the NB 0.5k LS CE-chirp, contrarily to what would be expected, latencies at 70 dB nHL were shorter than those at 90 dB nHL. However, this difference in latency was not significant.

5.4. Experiment 4

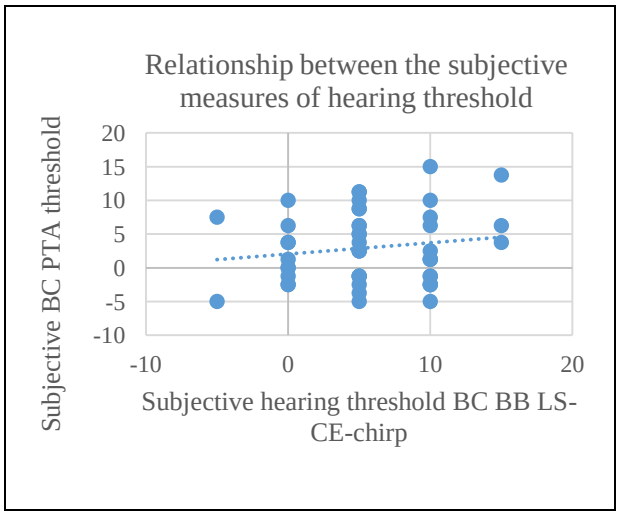
In this experiment, the agreement between subjective and objective measurements of hearing threshold is examined, using the ABR BC BB LS CE-chirp hearing threshold, the mean threshold of the bone-conduction screening audiogram (Pure Tone Average (PTA): average of the pure tone audiometry thresholds at 0.5, 1, 2 and 4 kHz) and a subjectively determined BC BB LS CE-chirp hearing threshold. Objective and subjective thresholds were determined in 48 participants (25 females, 23 males). Kolmogorov-Smirnov test of normality showed that only the PTA hearing threshold did not deviate significantly from a normal distribution ($D(51) = .117$, $p = .077$). Objective and subjective BB LS CE-chirp hearing threshold did deviate significantly from a normal distribution (respectively, $D(48) = .232$, $p < .001$ and $D(48) = .198$, $p < .001$). Therefore, Kendell's tau correlation coefficient was calculated. Kendell's tau showed a significant correlation between the objective hearing threshold and both subjectively established hearing thresholds, i.e. using pure tone audiometry and the BB LS CE-chirp (respectively, $r_\tau = .301$, $p < .01$ and $r_\tau = .335$, $p < .01$). However, between the two subjectively established hearing thresholds, no significant correlation has been found ($r_\tau = .071$, $p = .267$).



a) Objective and subjective BC BB LS CE-chirp hearing threshold



b) Subjective BC PTA and objective BC BB LS CE-chirp hearing threshold



c) Subjective BC PTA and BB LS CE-chirp hearing threshold

Figure 18 Scatterplots representing the relationship between a) objective and subjective BC BB LS CE-chirp hearing threshold, b) subjective BC PTA and objective BC BB LS CE-chirp hearing threshold, and c) subjective BC PTA and BB LS CE-chirp hearing threshold.

In 10% of all cases, the objective threshold was the same or better than the subjective PTA threshold. 27% of objective thresholds were within 5 dB of the subjective PTA threshold, 60% within 10 dB and 88% within 15 dB of the subjective PTA thresholds. The larges difference that has been found was 18,75 dB (1 case). Concerning the subjective BB LS CE-chirp hearing threshold, the objective hearing threshold was better than the subjective threshold for one case (2%). In 27% of all cases, subjective and objective thresholds were equal. 58% of objective thresholds were within 5 dB of the subjective threshold, 90% within 10 dB and 100% within 15 dB nHL (see also Table 12).

Table 12. Cumulative percentages of the difference in hearing threshold between the objective ABR measure and the two subjective measures.

Threshold difference	**Objective - subjective BC BB LS CE-chirp (cumulative percentages)**	**Objective BC BB LS CE-chirp - subjective BC PTA (cumulative percentages)**
≤ 0 dB nHL	29%	10%
≤ 5 dB nHL	58%	27%
≤ 10 dB nHL	90%	60%
≤ 15 dB nHL	100%	88%
≤ 20 dB nHL		100%

Furthermore, the relationship between the three measures of hearing threshold and the variables gender, age, handedness and ear measured has been examined. First, the distribution of the differential scores was examined. The Kolmogorov-Smirnov test shows that both differential scores, i.e. difference between objective threshold and PTA threshold and the difference between objective and subjective BB LS CE-chirp threshold, deviate significantly from a normal distribution (respectively, $D(51) = .359$, $p < .001$ and $D(51) = .380$, $p < .001$). Therefore, Kendell's tau correlation coefficient was calculated. Kendell's tau shows that the difference between objective and subjective hearing thresholds, PTA and BB LS CE-chirp, were not significantly correlated with gender (respectively, $r_\tau = -.016$, $p = .447$ and $r_\tau = -.141$, $p = .136$), age (respectively, $r_\tau = .103$, $p = .161$ and $r_\tau = .087$, $p = .216$), handedness (respectively, $r_\tau = -.075$, $p = .264$ and $r_\tau = .152$, $p = .118$) or the ear measured (respectively, $r_\tau = -.073$, $p = .270$ and $r_\tau = -.044$, $p = .365$). Thus, the objective-subjective hearing threshold differences were not significantly influenced by neither gender, age, handedness nor the measured ear of the subject.

6. Discussion

6.1. General set-up and procedures of the experiment

To the best of our knowledge, only three studies concerning LS CE-chirp evoked ABR have been published since its development (Cargnelutti, Cóser & Biaggio, 2016; Elberling et al., 2012; Kristensen & Elberling, 2012). Consequently, many aspects concerning the optimal set-up and procedure for LS CE-chirp evoked ABR measurements are still unclear. In the preparation of the present ABR project, published studies in the field of ABR have been reviewed regarding the acquisition parameters (see section 3.1.7.). Our research protocol is based on this literature study. Most literature, however, concerned ABRs evoked with the original CE-chirp, toneburst or click stimuli, instead of the newly developed LS CE-chirp. The present study serves, therefore, as an examination of the feasibility of the acquisition parameters for LS CE-chirp evoked ABR measurements and has led to the discovery of several uncertainties regarding these parameters that should be addressed in future research.

Stimulus rate

The stimulus rates used in de present study have been derived from the recommendations of the NHSP guidelines for AC and BC ABR testing (NHSP, 2014a) and have been conscientiously determined for the CE-chirp. This led to stimulus rates around 40 stimuli per second for the AC measurements, with a slight deviation for each stimulus type, i.e. the low frequency NB CE-chirps had a slightly lower stimulus rate (37.1/s, 39.1/s) and the stimulus rate of the higher frequency NB CE-chirps was slightly higher (45.1/s, 49.1/s). These stimulus rates have, in general, led to clearly visible waveforms. However, whether these rates are optimal for LS CE-chirp measurements remains uncertain. Regarding the highly variable results for the NB 0.5k and 1k LS CE-chirp, a lower stimulus rate would possibly have led to less variability and a smaller or even negligible shift in latency.

For the BC measurements on the other hand, a fairly low stimulus rate (19.1/s) has been used. This low stimulus rate has been determined for BC CE-chirp evoked ABRs to enhance the probability of observing wave I. It is unclear, however, whether such a low stimulus rate is necessary for BC LS CE-chirp evoked ABRs or that wave I can also be observed at higher stimulus rates. Future research should address this influence of stimulus rate on LS CE-chirp evoked ABR.

Presence of waveform components

The general goal of the present study was to assemble normative data for the broadband and narrowband LS CE-chirp stimuli obtained with air-conduction and bone-conduction BERA. The BC conditions were presented using a Radioear B-81 bone transducer and for the AC conditions, a TDH-39 supra-aural earphone was used. The TDH-39 was chosen to make a comparison between the obtained responses of the present study to those of an earlier study of our laboratory that generated CE-chirp evoked ABRs using the TDH-39 earphone (Van Bommel, 2014). This does not mean, however, that the assembled normative latency data only apply to ABRs obtained using the TDH-39. Research has shown that, except from a delay of approximately 0.8-0.9 ms due to the length of the tube of insert earphones, supra-aural and insert earphones lead to similar latencies (BCEHP, 2012; Beauchaine, Kaminski & Gorga, 1987; Hall, 2007; NHSP, 2014b). The normative latency data of the present study should thus apply to insert earphone ABR measurements too.

We even recommend the use of insert earphones in future ABR research and clinical practice. ABRs evoked using insert earphones namely present with significantly smaller stimulus artefacts thanks to the distance between the electrodes and transducer of the insert earphones (Hall, 2007). This might enhance the presence of early waveform components. This advantage applies in particular to wave I at high intensities. In the design of the LS CE-chirp, a delay of 1.5 ms in stimulus onset

compared to the CE-chirp has been introduced in order to approximate click evoked ABR latencies. However, at high intensities, wave I is located around 1.5 ms and might be obscured by stimulus artefact (see Figure 19 and 20). This reduces the reliability of normative data of wave I. The use of insert earphones might reduce the stimulus artefact substantially, as a result of which wave I might become (more clearly) visible and normative data obtained using the TDH-39 can be verified.

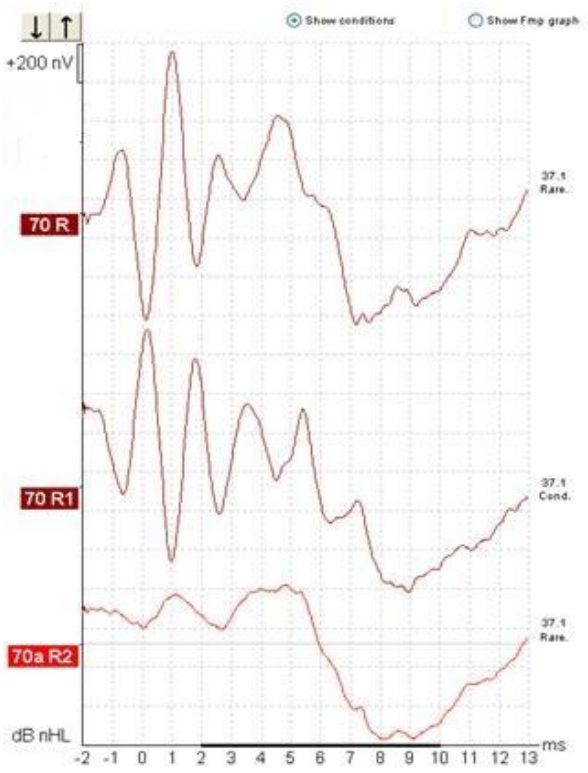


Figure 19 Stimulus artefact of the AC NB 0.5k LS CE-chirp at 70 dB nHL. Respectively the rarefaction, condensation and summation trace are shown.

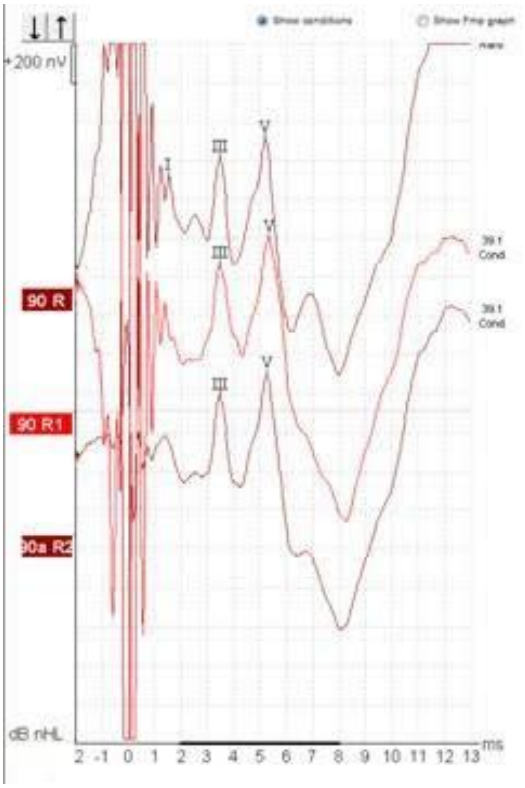


Figure 20 Stimulus artefact of the AC BB LS CE-chirp at 90 dB nHL. Respectively the rarefaction, condensation and summation trace are shown.

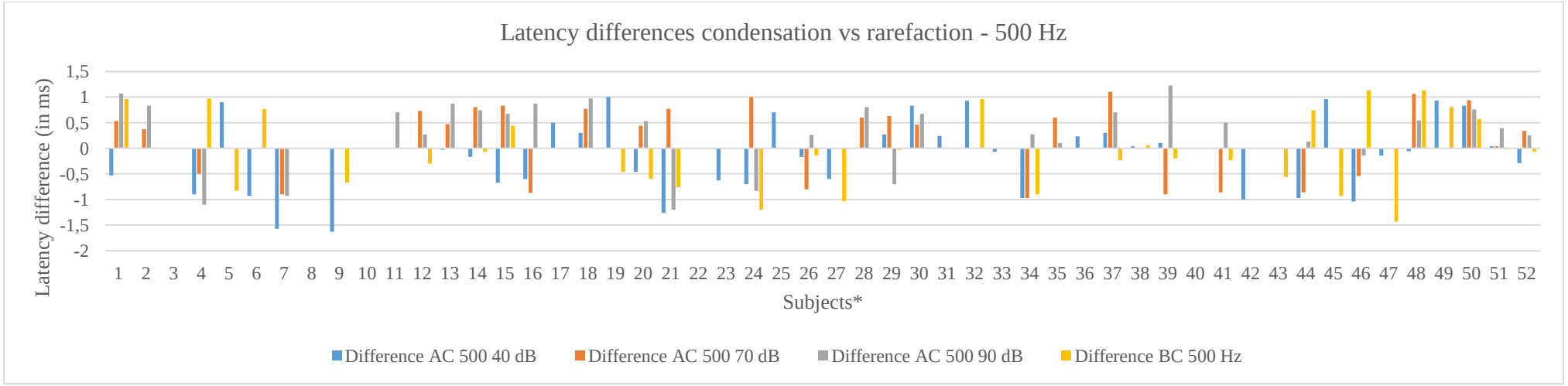
In addition to the uncertainties regarding wave I at high intensities as a result of stimulus artefact, the electrical artefact related to stimulus presentation has led to another concern during the present experiment. In several subjects, the AC NB 4k LS CE-chirp condition created a large electrical artefact that obscured the ABR waveform. After averaging of approximately 3000-4000 stimulus presentations, waves III and V were visible, but the whole waveform showed a trend upward and away from the baseline (see Appendix XII). We suspect that this artefact is caused by an interaction of the stimulus, the electrical artefact of the TDH-39 earphone and the proximity of the earphone to the ipsilateral recording electrode. Therefore, it is hypothesized that this difficulty in the measurement protocol might be resolved if insert earphones are used. Since the transducer of insert earphones is approximately 280 mm away from the ears, and thus the recording electrodes, the electrical artefact might be substantially reduced.

Condensation versus rarefaction polarity

Modern ABR systems often offer three polarity settings: condensation, rarefaction and alternating polarity. An explanation of these settings can be found in section 3.1.7.2. Since research involving broadband stimuli, mostly click stimuli, has not convincingly shown that there is an effect on the ABR of the stimulus polarity used (Schwartz, Morris & Jacobson, 1994; Borg & Lofqvist, 1981), most research groups in the field of chirp-evoked ABR use alternating polarity (e.g. Cargnelutti et al., 2016; Cobb & Stuart, 2016a,b; Elberling et al., 2010; Elberling et al., 2012; Ferm et al., 2013; Ferm & Lightfoot, 2015; Kristensen & Elberling, 2012; Rodrigues et al., 2013). However, earlier publications concerning tonal stimuli have shown that polarity can, in fact, influence ABR latency, in particular at lower frequencies (Orlando & Folsom, 1995; Salt & Thornton, 1984; Fowler, 1992; Don et al., 1996). Considering toneburst stimuli, it has been shown that the latency differences between polarities often approximate a half-period of the centre frequency of the stimulus (Sininger & Hyde, 2009). In case of a 500 Hz stimulus, this would imply a 1-ms difference in latency. Don et al. (1996) examined the latency difference for derived band stimuli and they have found smaller differences than the expected half-period of the theoretical centre frequency (Don et al., 1996).

In the present study, separate traces for condensation and rarefaction were obtained and subsequently summated into a third trace. We therefore had the opportunity to compare responses obtained with condensation and rarefaction polarity and evaluate whether the use of a summation curve or alternating polarity stimulus could be justified. For most conditions, differences between condensation and rarefaction traces were sufficiently small to conclude that they will have no consequences for the clinical evaluation of hearing function.

However, for the AC and BC NB 0.5k and, to a lesser extent, 1k LS CE-chirp, responses obtained with condensation and rarefaction polarity were often shifted in latency, as would be expected based on what has been found for tonebursts. These shifts in latency were irregular and very variable. There was no pattern found in the latency distribution of either polarity, neither was there a pattern in the curve on which the summation curve was based. Due to the lack of a pattern in the latency distribution, the mean latencies for the 0.5 and 1 kHz conditions do not adequately reflect the amount of latency shift. Since the polarity with the shortest latencies changes per subject, the mean latency of both polarities approximate each other and present with large standard deviations. Therefore, the amount of latency shift that we have seen for the low-frequency conditions is only presented adequately in the latencies of the individual subjects (see Figure 21). The figure shows that the amount of latency shift for the 500 Hz conditions centres around 0,5 ms and around 0,25 ms for the 1 kHz conditions. This is approximately one fourth of the period of the centre frequency and thus half of the expected latency shift for low-frequency toneburst stimuli. Future research should address this shift in latency and possible explanations for the phenomenon.



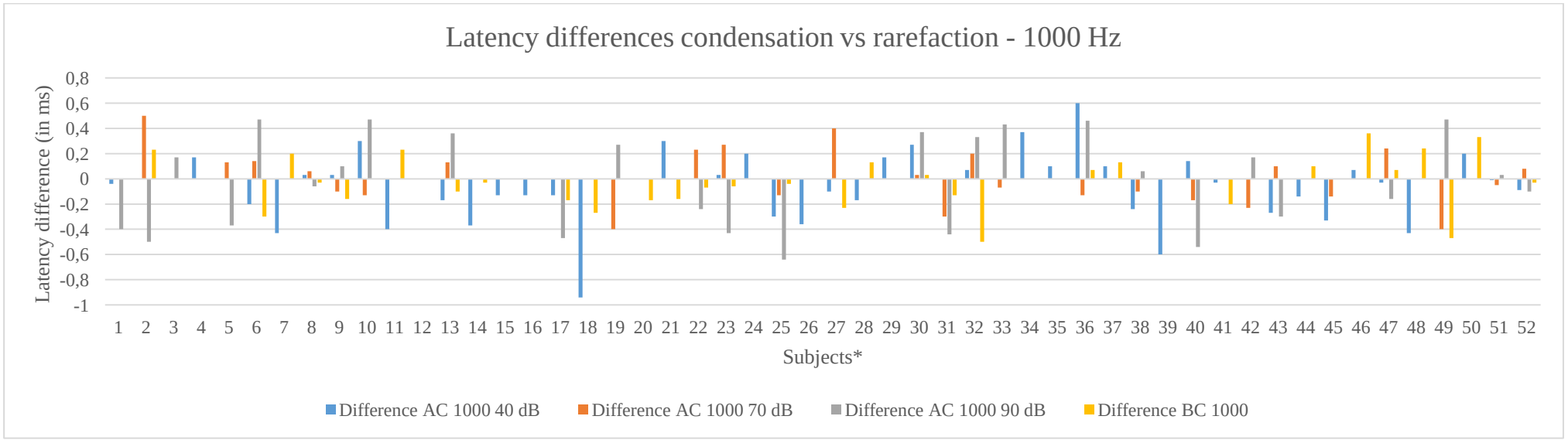
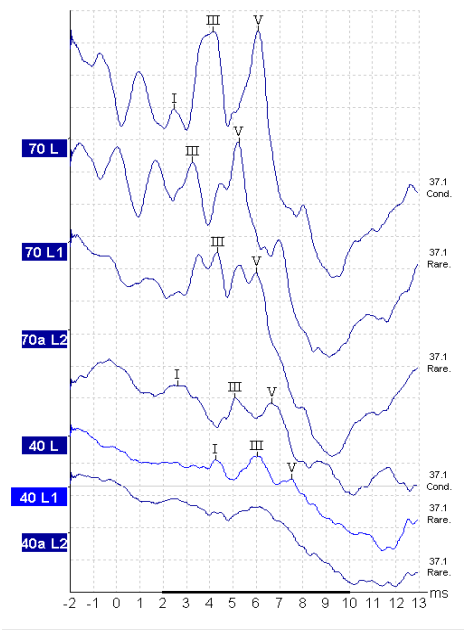
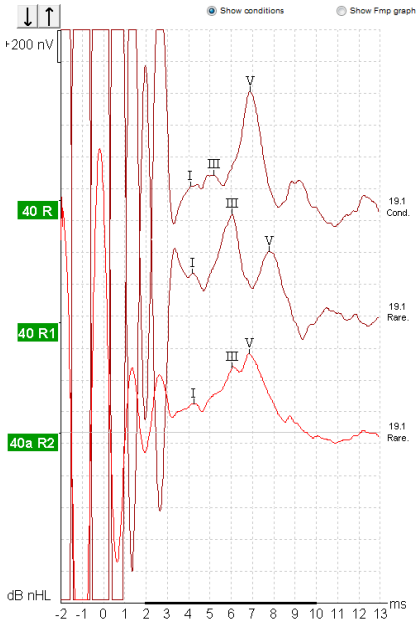


*Figure 21 The amount of latency shift per subject between condensation and rarefaction polarity for the AC and BC 500 and 1000 Hz conditions. *Subject number 52 reflects the difference in latency for the mean condensation and mean rarefaction trace. The latency difference is calculated by subtracting the latency of the rarefaction trace from that of the condensation trace. Data show the variability in ABR latency between polarities for the NB 0.5k and 1k LS CE-chirp and the lack of a pattern in the amount and direction of the difference in latency per polarity.*

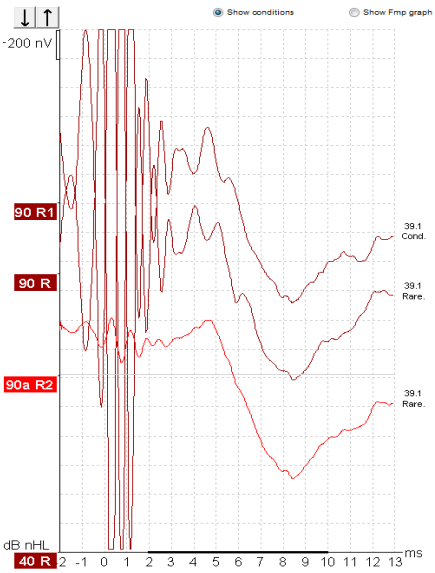
The present study shows that the summation/alternating polarity curves for the 500 Hz NB LS CE-chirp, and to a lesser extent the NB 1000 Hz LS CE-chirp, are not reliable (see Figure 22 for representative examples of NB 0.5k and 1k LS CE-chirp waveforms). Normative latency data for the 0.5k and 1k LS CE-chirp obtained with alternating polarity (Cargnelutti et al., 2016; Kristensen & Elberling, 2012) should be verified in future research using condensation and/or rarefaction polarity. Moreover, alternating polarity should not be used for ABR threshold measurements. Due to the shift in latency between polarities, ABR waves will cancel each other out when using alternating polarity and the threshold will be overestimated. In our opinion, the results of the present study imply that alternating polarity is not suitable for low-frequency LS CE-chirp ABR measurements and should not be used in clinical practice.



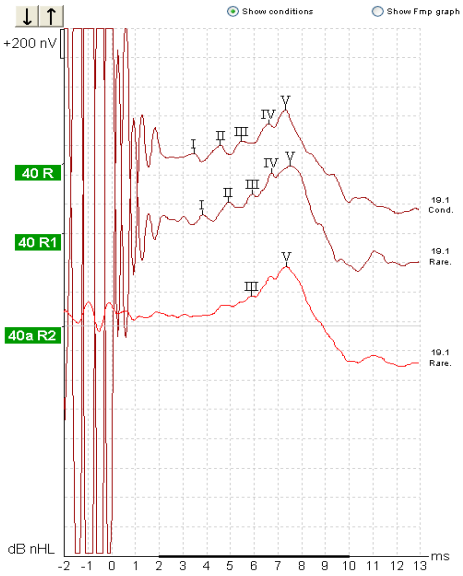
a) 500 Hz – AC



b) 500 Hz – BC



c) 1000 Hz – AC



d) 1000 Hz – BC

Figure 22 Representative examples of the latency shift evoked by low-frequency LS CE-chirps. Traces a and b represent the NB 0.5k LS CE-chirp evoked AC and BC ABR. There is a large shift in latency, resulting in opposite waveform patterns for condensation and rarefaction polarity. Trace c represents the amount of latency shift that we have seen often in the AC NB 1k LS CE-chirp condition. Even in the fairly good traces such as the depicted 1000 Hz BC stimulus condition (d, subject 40), a clear effect of the shift in latency is seen. Where all waveform components are present in the condensation and rarefaction traces, only wave V (and possibly wave III) remain valid in the summation trace.

6.2. Interpretation of the experiments

6.2.1. Experiment 1: air-conduction and bone-conduction BB and NB LS CE-chirp evoked ABRs

Latency differences between the LS CE-chirps

In experiment 1, normative latency data for the various LS CE-chirps have been assembled. The design of the LS CE-chirp theoretically implies similar latencies for all LS CE-chirps (Elberling et al., 2010; Kristensen & Elberling, 2012). The results of our study show similar latencies for the BC LS CE-chirp stimuli and the AC LS CE-chirps at high intensities, i.e. 90 and 70 dB nHL. However, at 40 dB nHL latencies a significant difference in wave V latency was found between the BB and NB 2k LS CE-chirp in the air-conduction condition for the female subjects. For the male subjects, the difference was not significant, but the ABR latencies did show a similar trend. This difference in latency between the BB and NB 2k LS CE-chirp can most likely be explained by the relatively large number of outliers (females: N=7, males: N=3) in the NB 2k LS CE-chirp condition.

To conclude, the latencies of the five LS CE-chirp do, overall, present with similar latencies as the theoretical design of the chirp implies. If these similar latencies are confirmed in future research, the LS CE-chirp has an important clinical advantage over the original broadband and narrowband CE-chirps. The original CE-chirp presented with substantial differences in latency between the chirps. As a result, clinicians need to know five sets of latency values by heart. The similar latencies for the five LS CE-chirps would mean this number can be reduced to one set of latency values (see also section 6.3.).

Latency differences between transduction methods

Research for click and toneburst stimuli has shown that ABR wave V latencies for bone-conduction ABR are longer than for air-conduction ABR (Gorga et al., 1993; Beattie, 1998; Sohmer & Freeman, 2002; Stenfelt & Goode, 2005a; Elsayed et al., 2015). In this study, we have compared wave V latencies of AC and BC LS CE-chirp evoked ABR. The data have been analysed separately for male and female subjects. Results show that for the female subjects only the BB and the 4k NB LS CE-chirp had significantly different latencies for the AC and BC conditions. For the male subjects, all chirp stimuli except the NB 1k LS CE-chirp showed significantly different latencies for AC and BC ABR. The lack of statistically significant differences for the NB 0.5k and 1k LS CE-chirp can most likely be explained by the large variance in wave V latency for these chirps. As a result, the long-latency outliers for the AC conditions and short-latency outliers for the BC conditions overlap. The explanation for the lack of statistical significance for the 2k condition in the female subjects can also be found in the outliers. Due to a relatively large number of outliers, the latency continuums for the AC and BC condition overlap.

Contrary to the expectations based on click and toneburst stimuli, the results of the present study do not always show prolonged latencies for BC ABR. For the BB, NB 0.5k and 2k, latencies of BC ABR are longer than AC ABR latencies. However, the NB 4k LS CE-chirp presents with significantly longer latencies for AC ABR in female (M= 7.17, SD= 0.28 ms) and male subjects (M=7.37, SD= 0.36 ms) compared to BC ABR for female (con: M= 6.81, SD= 0.36 ms, rar: M= 6.76, SD= 0.27 ms) as well as male subjects (M= 7.18, SD= 0.36 ms). For the 1k NB LS CE-chirp, no significant differences in latency have been found, but for the female subjects mean latency of BC ABR (M= 7.33, SD=0.34 ms) is shorter than AC ABR (M= 7.39, SD = 0.40 ms). For the male subjects, BC ABR mean latency (M= 7.58, SD= 0.54 ms) is longer than AC ABR (M= 7.54, SD= 0.28 ms). The differences in latency for the NB 1k LS CE-chirp are sufficiently small to assume they are

caused by the variability in the dataset. However, more research is needed to examine whether the shorter BC ABR latencies for the NB 4k LS CE-chirp can be reproduced and to study the underlying principles. At this point, it is unclear whether the unexpected latencies can be explained by the design of the LS CE-chirp or the acquisition parameters of the present study.

Additionally, standard deviations in latency for the BC conditions were larger than those of the AC conditions, except for the highly variable NB 0.5k and NB 1k LS CE-chirp stimuli in the female subjects (see Table 8 and 9). This variability in BC ABR measurements has been found earlier in click- and toneburst-evoked BC ABR and can most likely be explained by differences in skull characteristics between subjects (Elsayed et al., 2015; Gorga et al., 1993; Sohmer & Freeman, 2002). Since the stimulus needs to be transferred to the cochlea through the skull bone, skull characteristics of the subject, such as density, have a substantial influence on latency.

Moreover, the LS CE-chirp has been developed based on NB LS-CE chirp evoked air-conduction ABR data. Since air- and bone-conduction are substantially different transduction methods, the current design of the LS CE-chirp might not be optimal for bone-conduction ABR measurements. Future research should address the large variation found in LS CE-chirp evoked BC ABR and examine whether a change in the underlying model of the chirp based on BC ABR data results in less variant BC ABR waveforms.

Patient factors influencing wave V latency

In this study, the influence of gender, age, handedness and the measured ear on the latency of ABR wave V have been evaluated. Results showed a significant relationship between ABR latency and gender, in which ABR latencies for the male subjects were longer than those of the female subjects, regardless of the stimulus condition. This finding suggest the LS CE-chirp evoked ABR latencies are, as has been found for the click, tonebursts and CE-chirp (Don et al., 1993; Esteves et al., 2009; Li et al., 2013; Lotfi & Zamiri Abdollahi, 2012; Van Bommel, 2014), significantly different for male and female subjects. Earlier research concerning the LS CE-chirp (Cargnelutti et al., 2016; Elberling et al., 2012; Kristensen & Elberling, 2012) did not differentiate between male and female subjects. Moreover, the reported data used for the LS CE-chirp model itself consists of data from 25 young male and female subjects (48 ears), but the gender ratio has not been specified (Elberling & Don, 2010). The significance difference in latency that is consistently found between genders does suggest, however, that two different models underlying chirp stimuli for male and female subjects might lead to the best fit of the ABR data per gender.

Significant relationships between ABR latency and the other three patient factors have been shown for a small number of latency variables, but the results showed no pattern and were very variable. We therefore conclude that a relationship between ABR wave V latency and age, handedness or the measured ear has not been conclusively shown. However, earlier research does show a significant influence of age on ABR latency and this has been repeatedly shown for several stimulus types (e.g. Khullar & Babbar, 2011; Lotfi & Zamiri Abdollahi, 2012; Maloff & Hood, 2014). The lack of a relationship between ABR wave V latency and the age of the subject in the present study can be explained by the small range in age of the subjects.

Furthermore, the fact that a statistically significant relationship between the measured ear and the latency of ABR wave V has not been conclusively found, is in agreement with earlier research. Most researchers believe that ABRs to the right and left ears are identical and research publications typically do not mention the stimulated ear. However, several studies that did control for the stimulated ear did find subtle differences between the right and left ear in infants and adults (Eldredge & Salamy, 1996; Sininger & Cone-Wesson, 2006; Esteves et al., 2009). Esteves et al. (2009) examined differences in ABR latency for right and left ears in adults and found small differences in ABR I-V latency. When the difference was examined regardless of sex, the difference was not

significant. Most likely because the gender influence on the ABR levelling out the small difference caused by the ears. The present study also shows small differences in a few latency variables, but since the differences are small, variable and do not present over all five chirps, we join the opinion of Sininger and Hyde (2009) who state that the differences between the stimulated ear are sufficiently small to conclude they have no clinical significance (Sininger & Hyde, 2009).

In addition to the variable relationship between wave V latency and the measured ear, the relationship between the handedness of the subject and wave V latency also turned out to be variable. For most ABR wave V latencies, no significant relationship was found. However, for the NB 0.5k LS CE-chirp at 40 dB and the BC BB LS CE-chirp in the female subjects and the NB 0.5k LS CE-chirp at 70 dB and the NB 4k LS CE-chirp at 40 dB nHL in the male subjects. Since the number of stimulus conditions with a statistically significant relationship was minimal, no strict conclusions concerning the influence of handedness on ABR wave V latency are drawn.

Moreover, the subject pool of the present study consists of three subjects (6%) that reported a concussion without persisting symptoms and three subjects (6%) reported deviations in the tympanic membrane of the non-tested ear. The latency values of these patients fall within the normal range of the present subject pool. We therefore conclude that the injuries they reported did not influence ABR latencies. This is according to our expectations, based on the fact that the subjects did not reported any persisting symptoms and ABR measurements were performed on the ear with intact tympanic membrane.

6.2.2. Experiment 2: a traditional click stimulus vs. the BB LS CE-chirp in BC ABR measurements

In 2012, Kristensen and Elberling published a study concerning air-conduction ABR evoked by the broadband LS CE-chirp. In this study, latencies of ABRs evoked by a click stimulus, the broadband CE-chirp and the broadband LS CE-chirp are compared. Results show that wave V latencies of ABRs evoked by the BB LS CE-chirp at 80 and 60 dB nHL are significantly longer than those of ABRs evoked by a click or the BB CE-chirp. At 40 and 20 dB, no significant differences between the BB LS CE-chirp evoked and click-evoked ABR latencies can be found. There is, however, a significant difference in latency between the CE-chirp and the click/LS CE-chirp (Kristensen & Elberling, 2012).

The measures of the present study complement these findings by evaluating the ABR latencies for bone-conduction. Results of the present study show significantly longer latencies for BB LS CE-chirp evoked compared to click-evoked BC ABR. Thus, for air-conduction ABR at high intensities and bone-conduction ABR at 40 dB nHL, a significant difference in latency between click-evoked and BB LS CE-chirp evoked ABR was found. As Kristensen and Elberling (2012) have already argued, this difference in ABR latency can be explained by the temporal location of the stimulus. The LS CE-chirp is temporally aligned at 1.5 ms. The click stimulus, to the contrary, is located at the zero point on the time axis. This 0 ms-point corresponds approximately with the temporal location of the 2500 Hz component of the LS CE-chirp (Cargnelutti et al., 2016; Kristensen & Elberling, 2012). Therefore, all frequency components above 2500 Hz will reach the cochlea later than the corresponding components in the click stimulus. This will result in a longer latency of the LS CE-chirp evoked ABR compared to the ABR in response to the click. Kristensen and Elberling (2012) already showed this for AC ABR, and the latency results of the present study suggest that the same is true for BC ABR.

6.2.3. Experiment 3: Otoneurological assessment using the LS CE-chirp

Elberling and Don (2008) have shown that stimulus level has an influence on the relative cochlear-neural delay. Elberling et al. (2010) subsequently concluded that this has an influence on the optimal model for chirp-evoked ABR and that the optimal chirp should be level-dependent. This level

dependence of the chirp concerns the latency change with frequency: this change varies with stimulus level (Elberling and Don, 2008). Thus, the level specific CE-chirp does not cause an approximation of latency between stimulus levels measured within the same chirp (as has been shown in experiment three), but it evokes an approximation of ABR latencies evoked by the five different LS CE-chirps within one stimulus intensity (as has been shown in experiment one).

The LS CE-chirp stimuli thus react similarly to stimulation at various intensities as has been shown earlier for click, toneburst and CE-chirp stimuli (e.g. Beattie, 1998; Cobb & Stuart, 2016a,b; Elberling et al., 2010; Elberling & Don, 2010; Neely et al. 1988; Sininger & Hyde, 2009). As the results of experiment three of the present study show, significantly longer latencies were found the lower stimulus intensity (see also Table 11). The only exceptions were the NB 1k LS CE-chirp in the female subjects and the NB 2k LS CE-chip. This inconsistency might be due to the earlier mentioned variability in the NB 1k LS CE-chirp wave V latency and the relatively large number of outliers in the NB 2k LS CE-chirp condition.

6.2.4. Experiment 4: Agreement between objective and subjective estimates of bone-conduction hearing threshold

The results of the present study show a relatively good agreement between the objective measure and subjective measures of bone-conduction hearing threshold. For both subjective measures, almost all objective thresholds were within 15 dB of subjective thresholds. Considering the subjective measure of the BB LS CE-chirp, 90% of objective thresholds were even within 10 dB nHL. The larger differences between objective hearing threshold and subjective PTA thresholds are most likely caused by a limitation in the procedure of the screening audiogram. For the first 25 subjects, pure tone audiometry was performed while the computer for the ABR measurements was already turned on. The noise generated by the ventilator of this computer led to significantly higher thresholds for the 1000 Hz frequency, in particular for BC. Therefore, mean hearing thresholds of the first 25 subjects are biased by this overestimation of the true hearing threshold at 1 kHz. This bias in the PTA data is also the most likely explanation for the lack of a significant relationship between the two subjective measures of BC hearing threshold.

Due to the bias in the screening audiogram, the present study cannot determine a reliable correction factor nHL-eHL for the BC objective threshold to the estimated threshold in the pure tone audiometry. For the objective versus subjective BC BB LS CE-chirp hearing threshold, we recommend a correction factor of 10 dB.

6.2.5. Limitations

First, a limitation that applies to all studies examining latencies of ABR waveforms is the subjectivity of the interpretation of the waves and latency determination of the waveform components. Despite the fact that ABR is an objective measure, the interpretation remains subjective.

In addition to the subjectivity in the ABR interpretation, determination of PTA hearing threshold is subjective too. In this study, we only measured the PTA hearing thresholds once, i.e. before the start of the ABR experiments. In 13% of all cases, a difference between the objective and PTA hearing threshold of more than 15 dB was found. This might be explained by the audiogram of these subjects. For the correlation calculations of the objective and PTA hearing threshold, PTA hearing threshold at 500, 1000, 2000 and 4000 Hz are averaged. Since this is an average of only 4 values, a high threshold for one of the four frequencies, which can be due to a measurement error or a temporary decline in concentration of the subject, has a substantial influence on the final average. The objective hearing threshold, to the contrary, has been established using the broadband LS CE-chirp. A higher hearing threshold for one of the octave bands of the BB LS CE-chirp has significantly less

influence on the eventual objective hearing threshold, since the subject can resort to regions in which he or she has better hearing. The synchronised response of all octave bands will lead to a visible wave V in the ABR waveform. Moreover, as has been described earlier, the bone-conduction PTA hearing thresholds of the first 25 subjects are overestimated due to environmental noise.

A third limitation of the present study is that not every subject underwent the complete test protocol, due to available test time of the subject. As a consequence, the resulting data set includes missing values. Furthermore, the number of sweeps was not equal between subjects and experimental conditions. If the waveform interpretation was inconclusive, additional sweeps were collected. This potentially biased the percentages of identifiable waves.

Finally, the use of the TDH-39 for the AC ABR measurement limited the reliability of early waveform components at high intensities due to a large (and long) stimulus artefact. Based on the results of the present study, we conclude that supra-aural earphones might not be the optimal air-conduction transducers for AC ABR. For future research and clinical purposes, we recommend the use of insert earphones to enhance the visibility and reliability of early waveform components. Considering BC ABR measurement, more research is needed to examine the influence of bone vibrator placement on the generated stimulus artefact. Future research should undertake attempts to standardize the location of the bone transducers and EEG electrodes, in order to minimize the influence of the electromagnetic artefact on the ABR.

6.3. Latency differences between the original CE-chirp and the LS CE-chirp

The design of the LS CE-chirp introduced a delay of 1.5 ms in order to approximate latencies as they have been observed for click-evoked ABR. This implies a substantial increase in latency compared to the original CE-chirp, as can be seen in Tables 13 to 16. Most of the studies concerning (LS) CE-chirp-evoked ABR used air-conducted stimulation (Table 13 to 15), but recently two studies evaluating the CE-chirp using bone-conducted stimulation have been published (newborns: Cobb & Stuart, 2016a; adults: Cobb & Stuart, 2016sb). The BC CE-chirp latency data of the adults (Cobb & Stuart, 2016b) are compared to our BC LS CE-chirp latency data (Table 16). The study of Cobb & Stuart (2016b) and the present study are, to the best of our knowledge, the only two studies that measured bone conduction chirp ABR in adults. Unfortunately, Cobb and Stuart (2016b) did not measure BC ABR evoked by narrowband CE-chirps.

Furthermore, thanks to the design of the LS CE-chirp, latencies for the five LS CE-chirps at various intensities approximate each other. The results of the present study show similar latencies for ABRs evoked by the five chirps at the same intensity. If these similar latencies for the five LS CE-chirps are reproduced in future research, the LS CE-chirp has an important clinical advantage over the CE-chirp. Similar latencies for BB and NB versions of the LS CE-chirp would mean clinicians have to know only one set of latency values by heart instead of five to be able to consider at a first glance whether a patient appears to show pathological latency values.

Table 13. Latency differences in ms for the CE- and LS CE-chirp at 90 dB nHL. The present study used the TDH-39 as the transducer. ** The Interacoustics latency templates are only suggestive. They are not from a published study. They are entered in the software as an example.

Stimulus	**Study**	**N**	**Broadband**		**NB 0.5k Hz**		**NB 1k Hz**		**NB 2k Hz**		**NB 4k Hz**	
			mean	SD	mean	SD	mean	SD	mean	SD	mean	SD
CE-chirp	Latency template Interacoustics	**	3.86	0.90	2.21	0.25	3.61	0.51	3.94	0.62	5.07	0.08
LS-chirp	Latency template Interacoustics	**	5.33	0.28	4.95	0.25	4.95	0.51	4.95	0.62	4.95	0.08

LS-chirp	Present study	Males (N=25)	5.72	0.20	5.71	0.33	5.40	0.22	5.70	0.25	5.54	0.25
		Females (N=25)	5.52	0.15	5.62	0.32	1.30	0.20	1.39	0.17	1.70	0.17

Table 14. Latency differences in ms for the CE- and LS CE-chirp at 70, 80 and 85 dB nHL, measured using the TDH-39 (present study) or ER-3A insert earphones (Elberling & Don, 2010; Kristensen & Elberling, 2012).
* Gender distribution unknown.
** The Interacoustics latency templates are only suggestive. They are not from a published study. They are entered in the software as an example.

Stimulus	**Study**	**N**	**dB**	**Broadband**		**NB 0.5k Hz**		**NB 1k Hz**		**NB 2k Hz**		**NB 4k Hz**	
				mean	SD	mean	SD	mean	SD	mean	SD	mean	SD
CE-chirp	Elberling & Don (2010)	N=48*	80	2.85	0.84	0.74	0.46	2.19	0.56	2.89	0.5	3.78	0.21
CE-chirp	Kristensen & Elberling (2012)	N=10 (9f, 1m)	80	4.29	0.51								
CE-chirp	Latency template Interacou-stics	**	70	4.93	0.61	2.39	0.59	3.95	0.50	4.88	0.40	5.57	0.24
LS-chirp	Latency template Interacou-stics	**	70	5.51	0.33	5.60	0.59	5.60	0.50	5.60	0.40	5.60	0.24
LS-chirp	Kristensen & Elberling (2012)	N=10 (9f, 1m)	80	6.31	0.27								
LS-chirp	Present study	Males (N=25)	70	5.93	0.23	5.89	0.36	6.03	0.20	6.10	0.31	6.14	0.20
		Females (N=25)	70	5.71	0.18	1.64	0.12	1.70	0.25	1.60	0.17	1.78	0.11

Table 15. Latency differences in ms for the CE- and LS CE-chirp at 40 dB nHL, measured using the TDH-39 (Van Bommel, 2014; present study) or ER-3A insert earphones (Elberling & Don, 2010; Kristensen & Elberling, 2012).
* Gender distribution unknown.
** The Interacoustics latency templates are only suggestive. They are not from a published study. They are entered in the software as an example.

Stimulus	**Study**	**N**	**Broadband**		**NB 0.5k Hz**		**NB 1k Hz**		**NB 2k Hz**		**NB 4k Hz**	
			mean	SD	mean	SD	mean	SD	mean	SD	mean	SD
CE-chirp	Van Bommel (2014)	Males (N=18)			5.71	1.09	6.76	0.76	6.92	0.36	7.40	0.29
		Females (N=21)			5.60	0.50	6.14	0.73	6.63	0.35	7.11	0.30
CE-chirp	Elberling & Don (2010)	N=48*	5.17	0.40	3.90	1.15	5.21	0.81	5.03	0.38	5.36	0.52
CE-chirp	Kristensen & Elberling (2012)	N=10 (9f, 1m)	6.75	0.33								
CE-chirp	Latency template Interacou-stics	**	6.70	0.40	5.42	1.01	6.72	0.61	6.55	0.36	6.82	0.42
LS-chirp	Latency template Interacou-stics	**	6.71	0.41	6.82	1.01	6.82	0.61	6.82	0.36	6.82	0.42
LS-chirp	Kristensen & Elberling (2012)	N=10 (9f, 1m)	6.67	0.37								

LS-chirp	Present study	Males (N=25)	7.18	0.33	7.11	0.47	7.51	0.31	7.27	0.31	7.35	0.32
		Females (N=25)	6.99	0.30	2.29	0.44	1.74	0.30	1.67	0.17	1.75	0.17

Table 16. Latency differences in ms for the CE- and LS CE-chirp at 45 and 40 dB nHL, measured using a bone transducer (Cobb and Stuart: Radioear B-71, present study: Radioear B81).

Study	**N**	**dB nHL**	**Broadband**		**NB 0.5k Hz**		**NB 1k Hz**		**NB 2k Hz**		**NB 4k Hz**	
			mean	SD	mean	SD	mean	SD	mean	SD	mean	SD
CE-chirp	Males (N=10)	45	8.35	0.30								
Cobb & Stuart (2016b)	Females (N=10)	45	8.13	0.50								
LS CE-chirp	Males (N=25)	40	7.18	0.33	7.11	0.47	7.51	0.31	7.27	0.31	7.35	0.32
Present study	Females (N=25)	40	6.99	0.30	2.29	0.44	1.74	0.30	1.67	0.17	1.75	0.17

7. Future research and recommendations

The present study is the first step towards implementation of LS CE-chirp evoked ABR in the clinical practice of the Radboud University Medical Centre. Now that normative data have been collected in 50 normal-hearing young adults, the transfer to hearing impaired subjects has to be made. Future research should focus on the applicability of the normative data assembled in the present study to the hearing impaired population. The collected normative datasets include three intensity levels: 40, 70 and 90 dB nHL. However, instead of making a one-to-one comparison, a correction factor for the hearing loss must be applied on the normative dataset for patients that present with a conduction hearing loss. The question is whether 70 dB stimulation of a patient with 30 dB hearing loss, i.e. stimulation at 40 dB SL, leads to a similar ABR waveform as the 40 dB nHL data in our norm study.

Considering patients that present with a sensorineural hearing loss, the situation is more complicated. These patients generate normal ABRs at intensities distinctly above threshold. This is consistent with the cochlea being the lesion site and it indicates that the dysfunction within the auditory system is peripheral to the generator sites of the ABR waveform (Winston & Stoner, 2013). The latencies at 70 and 90 dB assembled in the present study should, thus, apply to patients with sensorineural hearing loss. However, at moderate intensities, sensorineural hearing loss is characterized by a prolonged wave I and wave V. Since wave V has a normal latency at high intensities, this will lead to an L-shaped latency-intensity function. The IWI's are normal or shortened (Winston & Stoner, 2013). The prolongation of wave V can be explained by a range of possible pathologies and as a result, in combination with patient factors, there is a great variation in wave V latency in patients with sensorineural hearing loss. Therefore, prolonged latency of wave V is not a reliable diagnostic criterion of sensorineural hearing loss. Instead, clinicians should examine at which stimulus intensity wave V threshold falls. Latency values in patients with sensorineural hearing loss can be used, however, in the differential diagnosis for otoneurological pathologies.

Moreover, the assembled normative dataset does not apply one-to-one to paediatric BERAs. As has been elaborated upon in chapter 2 of this publication, it takes up to 18 months after birth for the auditory brainstem response latencies to fully maturate (Hall, 2014). Thus, longer ABR latencies compared to our normative data found in children under 18 months of age do not necessarily mean that the child has difficulty hearing. Hearing loss can only be determined in paediatric BERAs if ABR latencies significantly deviate from the mean latency data for children in the age group of the patient.

It is therefore very important that separate normative latency datasets are assembled for children under 18 months of age. Since maturation of the brainstem leads to substantial changes in the ABR waveform between birth and the 18th month after birth, we recommend that separate normative datasets are assembled for neonates, six-month-olds, one-year-olds and 18-month-olds.

In addition to these patient related research recommendations, a more technical consideration for future research emerged during our study. Since, the new LS CE-chirps are developed only a few years ago, little is known about the frequency specificity of the narrowband LS CE-chirps. The LS CE-chirps are developed around four centre frequencies, i.e. 500, 1000, 2000 and 4000 Hz. However, their frequency spans over a certain bandwidth. To assess the frequency-specificity of the narrowband LS CE-chirps, it would be informative to measure NB LS CE-chirps evoked ABRs in patients presenting with a distinct ski slope audiogram, i.e. an abrupt change in hearing function at the higher frequencies (see Figure 23). If the NB LS CE-chirps are really frequency-specific, ABR wave V threshold at frequencies at which the patient has a loss in hearing function should be similar to the pure tone audiometry threshold at that frequency. If NB CE-chirp evoked ABR results in significantly better thresholds than the thresholds found using pure tone audiometry, that would suggest that the patient benefits from better hearing function at frequencies present in the bandwidth of the NB LS CE-chirp, despite the fact that these frequencies should, theoretically, receive less energy. This would indicate that the NB LS CE-chirp is not frequency-specific enough, i.e. the bandwidth of the stimulus is not restricted enough, to be able to adequately assess hearing functioning at specific frequencies. Future research should address this uncertainty regarding the frequency-specificity of the NB LS CE-chirps to ensure the clinical applicability of these stimuli.

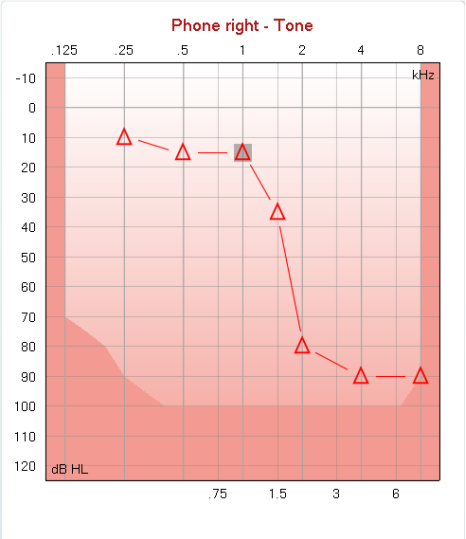


Figure 23 Example of a ski slope audiogram.

8. Clinical applicability

The present study shows the possibilities of ABR testing using the newly developed LS CE-chirp stimulus (Elberling et al., 2012; Kristensen & Elberling, 2012). We showed that it is possible to evoke reliable ABRs at various intensities. Moreover, our results show that, using the LS CE-chirp, it is possible to evoke bone-conduction ABR waveforms containing all important waveform components, i.e. wave I, III and V. This is a very positive development for clinical practice, since it would mean that the nature of hearing loss can be assessed with an objective measure. That way, clinicians can determine a conduction component in hearing loss, even in neonates. The conduction component in hearing loss can be assessed using a combination of AC and BC measures of hearing functioning, such as the objective ABR measures. Objective measures of hearing functioning are the only measures available in infants under six months of age.

To examine the conduction component in hearing loss, clinicians perform AC and BC ABR measurements and compare the obtained latencies. Air-conducted auditory signals enter the ear through the outer ear and complete the whole auditory pathway. When a conduction hearing loss is present in the middle ear, the processing of the auditory signal will thus be delayed and this is reflected in the latency of the ABR waveform components. Bone-conducted signals, however, skip the outer and middle ear and are directly transduced from the skull bone to the cochlea. Consequently, these signals will not be delayed by a conduction hearing loss and ABR waveform components will have comparable latencies to normal-hearing subjects. To conclude, when a patient presents with

delayed ABR latencies for all waveform components in AC ABR and normal waveform component latencies in BC ABR, a conduction hearing loss is present.

Theoretically, a total wave delay (TWD) in the AC ABR would be sufficient to determine the presence of a conduction hearing loss. However, this conclusion can only be drawn if all waveform components, including wave I, are present. As we have shown in the present study, AC LS CE-chirp evoked ABR wave I is often obscured or unreliable due to stimulus artefact and thus BC ABR latency data are needed to detect a conductive hearing loss. Moreover, BC ABR is needed to determine the degree of the conductive hearing loss. This can be established by measuring AC and BC ABR hearing threshold. The difference between those two threshold measurements reflects the degree of conductive hearing loss. This knowledge of the nature of hearing loss is highly significant in the process of adequate hearing revalidation provision, i.e. a hearing aid and potentially a cochlear implant.

Furthermore, the results of the present study show reliable results for NB LS CE-chirp evoked ABRs. Similar to the clinical value of bone-conduction ABR, frequency-specific BERA results can be used to provide infants with more adequate hearing revalidation adjusted to the hearing loss of the child measured at each centre frequency.

In addition to the advantage of frequency-specific BERA results in the process of hearing aid provision in infants, these frequency-specific results might also be advantageous in otoneurological assessment. Since the auditory nerve is tonotopically organised (see Figure 24), frequency-specific BERA results, in combination with pure tone audiometry to confirm unusual BERA results are not a consequence of hearing loss, might be informative in the location identification of a tumour.

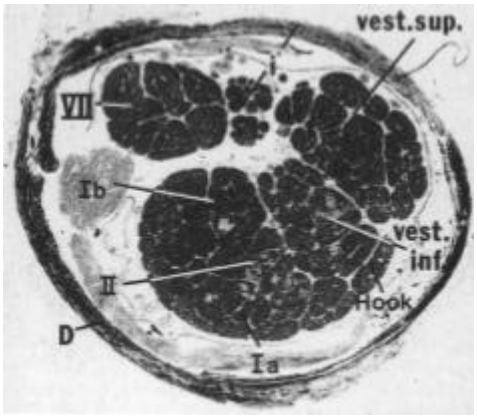


Figure 24 Tonotopic organisation of the human auditory nerve. This transverse section through the internal auditory canal of an 8-year-old child shows the position of the facial nerve (VII0, the superior (vest. sup.) and inferior (vest. inf.) division of the vestibular nerve, and the auditory nerve with the nerve fibres for the most basal end (Hook), for the lower basal turn (Ia), the upper basal turn (Ib), and the second and apical turns (II). Retrieved from Spoendlin and Schrott (1989).

9. Conclusions

This study examined the feasibility of the LS CE-chirp for AC and BC ABR measurements. In experiment 1, ABR wave V latencies for the BB and NB LS CE-chirps are examined. AC BB and NB LS CE-chirp latencies were similar within one intensity. This indicates that the latency changes with frequency defined per intensity in the model of the LS CE-chirp are an adequate compensation for the cochlear travelling wave delay. The frequencies of the various octave band chirps reach their basilar membrane location at approximately the same time, and this leads to a significantly more synchronized neural firing in the broadband LS CE-chirp.

In addition to the comparison of wave V latencies for the AC BB and NB LS CE-chirps within one intensity, the AC BB and NB LS CE-chirps are compared to their BC ABR counterpart (measured at 40 dB nHL). For the BB, NB 0.5k and NB 2k LS CE-chirp significantly longer latencies for the BC ABR measurements were found compared to their AC counterparts. This is in agreement with what has been previously found for click, toneburst and CE-chirp stimuli. For the BC NB 4k LS CE-chirp, however, significantly shorter latencies have been found for BC compared to AC ABR. It is unclear whether this finding is a result of the present research acquisition and stimulus parameters. Future research should examine whether the results can be reproduced and study the underlying principles. For the NB 1k LS CE-chirp, no significant differences in latency were found between the AC and BC ABR measurements.

Additionally, a significant relationship between ABR wave V latency and gender was found, in which male subjects presented with significantly longer latencies than female subjects. The relationship between wave V latency and age, handedness and the measured ear was only shown for a minimal number of wave V variables. Therefore, no strict conclusions are drawn.

In experiment 2, significant differences in latency were found between click- and BB LS CE-chirp evoked BC ABR for wave I, III and V. BB LS CE-chirp evoked ABR latencies were longer than those of click-evoked BC ABR. This is in agreement with the study of Kristensen and Elberling (2012), who found significantly longer latencies for the BB LS CE-chirp compared to the click in insert earphone AC ABR measurements.

In experiment 3, ABR latencies to three different intensities were examined for each LS CE-chirp. A normative data pool for otoneurological assessment containing the mean latency and standard deviation of wave I, III and V and interwave interval I-III, I-V and III-V at 40, 70 and 90 dB nHL is assembled and will be implemented in the Interacoustics Eclipse EP25 system of the Radboudumc for clinical purposes. All LS CE-chirps, except the NB 2k, showed significant differences in latency between frequencies: the lower stimulus intensity, the longer ABR latency. This is in agreement with what has been found earlier for click, toneburst and CE-chirp stimuli. The results of the present study show that LS CE-chirp evoked ABRs at 70 and 90 dB nHL are a feasible measure to assess otoneurological pathologies.

Furthermore, the agreement between objective ABR threshold measurements and subjectively determined hearing thresholds is examined in experiment 4. The results show generally good agreement between the objective and subjective measures of hearing threshold. For 88% of all subjects, objective BC BB LS CE-chirp hearing threshold fell within 15 dB nHL of the subjective BC PTA threshold. The agreement between objective and subjective BC BB LS CE-chirp hearing threshold was even better. For 58% of the subjects, objective hearing threshold fell within 5 dB nHL of the subjective hearing threshold and in 90% of all cases the objective-subjective hearing threshold difference fell within 10 dB nHL. This exploratory experiment shows that it is possible to perform threshold measurements using BB LS CE-chirp evoked BC ABR.

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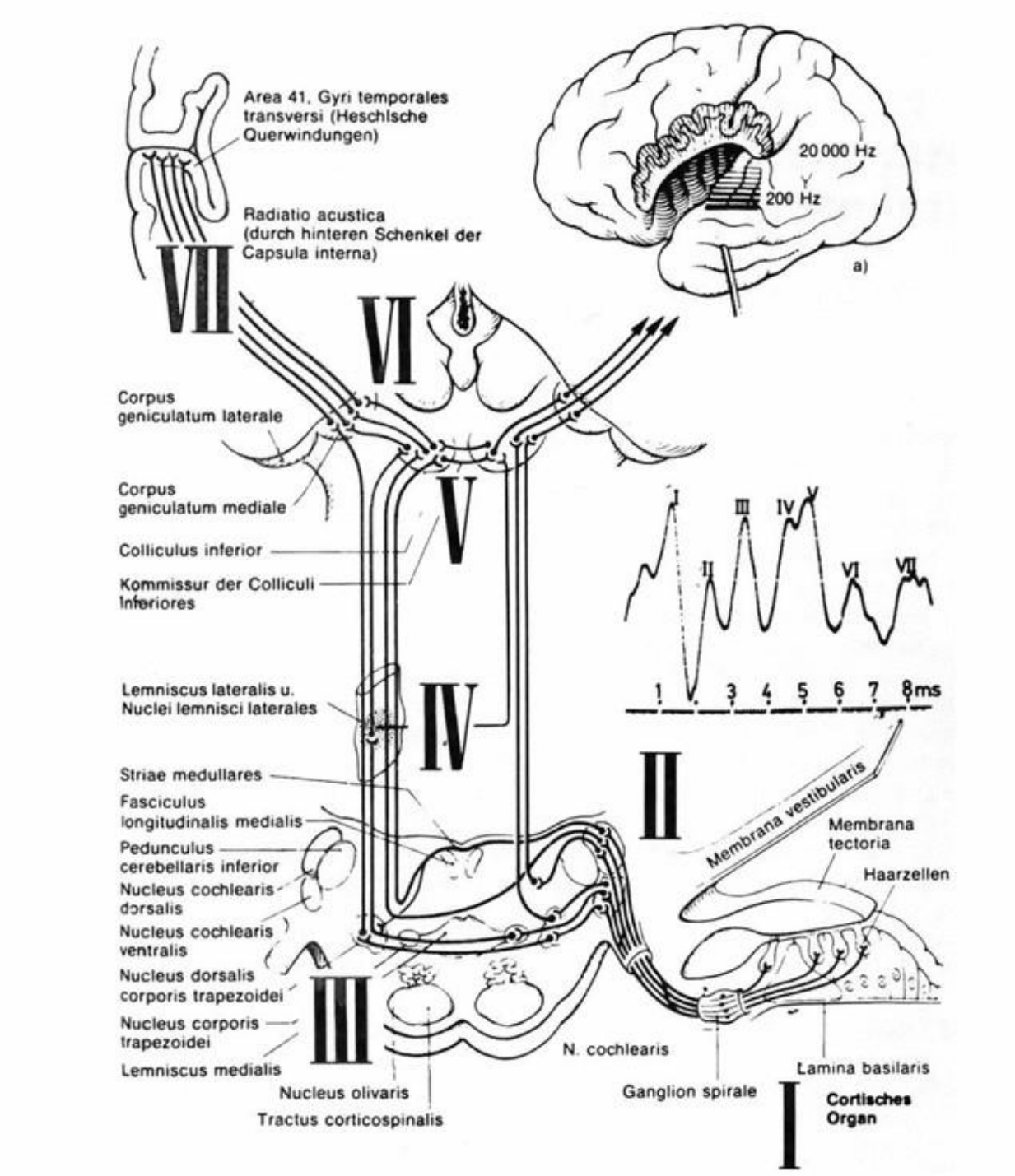
Appendices

Appendix I – Generation sites of the auditory brainstem potentials. Retrieved from Maurer, Leitner and Schäfer (1980)



Appendix II – Stimulus waveform of the BB CE-chirp, NB CE-chirps and tonebursts

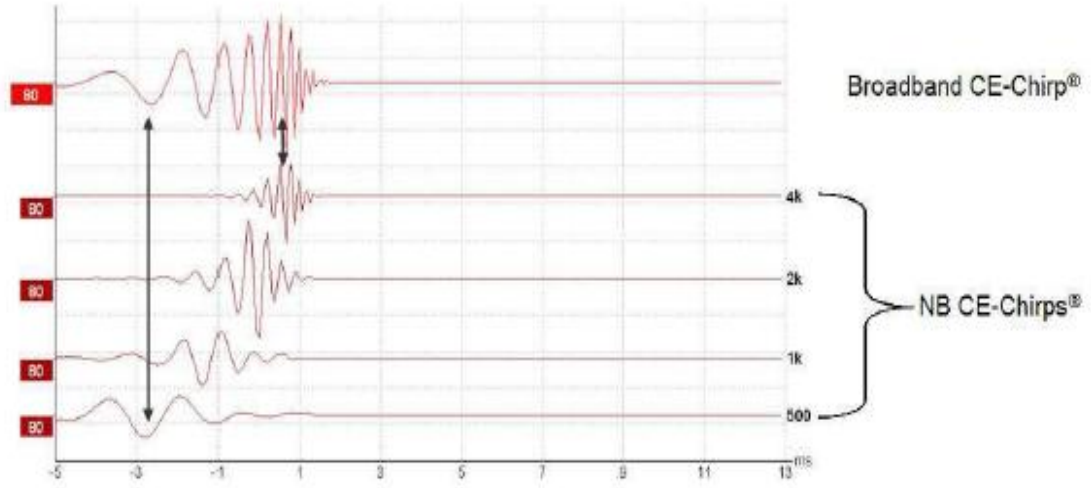


Figure 1 Decomposition of the broadband CE-chirp into the narrowband CE-chirps (Interacoustics, retrieved July 6th, 2016).

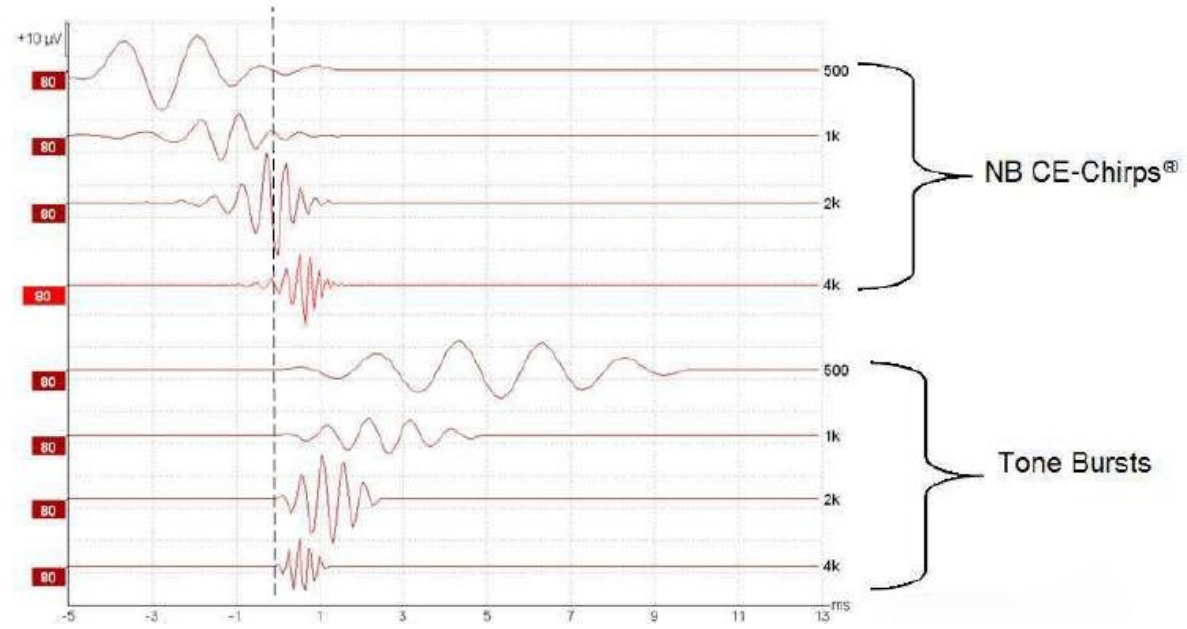


Figure 2 Comparison of timing presentation between NB CE-chirp and toneburst stimuli. Stimulus onset of all four NB CE-chirps precedes the 0-ms point, whereas toneburst onset is at 0-ms (Interacoustics, retrieved July 6th, 2016).

Appendix III – Subjects of the present study

SUBJECT NUMBER	AGE	GENDER	HANDEDNESS	PROBLEMS REGARDING HEARING	CONCUSSION?
1	22	Female	Left	No	No
2	22	Female	Right	No	No
3	24	Female	Right	No	No
4	24	Female	Right	No	Yes, no persisting symptoms
5	23	Male	Left	No	No
6	20	Female	Right	No	No
8	21	Female	Right	No	No
9	24	Female	Left	No	No
10	23	Female	Right	No	No
11	20	Female	Right	No	No
12	22	Male	Right	No	No
13	23	Female	Right	Devious tympanic membrane	No
14	23	Female	Right	No	No
15	22	Female	Left	No	No
16	21	Female	Right	No	No
17	24	Male	Right	No	No
18	23	Female	Right	No	No
19	22	Male	Right	No	No
20	24	Male	Right	No	No
21	33	Male	Left	No	No
22	22	Female	Right	No	No
23	23	Male	Right	No	No
24	18	Male	Right	No	No
25	23	Female	Right	No	Yes, no persisting symptoms
26	21	Female	Right	No	No
27	18	Female	Right	No	No
28	22	Female	Right	No	No
29	24	Male	Right	No	No
30	20	Male	Right	No	No
32	24	Male	Right	No	No
33	25	Female	Right	No	No
34	23	Male	Right	No	No
35	28	Male	Right	No	No
36	22	Female	Left	No	No
37	22	Female	Right	No	No
38	19	Male	Right	No	No
39	20	Male	Right	No	No
40	23	Male	Right	no	no
41	22	Female	Right	No	no
42	28	Male	Right	No	no
43	23	Female	Right	No	Yes, no persisting symptoms
44	30	Female	Right	No	No
45	29	Male	Left	No	No
46	28	Male	Right	No	No
47	23	Male	Left	No	No

48	23	Male	Right	Tympanic membrane perforation (right ear, two weeks ago)	No
49	27	Male	Right	Tympanic membrane perforation as a result of tympanostomy tubes (right ear)	No
50	26	Male	Right	No	No
51	22	Male	Left	No	No
52	27	Male	Right	No	No

Appendix IV – Parameter settings air-conduction measurements

Parameter	Setting				
	0.5 kHz	1.0 kHz	2.0 kHz	4.0 kHz	BB
Stimulus type	LS CE-chirp	LS CE-chirp	LS CE-chirp	LS CE-chirp	LS CE-chirp
Stimulus rate	37.1/s	39.1/s	45.1/s	49.1/s	39.1/s
Polarity	Condensation Rarefaction	Condensation Rarefaction	Condensation Rarefaction	Condensation Rarefaction	Condensation Rarefaction
Filter settings EEG	30 – 3000 Hz	30 – 3000 Hz	30 – 3000 Hz	30 – 3000 Hz	30 – 3000 Hz
Preliminary display	30 – 3000 Hz	30 – 3000 Hz	30 – 3000 Hz	30 – 3000 Hz	30 – 3000 Hz
Masking level	-40 dB	-40 dB	-40 dB	-40 dB	-40 dB
Number of stimuli	≥2x1000 per polarity	≥2x1000 per polarity	≥2x1000 per polarity	≥2x1000 per polarity	≥2x1000 per polarity
Type of stimulation	TDH-39	TDH-39	TDH-39	TDH-39	TDH-39
Residual noise target line	40 nV	40 nV	40 nV	40 nV	40 nV
Response confidence	Detection=99 % (Fmp ≥ 3.1)	Detection=99 % (Fmp ≥ 3.1)	Detection=99 % (Fmp ≥ 3.1)	Detection=99 % (Fmp ≥ 3.1)	Detection=99 % (Fmp ≥ 3.1)
Fmp range	0 – 10 ms	0 – 10 ms	0 – 10 ms	0 – 10 ms	0 – 10 ms
Recording display	-2 – 15 ms	-2 – 15 ms	-2 – 15 ms	-2 – 15 ms	-2 – 15 ms
Rejection level	±40 µV	±40 µV	±40 µV	±40 µV	±40 µV
Optimize recording	Bayesian weighting; minimize interference	Bayesian weighting; minimize interference	Bayesian weighting; minimize interference	Bayesian weighting; minimize interference	Bayesian weighting; minimize interference
Wave reproduc-tion	2 – 10 ms	2 – 10 ms	2 – 10 ms	2 – 10 ms	2 – 10 ms

Appendix V – Parameter settings bone-conduction measurements

Parameter	Setting				
	0.5 kHz	1.0 kHz	2.0 kHz	4.0 kHz	BB
Stimulus type	LS CE-chirp	LS CE-chirp	LS CE-chirp	LS CE-chirp	LS CE-chirp; click
Stimulus rate	19.1/s	19.1/s	19.1/s	19.1/s	19.1/s
Polarity	Condensation Rarefaction	Condensation Rarefaction	Condensation Rarefaction	Condensation Rarefaction	Condensation Rarefaction
Filter settings EEG	30 – 3000 Hz	30 – 3000 Hz	30 – 3000 Hz	30 – 3000 Hz	30 – 3000 Hz
Prelimi-nary display settings	30 – 3000 Hz	30 – 3000 Hz	30 – 3000 Hz	30 – 3000 Hz	30 – 3000 Hz
Masking level	+10 dB	+10 dB	+10 dB	+10 dB	+10 dB
Type of masking	White noise	White noise	White noise	White noise	White noise
Transduce r masking	3M E-A-R-TONE	3M E-A-R-TONE	3M E-A-R-TONE	3M E-A-R-TONE	3M E-A-R-TONE
Number of stimuli	≥2x2000 per polarity	≥2x2000 per polarity	≥2x2000 per polarity	≥2x2000 per polarity	≥2x2000 per polarity
Type of stimulation	Radioear B-81	Radioear B-81	Radioear B-81	Radioear B-81	Radioear B-81
Residual noise target line	40 nV	40 nV	40 nV	40 nV	40 nV
Response confidence	Detection=99 % (Fmp ≥ 3.1)	Detection=99 % (Fmp ≥ 3.1)	Detection=99 % (Fmp ≥ 3.1)	Detection=99 % (Fmp ≥ 3.1)	Detection=99 % (Fmp ≥ 3.1)
Fmp range	0 – 10 ms	0 – 10 ms	0 – 10 ms	0 – 10 ms	0 – 10 ms
Recording display	-2 – 15 ms	-2 – 15 ms	-2 – 15 ms	-2 – 15 ms	-2 – 15 ms
Rejection level	±40 µV	±40 µV	±40 µV	±40 µV	±40 µV
Optimize recording	Bayesian weighting; minimize interference	Bayesian weighting; minimize interference	Bayesian weighting; minimize interference	Bayesian weighting; minimize interference	Bayesian weighting; minimize interference
Wave reproduc-tion	2 – 10 ms	2 – 10 ms	2 – 10 ms	2 – 10 ms	2 – 10 ms

Appendix VI – Normative data for the AC LS CE-chirp at 40 dB nHL

			Means and standard deviations (ms)																							
LS CE-chirps	**Broadband**	Polarity	**I**				**III**				**V**				**I-III**				**I-V**				**III-V**			
	males n=25		**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**
	SUM-ipsi		**3.22**	0.19	2.84	**3.60**	**5.36**	0.30	4.76	**5.96**	**7.18**	0.33	6.52	**7.84**	**2.02**	0.28	1.46	**2.58**	**3.87**	0.24	3.39	**4.35**	**1.77**	0.21	1.35	**2.19**
	COND-ipsi	+	**3.15**	0.16	2.83	**3.47**	**5.38**	0.32	4.74	**6.02**	**7.18**	0.31	6.56	**7.80**	**2.24**	0.29	1.66	**2.82**	**4.03**	0.33	3.37	**4.69**	**1.76**	0.20	1.36	**2.16**
	RARE-ipsi	-	**3.12**	0.23	2.66	**3.58**	**5.39**	0.29	4.81	**5.97**	**7.19**	0.35	6.49	**7.89**	**2.18**	0.19	1.80	**2.56**	**4.00**	0.22	3.56	**4.44**	**1.76**	0.22	1.32	**2.20**
	Broadband	Polarity	**I**				**III**				**V**				**I-III**				**I-V**				**III-V**			
	females n=25		**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**
	SUM-ipsi		**3.28**	0.26	2.76	**3.80**	**5.37**	0.30	4.77	**5.97**	**6.99**	0.30	6.39	**7.59**	**1.94**	0.35	1.24	**2.64**	**3.57**	0.39	2.79	**4.35**	**1.59**	0.19	1.21	**1.97**
	COND-ipsi	+	**3.35**	0.26	2.83	**3.87**	**5.36**	0.29	4.78	**5.94**	**7.01**	0.29	6.43	**7.59**	**1.94**	0.29	1.36	**2.52**	**3.53**	0.29	2.95	**4.11**	**1.62**	0.21	1.20	**2.04**
	RARE-ipsi	-	**3.37**	0.26	2.85	**3.89**	**5.35**	0.33	4.69	**6.01**	**6.99**	0.30	6.39	**7.59**	**1.90**	0.42	1.06	**2.74**	**3.54**	0.38	2.78	**4.30**	**1.59**	0.19	1.21	**1.97**
	NB 0.5k	Polarity	**I**				**III**				**V**				**I-III**				**I-V**				**III-V**			
	males n=25		**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**
	SUM-ipsi		-	-	-	-	**5.08**	0.53	4.02	**6.14**	**7.11**	0.47	6.17	**8.05**	-	-	-	-	-	-	-	-	**2.14**	0.35	1.44	**2.84**
	COND-ipsi	+	-	-	-	-	**5.03**	0.28	4.47	**5.59**	**7.10**	0.38	6.34	**7.86**	-	-	-	-	-	-	-	-	**2.16**	0.39	1.38	**2.94**
	RARE-ipsi	-	-	-	-	-	**5.31**	0.78	3.75	**6.87**	**7.06**	0.65	5.76	**8.36**	-	-	-	-	-	-	-	-	**2.00**	0.31	1.38	**2.62**
	NB 0.5k	Polarity	**I**				**III**				**V**				**I-III**				**I-V**				**III-V**			
	females n=25		**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**
	SUM-ipsi		-	-	-	-	**5.63**	0.23	5.17	**6.09**	**7.31**	0.52	6.27	**8.35**	-	-	-	-	-	-	-	-	-	-	-	-
	COND-ipsi	+	-	-	-	-	**5.23**	0.28	4.67	**5.79**	**7.06**	0.51	6.04	**8.08**	-	-	-	-	-	-	-	-	-	-	-	-
	RARE-ipsi	-	-	-	-	-	**5.80**	0.15	5.50	**6.10**	**7.35**	0.66	6.03	**8.67**	-	-	-	-	-	-	-	-	-	-	-	-
	NB 1k	Polarity	**I**				**III**				**V**				**I-III**				**I-V**				**III-V**			
	males n=25		**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**
	SUM-ipsi		**3.07**	0.12	2.83	**3.31**	**5.61**	0.47	4.67	**6.55**	**7.51**	0.31	6.89	**8.13**	**2.82**	0.38	2.06	**3.58**	**4.62**	0.29	4.04	**5.20**	**1.92**	0.14	1.64	**2.20**
	COND-ipsi	+	**3.14**	0.17	2.80	**3.48**	**5.52**	0.48	4.56	**6.48**	**7.51**	0.32	6.87	**8.15**	**2.24**	0.20	1.84	**2.64**	**4.46**	0.32	3.82	**5.10**	**1.99**	0.26	1.47	**2.51**
	RARE-ipsi	-	**3.11**	0.16	2.79	**3.43**	**5.58**	0.40	4.78	**6.38**	**7.52**	0.37	6.78	**8.26**	**2.56**	0.34	1.88	**3.24**	**4.45**	0.21	4.03	**4.87**	**1.95**	0.24	1.47	**2.43**
	NB 1k	Polarity	**I**				**III**				**V**				**I-III**				**I-V**				**III-V**			
	females n=25		**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**
	SUM-ipsi		**2.81**	0.35	2.11	**3.51**	**5.64**	0.39	4.86	**6.42**	**7.45**	0.46	6.53	**8.37**	**2.63**	0.28	2.07	**3.19**	**3.97**	0.35	3.27	**4.67**	**1.74**	0.30	1.14	**2.34**
	COND-ipsi	+	**2.92**	0.36	2.20	**3.64**	**5.55**	0.34	4.87	**6.23**	**7.34**	0.49	6.36	**8.32**	**2.52**	0.44	1.64	**3.40**	**3.68**	0.12	3.44	**3.92**	**1.72**	0.27	1.18	**2.26**
	RARE-ipsi	-	**2.77**	0.33	2.11	**3.43**	**5.61**	0.43	4.75	**6.47**	**7.43**	0.42	6.59	**8.27**	**2.70**	0.26	2.18	**3.22**	**4.08**	0.41	3.26	**4.90**	**1.85**	0.38	1.09	**2.61**

			Means and standard deviations (ms)																							
LS CE-chirps	**NB 2k**	Polarity	**I**				**III**				**V**				**I-III**				**I-V**				**III-V**			
	males n=25		**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**
	SUM-ipsi		**3.39**	0.28	2.83	**3.95**	**5.42**	0.31	4.80	**6.04**	**7.27**	0.31	6.65	**7.89**	**2.09**	0.24	1.61	**2.57**	**3.91**	0.23	3.45	**4.37**	**1.82**	0.25	1.32	**2.32**
	COND-ipsi	+	**3.28**	0.34	2.60	**3.96**	**5.43**	0.29	4.85	**6.01**	**7.24**	0.29	6.66	**7.82**	**2.22**	0.29	1.64	**2.80**	**4.04**	0.30	3.44	**4.64**	**1.79**	0.27	1.25	**2.33**
	RARE-ipsi	-	**3.47**	0.24	2.99	**3.95**	**5.47**	0.35	4.77	**6.17**	**7.28**	0.32	6.64	**7.92**	**2.04**	0.27	1.50	**2.58**	**3.82**	0.11	3.60	**4.04**	**1.75**	0.20	1.35	**2.15**
	NB 2k	Polarity	**I**				**III**				**V**				**I-III**				**I-V**				**III-V**			
	females n=25		**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**
	SUM-ipsi		**3.22**	0.15	2.92	**3.52**	**5.37**	0.32	4.73	**6.01**	**7.12**	0.32	6.48	**7.76**	**1.93**	0.20	1.53	**2.33**	**3.67**	0.19	3.29	**4.05**	**1.67**	0.17	1.33	**2.01**
	COND-ipsi	+	**3.18**	0.20	2.78	**3.58**	**5.32**	0.26	4.80	**5.84**	**7.10**	0.30	6.50	**7.70**	**2.00**	0.29	1.42	**2.58**	**3.72**	0.22	3.28	**4.16**	**1.72**	0.17	1.38	**2.06**
	RARE-ipsi	-	**3.26**	0.16	2.94	**3.58**	**5.32**	0.33	4.66	**5.98**	**7.15**	0.33	6.49	**7.81**	**1.91**	0.23	1.45	**2.37**	**3.65**	0.21	3.23	**4.07**	**1.73**	0.19	1.35	**2.11**
	NB 4k	Polarity	**I**				**III**				**V**				**I-III**				**I-V**				**III-V**			
	males n=25		**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**
	SUM-ipsi		**3.53**	0.13	3.27	**3.79**	**5.67**	0.27	5.13	**6.21**	**7.35**	0.32	6.71	**7.99**	**2.10**	0.24	1.62	**2.58**	**3.82**	0.25	3.32	**4.32**	**1.74**	0.11	1.52	**1.96**
	COND-ipsi	+	**3.51**	0.13	3.25	**3.77**	**5.65**	0.29	5.07	**6.23**	**7.34**	0.33	6.68	**8.00**	**2.16**	0.20	1.76	**2.56**	**3.83**	0.21	3.41	**4.25**	**1.75**	0.16	1.43	**2.07**
	RARE-ipsi	-	**3.40**	0.20	3.00	**3.80**	**5.70**	0.27	5.16	**6.24**	**7.36**	0.33	6.70	**8.02**	**2.24**	0.26	1.72	**2.76**	**3.95**	0.27	3.41	**4.49**	**1.71**	0.11	1.49	**1.93**
	NB 4k	Polarity	**I**				**III**				**V**				**I-III**				**I-V**				**III-V**			
	females n=25		**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**
	SUM-ipsi		**3.38**	0.16	3.06	**3.70**	**5.41**	0.26	4.89	**5.93**	**7.14**	0.26	6.62	**7.66**	**1.96**	0.28	1.40	**2.52**	**3.75**	0.29	3.17	**4.33**	**1.75**	0.17	1.41	**2.09**
	COND-ipsi	+	**3.44**	0.12	3.20	**3.68**	**5.34**	0.24	4.86	**5.82**	**7.15**	0.24	6.67	**7.63**	**1.92**	0.18	1.56	**2.28**	**3.68**	0.17	3.34	**4.02**	**1.78**	0.20	1.38	**2.18**
	RARE-ipsi	-	**3.41**	0.21	2.99	**3.83**	**5.41**	0.26	4.89	**5.93**	**7.14**	0.27	6.60	**7.68**	**1.98**	0.35	1.28	**2.68**	**3.72**	0.36	3.00	**4.44**	**1.73**	0.17	1.39	**2.07**

Appendix VII - Normative data for the BC LS CE-chirp at 40 dB nHL

			Means and standard deviations (ms)																							
LS CE-chirps	**Click**	Polarity	**I**				**III**				**V**				**I-III**				**I-V**				**III-V**			
	males n=25		**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**
	SUM-ipsi		**3.31**	0.19	2.93	**3.69**	**5.48**	0.29	4.90	**6.06**	**7.42**	0.34	6.74	**8.10**	**2.20**	0.24	1.72	**2.68**	**4.04**	0.23	3.58	**4.50**	**1,89**	0.23	1.43	**2.35**
	COND-ipsi	+	**3.34**	0.22	2.90	**3.78**	**5.51**	0.33	4.85	**6.17**	**7.45**	0.34	6.77	**8.13**	**2.19**	0.28	1.63	**2.75**	**4.04**	0.24	3.56	**4.52**	**1,87**	0.25	1.37	**2.37**
	RARE-ipsi	-	**3.30**	0.26	2.78	**3.82**	**5.49**	0.29	4.91	**6.07**	**7.41**	0.33	6.75	**8.07**	**2.21**	0.31	1.59	**2.83**	**4.04**	0.32	3.40	**4.68**	**1,87**	0.23	1.41	**2.33**
	Click	Polarity	**I**				**III**				**V**				**I-III**				**I-V**				**III-V**			
	females n=25		**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**
	SUM-ipsi		**3.11**	0.13	2.85	**3.37**	**5.22**	0.24	4.74	**5.70**	**6.98**	0.27	6.44	**7.52**	**2.07**	0.17	1.73	**2.41**	**3.84**	0.25	3.34	**4.34**	**1.75**	0.21	1.33	**2.17**
	COND-ipsi	+	**3.14**	0.16	2.82	**3.46**	**5.21**	0.24	4.73	**5.69**	**7.01**	0.27	6.47	**7.55**	**2.10**	0.21	1.68	**2.52**	**3.82**	0.23	3.36	**4.38**	**1.74**	0.17	1.40	**2.08**
	RARE-ipsi	-	**3.08**	0.16	2.76	**3.40**	**5.22**	0.22	4.78	**5.66**	**6.97**	0.28	6.41	**7.53**	**2.04**	0.16	1.72	**2.36**	**3.81**	0.18	3.45	**4.17**	**1.77**	0.21	1.35	**2.19**
	Broadband	Polarity	**I**				**III**				**V**				**I-III**				**I-V**				**III-V**			
	males n=25		**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**
	SUM-ipsi		**3.86**	0.35	3.16	**4.56**	**6.05**	0.29	5.47	**6.63**	**7.58**	0.43	6.72	**8.44**	**2.13**	0.21	1.71	**2.55**	**3.66**	0.38	2.90	**4.42**	**1.61**	0.24	1.13	**2.09**
	COND-ipsi	+	**3.86**	0.34	3.18	**4.54**	**6.03**	0.29	5.45	**6.61**	**7.59**	0.43	6.73	**8.45**	**2.02**	0.27	1.48	**2.56**	**3.64**	0.37	2.90	**4.38**	**1.65**	0.29	1.07	**2.23**
	RARE-ipsi	-	**3.81**	0.35	3.11	**4.51**	**6.08**	0.23	5.62	**6.54**	**7.58**	0.45	6.68	**8.48**	**2.18**	0.20	1.78	**2.58**	**3.81**	0.41	2.99	**4.63**	**1.61**	0.27	1.07	**2.15**
	Broadband	Polarity	**I**				**III**				**V**				**I-III**				**I-V**				**III-V**			
	females n=25		**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**
	SUM-ipsi		**3.40**	0.31	2.78	**4.02**	**5.52**	0.38	4.76	**6.28**	**7.22**	0.37	6.48	**7.96**	**2.16**	0.28	1.60	**2.72**	**3.79**	0.32	3.15	**4.43**	**1.66**	0.27	1.12	**2.20**
	COND-ipsi	+	**3.42**	0.33	2.76	**4.08**	**5.52**	0.36	4.80	**6.24**	**7.26**	0.37	6.52	**8.00**	**2.15**	0.22	1.71	**2.59**	**3.83**	0.33	3.17	**4.49**	**1.71**	0.23	1.25	**2.17**
	RARE-ipsi	-	**3.39**	0.33	2.73	**4.05**	**5.58**	0.41	4.76	**6.40**	**7.21**	0.39	6.43	**7.99**	**2.19**	0.39	1.41	**2.97**	**3.79**	0.35	3.09	**4.49**	**1.60**	0.26	1.08	**2.12**
	NB 0.5k	Polarity	**I**				**III**				**V**				**I-III**				**I-V**				**III-V**			
	males n=19		**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**
	SUM-ipsi		-	-	-	-	**5.72**	0.45	4.82	**6.62**	**7.58**	0.55	6.48	**8.68**	-	-	-	-	-	-	-	-	**1.84**	0.57	0.70	**2.98**
	COND-ipsi	+	-	-	-	-	**5.77**	0.65	4.47	**7.07**	**7.61**	0.64	6.33	**8.89**	-	-	-	-	-	-	-	-	**1.89**	0.25	1.39	**2.39**
	RARE-ipsi	-	-	-	-	-	**5.70**	0.56	4.58	**6.82**	**7.63**	0.57	6.49	**8.77**	-	-	-	-	-	-	-	-	**1.99**	0.52	0.95	**3.03**
	NB 0.5k	Polarity	**I**				**III**				**V**				**I-III**				**I-V**				**III-V**			
	females n=17		**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**
	SUM-ipsi		-	-	-	-	**5.49**	0.37	4.75	**6.23**	**7.46**	0.45	6.56	**8.36**	-	-	-	-	-	-	-	-	**1.77**	0.46	0.85	**2.69**
	COND-ipsi	+	-	-	-	-	**5.46**	0.48	4.50	**6.42**	**7.45**	0.43	6.59	**8.31**	-	-	-	-	-	-	-	-	**1.98**	0.36	1.26	**2.70**
	RARE-ipsi	-	-	-	-	-	**5.44**	0.46	4.52	**6.36**	**7.52**	0.48	6.56	**8.48**	-	-	-	-	-	-	-	-	**2.07**	0.43	1.21	**2.93**

			Means and standard deviations (ms)																							
LS CE-chirps	**NB 1k**	Polarity	**I**				**III**				**V**				**I-III**				**I-V**				**III-V**			
	males n=19		**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**
	SUM-ipsi		-	-	-	-	**6.14**	0.56	5.02	**7.26**	**7.68**	0,52	6.64	**8.72**	-	-	-	-	-	-	-	-	**1.68**	0.38	0.92	**2.44**
	COND-ipsi	+	**3.93**	0.52	2.89	**4.97**	**5.83**	0.46	4.91	**6.75**	**7.68**	0.52	6.64	**8.72**	**2.01**	0.29	1.43	**2.59**	**3.72**	0.37	2.98	**4.46**	**1.79**	0.37	1.05	**2.53**
	RARE-ipsi	-	**3.84**	0.53	2.78	**4.90**	**5.96**	0.61	4.74	**7.18**	**7.68**	0.56	6.56	**8.80**	**2.05**	0.41	1.23	**2.87**	**3.64**	0.35	2.94	**4.34**	**1.62**	0.19	1.24	**2.00**
	NB 1k	Polarity	**I**				**III**				**V**				**I-III**				**I-V**				**III-V**			
	females n=18		**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**
	SUM-ipsi		**3.13**	0.32	2.49	**3.77**	**5.67**	0.42	4.83	**6.51**	**7.31**	0.33	6.65	**7.97**	**2.56**	0.52	1.52	**3.60**	**4.25**	0.39	3.47	**5.03**	**1.68**	0.21	1.26	**2.10**
	COND-ipsi	+	**3.27**	0.54	2.19	**4.35**	**5.64**	0.36	4.92	**6.36**	**7.33**	0.34	6.65	**8.01**	**2.38**	0.55	1.28	**3.48**	**4.11**	0.44	3.23	**4.99**	**1.70**	0.19	1.32	**2.08**
	RARE-ipsi	-	**3.24**	0.34	2.56	**3.92**	**5.71**	0.33	5.05	**6.37**	**7.36**	0.35	6.66	**8.06**	**2.60**	0.55	1.50	**3.70**	**4.23**	0.47	3.29	**5.17**	**1.75**	0.20	1.35	**2.15**
	NB 2k	Polarity	**I**				**III**				**V**				**I-III**				**I-V**				**III-V**			
	males n=19		**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**
	SUM-ipsi		**3.63**	0.45	2.73	**4.53**	**5.74**	0.50	4.74	**6.74**	**7.49**	0.51	6.47	**8.51**	**2.09**	0.31	1.47	**2.71**	**3.84**	0.33	3.18	**4.50**	**1.69**	0.20	1.29	**2.09**
	COND-ipsi	+	**3.68**	0.42	2.84	**4.52**	**5.70**	0.50	4.70	**6.70**	**7.47**	0.51	6.45	**8.49**	**1.90**	0.31	1.28	**2.52**	**3.55**	0.37	2.81	**4.29**	**1.69**	0.22	1.25	**2.13**
	RARE-ipsi	-	**3.67**	0.42	2.83	**4.51**	**5.81**	0.42	4.97	**6.65**	**7.51**	0.52	6.47	**8.55**	**2.08**	0.25	1.58	**2.58**	**3.82**	0.25	3.32	**4.32**	**1.72**	0.24	1.24	**2.20**
	NB 2k	Polarity	**I**				**III**				**V**				**I-III**				**I-V**				**III-V**			
	females n=18		**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**
	SUM-ipsi		**3.21**	0.19	2.83	**3.59**	**5.28**	0.50	4.28	**6.28**	**6.93**	0.48	5.97	**7.89**	**1.96**	0.18	1.60	**2.32**	**3.61**	0.21	3.19	**4.03**	**1.67**	0.14	1.39	**1.95**
	COND-ipsi	+	**3.27**	0.17	2.93	**3.61**	**5.26**	0.53	4.20	**6.32**	**6.95**	0.48	5.99	**7.91**	**1.85**	0.12	1.61	**2.09**	**3.53**	0.21	3.11	**3.95**	**1.69**	0.12	1.45	**1.93**
	RARE-ipsi	-	**3.24**	0.19	2.86	**3.62**	**5.30**	0.53	4.24	**6.36**	**6.93**	0.48	5.97	**7.89**	**1.93**	0.26	1.41	**2.45**	**3.57**	0.22	3.13	**4.01**	**1.67**	0.14	1.39	**1.95**
	NB 4k	Polarity	**I**				**III**				**V**				**I-III**				**I-V**				**III-V**			
	males n=19		**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**
	SUM-ipsi		**3.02**	0.25	2.52	**3.52**	**5.31**	0.33	4.65	**5.97**	**7.18**	0.35	6.48	**7.88**	**2.19**	0.25	1.69	**2.69**	**4.00**	0.25	3.50	**4.50**	**1.84**	0.16	1.52	**2.16**
	COND-ipsi	+	**3.01**	0.24	2.53	**3.49**	**5.28**	0.36	4.56	**6.00**	**7.20**	0.36	6.48	**7.92**	**2.22**	0.26	1.70	**2.74**	**4.03**	0.26	3.51	**4.55**	**1.85**	0.22	1.41	**2.29**
	RARE-ipsi	-	**3.04**	0.26	2.52	**3.56**	**5.31**	0.36	4.59	**6.03**	**7.20**	0.34	6.52	**7.88**	**2.22**	0.28	1.66	**2.78**	**3.99**	0.27	3.45	**4.53**	**1.84**	0.16	1.52	**2.16**
	NB 4k	Polarity	**I**				**III**				**V**				**I-III**				**I-V**				**III-V**			
	females n=17		**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**
	SUM-ipsi		**3.00**	0.18	2.64	**3.36**	**5.10**	0.39	4.32	**5.88**	**6.78**	0.34	6.10	**7.46**	**1.93**	0.16	1.61	**2.25**	**3.71**	0.16	3.39	**4.03**	**1.73**	0.22	1.29	**2.17**
	COND-ipsi	+	**2.95**	0.13	2.69	**3.21**	**5.10**	0.39	4.32	**5.88**	**6.80**	0.34	6.12	**7.48**	**1.99**	0.15	1.69	**2.29**	**3.77**	0.20	3.37	**4.17**	**1.76**	0.21	1.34	**2.18**
	RARE-ipsi	-	**3.01**	0.19	2.63	**3.39**	**5.09**	0.40	4.29	**5.89**	**6.75**	0.35	6.05	**7.45**	**1.88**	0.16	1.56	**2.20**	**3.69**	0.15	3.39	**3.99**	**1.70**	0.23	1.24	**2.16**

Appendix VIII – Normative data for otoneurological assessment using the LS CE-chirp

			Means and standard deviations (ms)																							
LS CE-chirps 90 dB	**Broadband**	Polarity	**I**				**III**				**V**				**I-III**				**I-V**				**III-V**			
	males n=25		**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**
	SUM-ipsi		**1.52**	0.12	1.28	**1.76**	**3.80**	0.19	3.42	**4.18**	**5.72**	0.20	5.32	**6.12**	**2.29**	0.19	1.91	**2.67**	**4.20**	0.22	3.76	**4.64**	**1.92**	0.12	1.68	**2.16**
	COND-ipsi	+	**1.57**	0.15	1.27	**1.87**	**3.87**	0.20	3.47	**4.27**	**5.80**	0.21	5.38	**6.22**	**2.32**	0.19	1.94	**2.70**	**4.23**	0.22	3.79	**4.67**	**1.93**	0.13	1.67	**2.19**
	RARE-ipsi	-	**1.54**	0.10	1.34	**1.74**	**3.76**	0.19	3.38	**4.14**	**5.66**	0.24	5.18	**6.14**	**2.23**	0.18	1.87	**2.59**	**4.12**	0.25	3.62	**4.62**	**1.89**	0.16	1.57	**2.21**
	Broadband	Polarity	**I**				**III**				**V**				**I-III**				**I-V**				**III-V**			
	females n=25		**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**
	SUM-ipsi		**1.51**	0.09	1.33	**1.69**	**3.69**	0.15	3.39	**3.99**	**5.52**	0.15	5.22	**5.82**	**2.19**	0.16	1.87	**2.51**	**4.02**	0.17	3.68	**4.36**	**1.83**	0.11	1.61	**2.05**
	COND-ipsi	+	**1.57**	0.12	1.33	**1.81**	**3.74**	0.19	3.36	**4.12**	**5.59**	0.17	5.25	**5.93**	**2.18**	0.19	1.80	**2.56**	**3.95**	0.20	3.55	**4.35**	**1.85**	0.13	1.59	**2.11**
	RARE-ipsi	-	**1.52**	0.13	1.26	**1.78**	**3.66**	0.15	3.36	**3.96**	**5.46**	0.19	5.08	**5.84**	**2.15**	0.21	1.73	**2.57**	**4.03**	0.24	3.55	**4.51**	**1.80**	0.13	1.54	**2.06**
	NB 0.5k	Polarity	**I**				**III**				**V**				**I-III**				**I-V**				**III-V**			
	males n=13		**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**
	SUM-ipsi		-	-	-	-	-	-	-	-	**5.71**	0.33	5.05	**6.37**	-	-	-	-	-	-	-	-	-	-	-	-
	COND-ipsi	+	-	-	-	-	-	-	-	-	**5.97**	0.53	4.91	**7.03**	-	-	-	-	-	-	-	-	-	-	-	-
	RARE-ipsi	-	-	-	-	-	-	-	-	-	**5.58**	0.28	5.02	**6.14**	-	-	-	-	-	-	-	-	-	-	-	-
	NB 0.5k	Polarity	**I**				**III**				**V**				**I-III**				**I-V**				**III-V**			
	females n=14		**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**
	SUM-ipsi		-	-	-	-	-	-	-	-	**5.62**	0.32	4.98	**6.26**	-	-	-	-	-	-	-	-	-	-	-	-
	COND-ipsi	+	-	-	-	-	-	-	-	-	**5.97**	0.45	5.07	**6.87**	-	-	-	-	-	-	-	-	-	-	-	-
	RARE-ipsi	-	-	-	-	-	-	-	-	-	**5.72**	0.63	4.46	**6.98**	-	-	-	-	-	-	-	-	-	-	-	-
	NB 1k	Polarity	**I**				**III**				**V**				**I-III**				**I-V**				**III-V**			
	males n=13		**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**
	SUM-ipsi		-	-	-	-	**4.19**	0.14	3.91	**4.47**	**5.40**	0.22	4.96	**5.84**	-	-	-	-	-	-	-	-	**1.33**	0.25	0.83	**1.83**
	COND-ipsi	+	-	-	-	-	**4.25**	0.17	3.91	**4.59**	**5.46**	0.27	4.92	**6.00**	-	-	-	-	-	-	-	-	**1.26**	0.24	0.78	**1.74**
	RARE-ipsi	-	-	-	-	-	**4.08**	0.19	3.70	**4.46**	**5.43**	0.32	4.79	**6.07**	-	-	-	-	-	-	-	-	**1.41**	0.39	0.63	**2.19**
	NB 1k	Polarity	**I**				**III**				**V**				**I-III**				**I-V**				**III-V**			
	females n=14		**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**
	SUM-ipsi		-	-	-	-	**4.19**	0.15	3.89	**4.49**	**5.47**	0.22	5.03	**5.91**	-	-	-	-	-	-	-	-	**1.30**	0.20	0.90	**1.70**
	COND-ipsi	+	-	-	-	-	**4.05**	0.37	3.31	**4.79**	**5.45**	0.27	4.91	**5.99**	-	-	-	-	-	-	-	-	**1.41**	0.36	0.69	**2.13**
	RARE-ipsi	-	-	-	-	-	**4.14**	0.32	3.50	**4.78**	**5.55**	0.30	4.95	**6.15**	-	-	-	-	-	-	-	-	**1.41**	0.33	0.75	**2.07**

			Means and standard deviations (ms)																									
LS CE-chirps 90 dB	**NB 2k**	Polarity	**I**				**III**				**V**				**I-III**								**I-V**				**III-V**			
	males n=13		**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**
	SUM-ipsi		-	-	-	-	**4.19**	0.27	3.65	**4.73**	**5.70**	0.25	5.20	**6.20**	-	-	-	-	-	-	-	-	**1.50**	0.14	1.22	**1.78**				
	COND-ipsi	+	-	-	-	-	**4.15**	0.29	3.57	**4.73**	**5.71**	0.23	5.25	**6.17**	-	-	-	-	-	-	-	-	**1.56**	0.26	1.04	**2.08**				
	RARE-ipsi	-	-	-	-	-	**4.23**	0.32	3.59	**4.87**	**5.73**	0.27	5.19	**6.27**	-	-	-	-	-	-	-	-	**1.48**	0.18	1.12	**1.84**				
	NB 2k	Polarity	**I**				**III**				**V**				**I-III**								**I-V**				**III-V**			
	females n=15		**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**
	SUM-ipsi		-	-	-	-	**4.24**	0.32	3.60	**4.88**	**5.62**	0.27	5.08	**6.16**	-	-	-	-	-	-	-	-	**1.39**	0.17	1.05	**1.73**				
	COND-ipsi	+	-	-	-	-	**4.30**	0.28	3.74	**4.86**	**5.65**	0.29	5.07	**6.23**	-	-	-	-	-	-	-	-	**1.43**	0.19	1.05	**1.81**				
	RARE-ipsi	-	-	-	-	-	**4.23**	0.33	3.57	**4.89**	**5.62**	0.31	5.00	**6.24**	-	-	-	-	-	-	-	-	**1.38**	0.17	1.04	**1.72**				
	NB 4k	Polarity	**I**				**III**				**V**				**I-III**								**I-V**				**III-V**			
	males n=14		**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**
	SUM-ipsi		-	-	-	-	**3.82**	0.19	3.44	**4.20**	**5.54**	0.25	5.04	**6.04**	-	-	-	-	-	-	-	-	**1.69**	0.15	1.38	**2.00**				
	COND-ipsi	+	-	-	-	-	**3.83**	0.17	3.49	**4.17**	**5.51**	0.26	4.99	**6.03**	-	-	-	-	-	-	-	-	**1.65**	0.13	1.39	**1.91**				
	RARE-ipsi	-	-	-	-	-	**3.81**	0.24	3.33	**4.29**	**5.47**	0.27	4.93	**6.01**	-	-	-	-	-	-	-	-	**1.65**	0.25	1.15	**2.15**				
	NB 4k	Polarity	**I**				**III**				**V**				**I-III**								**I-V**				**III-V**			
	females n=15		**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**
	SUM-ipsi		-	-	-	-	**3.66**	0.18	3.30	**4.02**	**5.36**	0.28	4.80	**5.92**	-	-	-	-	-	-	-	-	**1.70**	0.17	1.36	**2.04**				
	COND-ipsi	+	-	-	-	-	**3.69**	0.15	3.39	**3.99**	**5.38**	0.28	4.82	**5.94**	-	-	-	-	-	-	-	-	**1.69**	0.17	1.35	**2.03**				
	RARE-ipsi	-	-	-	-	-	**3.65**	0.19	3.27	**4.03**	**5.37**	0.29	4.79	**5.95**	-	-	-	-	-	-	-	-	**1.72**	0.20	1.32	**2.12**				

			Means and standard deviations (ms)																							
LS CE-chirps 70 dB	**Broadband**	Polarity	**I**				**III**				**V**				**I-III**				**I-V**				**III-V**			
	males n=25		**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**
	SUM-ipsi		**1.90**	0.14	1.62	**2.18**	**4.07**	0.18	3.71	**4.43**	**5.93**	0.23	5.47	**6.39**	**2.17**	0.16	1.85	**2.49**	**4.03**	0.19	3.65	**4.41**	**1.86**	0.08	1.70	**2.02**
	COND-ipsi	+	**1.92**	0.16	1.60	**2.24**	**4.03**	0.17	3.69	**4.37**	**5.92**	0.25	5.42	**6.42**	**2.11**	0.17	1.77	**2.45**	**4.01**	0.23	3.55	**4.47**	**1.89**	0.13	1.63	**2.15**
	RARE-ipsi	-	**1.91**	0.13	1.65	**2.17**	**4.09**	0.21	3.67	**4.51**	**5.95**	0.22	5.51	**6.39**	**2.17**	0.21	1.76	**2.60**	**4.04**	0.21	3.62	**4.46**	**1.86**	0.11	1.64	**2.08**
	Broadband	Polarity	**I**				**III**				**V**				**I-III**				**I-V**				**III-V**			
	females n=25		**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**
	SUM-ipsi		**1.89**	0.15	1.59	**2.19**	**3.94**	0.15	3.64	**4.24**	**5.71**	0.18	5.35	**6.07**	**2.04**	0.13	1.78	**2.30**	**3.80**	0.13	3.54	**4.06**	**1.77**	0.11	1.55	**1.99**
	COND-ipsi	+	**1.88**	0.14	1.60	**2.16**	**3.91**	0.17	3.57	**4.25**	**5.72**	0.19	5.34	**6.10**	**2.03**	0.15	1.73	**2.33**	**3.82**	0.15	3.52	**4.12**	**1.81**	0.11	1.59	**2.03**
	RARE-ipsi	-	**1.90**	0.16	1.58	**2.22**	**3.97**	0.26	3.65	**4.29**	**5.72**	0.19	5.34	**6.10**	**2.06**	0.13	1.80	**2.32**	**3.81**	0.14	3.53	**4.09**	**1.75**	0.11	1.53	**1.97**
	NB 0.5k	Polarity	**I**				**III**				**V**				**I-III**				**I-V**				**III-V**			
	males n=13		**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**
	SUM-ipsi		-	-	-	-	**3.94**	0.60	2.74	**5.14**	**5.89**	0.36	5.17	**6.61**	-	-	-	-	-	-	-	-	**1.99**	0.29	1.41	**2.57**
	COND-ipsi	+	-	-	-	-	**3.89**	0.39	3.11	**4.67**	**6.00**	0.36	5.28	**6.72**	-	-	-	-	-	-	-	-	**2.03**	0.07	1.89	**2.17**
	RARE-ipsi	-	-	-	-	-	**4.23**	0.41	3.41	**5.05**	**5.96**	0.59	4.78	**7.14**	-	-	-	-	-	-	-	-	**1.89**	0.29	1.25	**2.41**
	NB 0.5k	Polarity	**I**				**III**				**V**				**I-III**				**I-V**				**III-V**			
	females n=14		**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**
	SUM-ipsi		-	-	-	-	-	-	-	-	**5.73**	0.40	4.93	**6.53**	-	-	-	-	-	-	-	-	-	-	-	-
	COND-ipsi	+	-	-	-	-	-	-	-	-	**5.67**	0.17	5.33	**6.01**	-	-	-	-	-	-	-	-	-	-	-	-
	RARE-ipsi	-	-	-	-	-	-	-	-	-	**5.33**	0.62	4.09	**6.57**	-	-	-	-	-	-	-	-	-	-	-	-
	NB 1k	Polarity	**I**				**III**				**V**				**I-III**				**I-V**				**III-V**			
	males n=13		**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**
	SUM-ipsi		-	-	-	-	**4.45**	0.19	4.07	**4.83**	**6.03**	0.20	5.63	**6.43**	-	-	-	-	-	-	-	-	**1.61**	0.16	1.85	**2.49**
	COND-ipsi	+	-	-	-	-	**4.24**	0.19	3.86	**4.62**	**6.04**	0.23	5.58	**6.50**	-	-	-	-	-	-	-	-	**1.80**	0.17	1.77	**2.45**
	RARE-ipsi	-	-	-	-	-	**4.48**	0.29	3.90	**5.06**	**6.09**	0.27	5.55	**6.63**	-	-	-	-	-	-	-	-	**1.61**	0.21	1.76	**2.60**
	NB 1k	Polarity	**I**				**III**				**V**				**I-III**				**I-V**				**III-V**			
	females n=14		**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**
	SUM-ipsi		-	-	-	-	**4.26**	0.21	3.84	**4.68**	**5.92**	0.33	5.26	**6.58**	-	-	-	-	-	-	-	-	**1.70**	0.25	1.20	**2.20**
	COND-ipsi	+	-	-	-	-	**4.26**	0.27	3.72	**4.80**	**6.00**	0.28	5.44	**6.56**	-	-	-	-	-	-	-	-	**1.76**	0.23	1.30	**2.22**
	RARE-ipsi	-	-	-	-	-	**4.16**	0.21	3.74	**4.58**	**5.92**	0.40	5.12	**6.72**	-	-	-	-	-	-	-	-	**1.83**	0.28	1.27	**2.39**

			Means and standard deviations (ms)																							
LS CE-chirps 70 dB	**NB 2k**	Polarity		**I**				**III**				**V**				**I-III**				**I-V**				**III-V**			
	males n=13		**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**
	SUM-ipsi		**2.36**	0.19	1.98	**2.74**	**4.29**	0.27	3.75	**4.83**	**6.10**	0.31	5.48	**6.72**	**1.99**	0.21	1.57	**2.41**	**3.75**	0.23	3.29	**4.21**	**1.81**	0.16	1.49	**2.13**
	COND-ipsi	+	**2.31**	0.21	1.89	**2.73**	**4.28**	0.32	3.64	**4.92**	**6.07**	0.29	5.49	**6.65**	**2.04**	0.29	1.46	**2.62**	**3.77**	0.25	3.27	**4.27**	**1.79**	0.21	1.37	**2.21**
	RARE-ipsi	-	**2.41**	0.17	2.07	**2.75**	**4.31**	0.28	3.75	**4.87**	**6.11**	0.33	5.45	**6.77**	**1.97**	0.20	1.57	**2.37**	**3.74**	0.27	3.20	**4.28**	**1.78**	0.16	1.46	**2.10**
	NB 2k	Polarity		**I**				**III**				**V**				**I-III**				**I-V**				**III-V**			
	females n=15		**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**
	SUM-ipsi		**2.30**	0.15	2.00	**2.60**	**4.31**	0.19	3.93	**4.69**	**5.91**	0.25	5.41	**6.41**	**2.00**	0.17	1.66	**2.34**	**3.60**	0.19	3.22	**3.98**	**1.60**	0.17	1.26	**1.94**
	COND-ipsi	+	**2.35**	0.16	2.03	**2.67**	**4.25**	0.20	3.85	**4.65**	**5.90**	0.26	5.38	**6.42**	**1.93**	0.21	1.51	**2.35**	**3.52**	0.20	3.12	**3.92**	**1.64**	0.22	1.20	**2.08**
	RARE-ipsi	-	**2.30**	0.15	2.00	**2.60**	**4.39**	0.13	4.13	**4.65**	**5.96**	0.23	5.50	**6.42**	**2.02**	0.20	1.62	**2.42**	**3.51**	0.20	3.11	**3.91**	**1.61**	0.16	1.29	**1.93**
	NB 4k	Polarity		**I**				**III**				**V**				**I-III**				**I-V**				**III-V**			
	males n=14		**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**
	SUM-ipsi		**2.23**	0.15	1.93	**2.53**	**4.34**	0.19	3.96	**4.72**	**6.14**	0.20	5.74	**6.54**	**2.11**	0.15	1.80	**2.42**	**3.91**	0.16	3.59	**4.23**	**1.81**	0.13	1.55	**2.07**
	COND-ipsi	+	**2.25**	0.16	1.93	**2.57**	**4.30**	0.17	3.96	**4.64**	**6.13**	0.22	5.69	**6.57**	**2.06**	0.18	1.70	**2.42**	**3.88**	0.18	3.52	**4.24**	**1.82**	0.11	1.60	**2.04**
	RARE-ipsi	-	**2.21**	0.16	1.89	**2.53**	**4.33**	0.17	3.99	**4.67**	**6.16**	0.20	5.76	**6.56**	**2.12**	0.18	1.76	**2.48**	**3.95**	0.23	3.49	**4.41**	**1.83**	0.13	1.57	**2.09**
	NB 4k	Polarity		**I**				**III**				**V**				**I-III**				**I-V**				**III-V**			
	females n=15		**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**
	SUM-ipsi		**2.13**	0.12	1.89	**2.37**	**4.18**	0.16	3.86	**4.50**	**5.95**	0.21	5.53	**6.37**	**2.03**	0.11	1.81	**2.25**	**3.80**	0.18	3.44	**4.16**	**1.78**	0.11	1.56	**2.00**
	COND-ipsi	+	**2.14**	0.12	1.90	**2.38**	**4.15**	0.17	3.81	**4.49**	**5.95**	0.21	5.53	**6.37**	**2.00**	0.13	1.74	**2.26**	**3.78**	0.20	3.38	**4.18**	**1.79**	0.11	1.57	**2.01**
	RARE-ipsi	-	**2.14**	0.15	1.84	**2.44**	**4.20**	0.15	3.90	**4.50**	**5.98**	0.20	5.58	**6.38**	**2.04**	0.13	1.78	**2.30**	**3.82**	0.17	3.48	**4.16**	**1.78**	0.10	1.58	**1.98**

Appendix IX – Normative data for otoneurological assessment using a click stimulus (Feijen, 2013; Van Bommel, 2014)

LS CE-chirps

Means and standard deviations (ms)

90 dB	Polarity	I				III				V				I-III				I-V				III-V			
males n=24		**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**
SUM-ipsi		**1.36**	0.11	1.14	**1.58**	**3.58**	0.14	3.29	**3.86**	**5.49**	0.19	5.11	**5.88**	**2.22**	0.12	1.98	**2.45**	**4.13**	0.19	3.76	**4.51**	**1.90**	0.17	1.56	**2.25**
COND-ipsi	+	**1.41**	0.14	1.13	**1.70**	**3.61**	0.15	3.30	**3.92**	**5.50**	0.21	5.07	**5.93**	**2.20**	0.13	1.93	**2.47**	**4.09**	0.21	3.67	**4.50**	**1.88**	0.18	1.53	**2.24**
RARE-ipsi	-	**1.38**	0.13	1.12	**1.65**	**3.56**	0.18	3.20	**3.92**	**5.50**	0.19	5.11	**5.88**	**2.18**	0.17	1.84	**2.52**	**4.12**	0.21	3.70	**4.54**	**1.92**	0.17	1.59	**2.25**

90 dB	Polarity	I				III				V				I-III				I-V				III-V			
females n=31		**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**
SUM-ipsi		**1.32**	0.08	1.15	**1.49**	**3.43**	0.12	3.18	**3.68**	**5.23**	0.21	4.81	**5.65**	**2.11**	0.10	1.90	**2.32**	**3.91**	0.18	3.55	**4.27**	**1.80**	0.16	1.48	**2.12**
COND-ipsi	+	**1.34**	0.11	1.12	**1.55**	**3.48**	0.14	3.19	**3.76**	**5.20**	0.23	4.74	**5.66**	**2.15**	0.12	1.90	**2.39**	**3.86**	0.19	3.47	**4.25**	**1.73**	0.19	1.34	**2.11**
RARE-ipsi	-	**1.32**	0.09	1.14	**1.50**	**3.38**	0.13	3.13	**3.63**	**5.24**	0.23	4.78	**5.70**	**2.06**	0.13	1.80	**2.33**	**3.91**	0.23	3.45	**4.37**	**1.86**	0.19	1.48	**2.24**

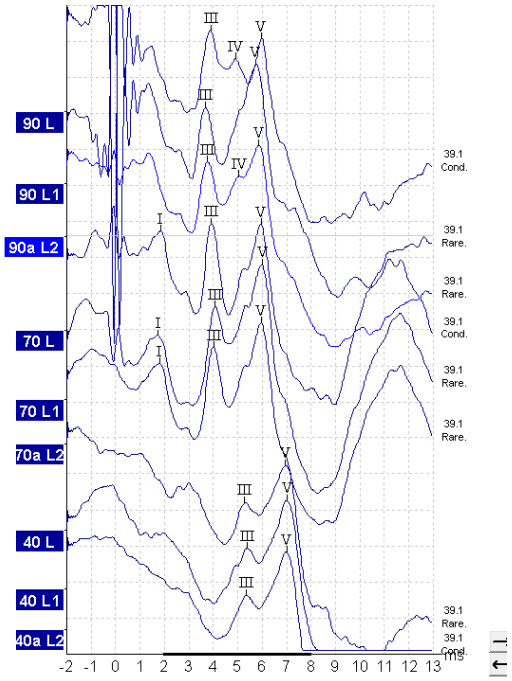
70 dB	Polarity	I				III				V				I-III				I-V				III-V			
males n=27		**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**
SUM-ipsi		**1.65**	0.14	1.37	**1.93**	**3.85**	0.22	3.41	**4.28**	**5.73**	0.27	5.18	**6.28**	**2.19**	0.15	1.89	**2.50**	**4.07**	0.23	3.61	**4.53**	**1.88**	0.18	1.51	**2.24**
COND-ipsi	+	**1.60**	0.13	1.33	**1.87**	**3.81**	0.21	3.39	**4.23**	**5.75**	0.24	5.28	**6.23**	**2.18**	0.15	1.87	**2.49**	**4.12**	0.17	3.78	**4.46**	**1.92**	0.16	1.60	**2.25**
RARE-ipsi	-	**1.70**	0.19	1.32	**2.07**	**3.87**	0.19	3.49	**4.24**	**5.73**	0.24	5.26	**6.20**	**2.17**	0.15	1.86	**2.48**	**4.02**	0.24	3.54	**4.49**	**1.84**	0.15	1.54	**2.13**

70 dB	Polarity	I				III				V				I-III				I-V				III-V			
females n=35		**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**
SUM-ipsi		**1.63**	0.15	1.32	**1.93**	**3.69**	0.17	3.35	**4.03**	**5.49**	0.19	5.11	**5.87**	**2.06**	0.09	1.89	**2.24**	**3.85**	0.15	3.54	**4.16**	**1.79**	0.12	1.55	**2.02**
COND-ipsi	+	**1.57**	0.14	1.28	**1.86**	**3.64**	0.21	3.22	**4.06**	**5.49**	0.21	5.07	**5.90**	**2.04**	0.13	1.79	**2.30**	**3.90**	0.18	3.54	**4.25**	**1.85**	0.18	1.49	**2.20**
RARE-ipsi	-	**1.66**	0.17	1.32	**1.99**	**3.74**	0.17	3.40	**4.08**	**5.48**	0.21	5.07	**5.90**	**2.08**	0.13	1.82	**2.34**	**3.82**	0.18	3.46	**4.17**	**1.74**	0.16	1.42	**2.06**

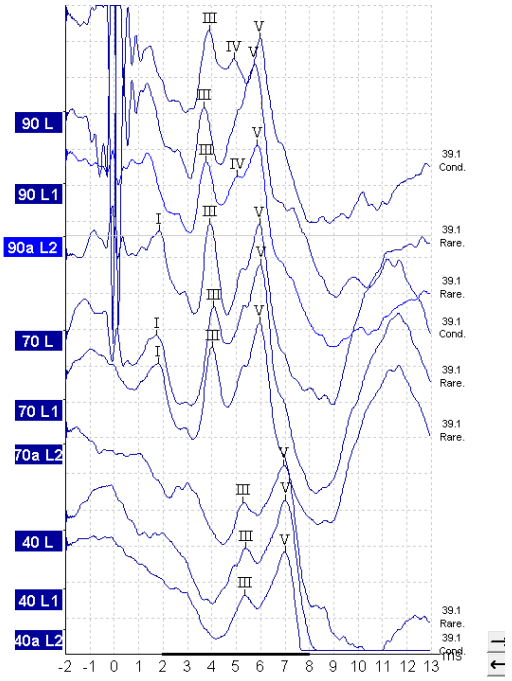
80 dB	Polarity	I				III				V				I-III				I-V				III-V			
males n=15		**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**
SUM-ipsi		**1.52**	0.10	1.31	**1.72**	**3.71**	0.12	3.46	**3.96**	**5.47**	0.15	5.17	**5.76**	**2.19**	0.11	1.98	**2.40**	**3.96**	0.15	3.66	**4.25**	**1.79**	0.14	1.52	**2.06**
COND-ipsi	+	**1.49**	0.10	1.28	**1.69**	**3.70**	0.12	3.46	**3.95**	**5.49**	0.17	5.16	**5.83**	**2.22**	0.12	1.98	**2.45**	**4.02**	0.25	3.53	**4.52**	**1.81**	0.16	1.49	**2.13**
RARE-ipsi	-	**1.54**	0.11	1.31	**1.77**	**3.71**	0.13	3.44	**3.97**	**5.47**	0.13	5.22	**5.73**	**2.17**	0.15	1.86	**2.47**	**3.93**	0.15	3.62	**4.23**	**1.81**	0.20	1.40	**2.21**

80 dB	Polarity	I				III				V				I-III				I-V				III-V			
females n=18		**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**	**mean**	sd	-2sd	**+2sd**
SUM-ipsi		**1.48**	0.12	1.23	**1.72**	**3.58**	0.11	3.36	**3.81**	**5.38**	0.17	5.05	**5.71**	**2.11**	0.11	1.88	**2.33**	**3.90**	0.18	3.54	**4.26**	**1.79**	0.11	1.58	**2.01**
COND-ipsi	+	**1.45**	0.10	1.25	**1.64**	**3.56**	0.11	3.35	**3.77**	**5.37**	0.20	4.97	**5.77**	**2.12**	0.10	1.92	**2.31**	**3.93**	0.23	3.46	**4.39**	**1.81**	0.18	1.45	**2.17**
RARE-ipsi	-	**1.51**	0.15	1.22	**1.80**	**3.61**	0.16	3.29	**3.92**	**5.37**	0.17	5.02	**5.71**	**2.10**	0.13	1.83	**2.37**	**3.86**	0.16	3.54	**4.19**	**1.76**	0.16	1.44	**2.08**

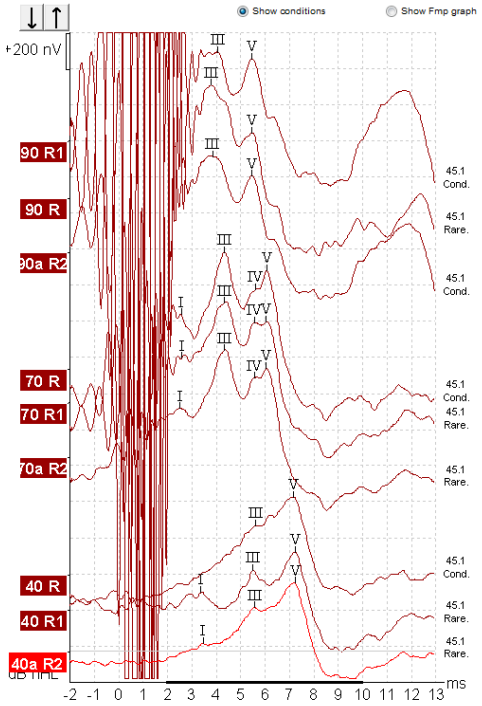
Appendix X – Representative examples of ABR waveforms evoked by the five LS CE-chirps



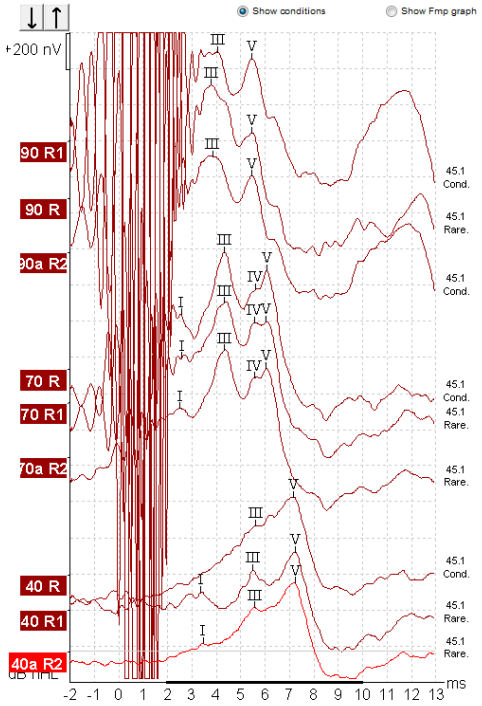
Broadband LS CE-chirp



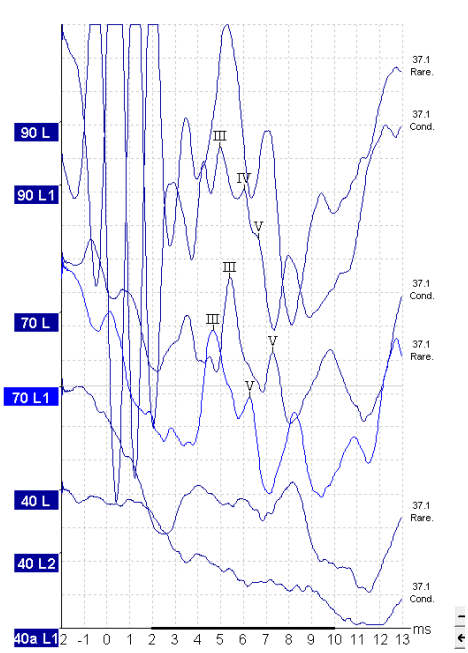
NB 4k LS CE-chirp



NB 2k LS CE-chirp

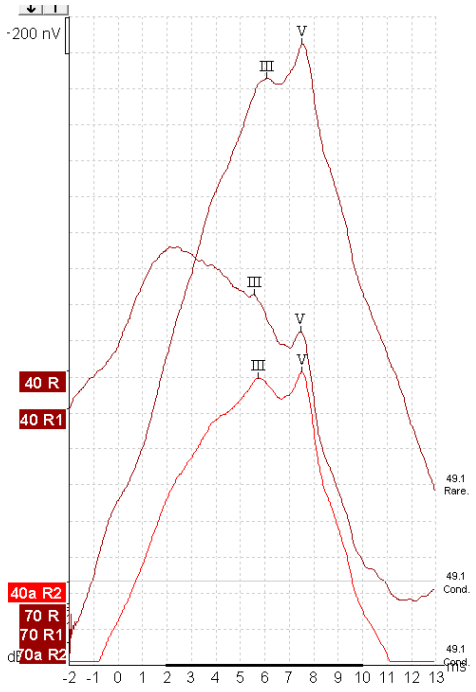


NB 1k LS CE-chirp

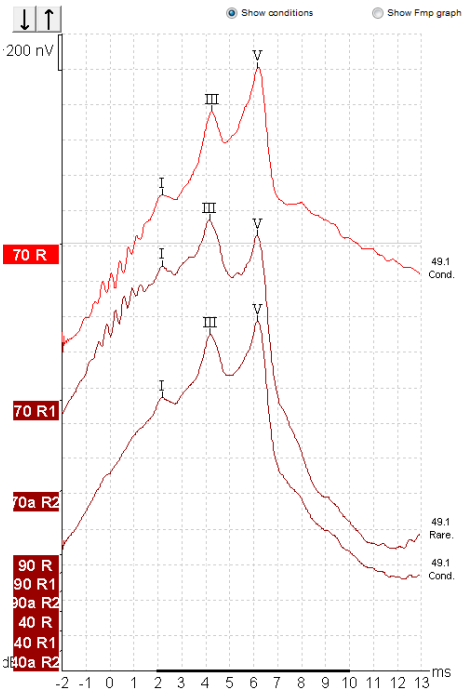


NB 0.5k LS CE-chirp

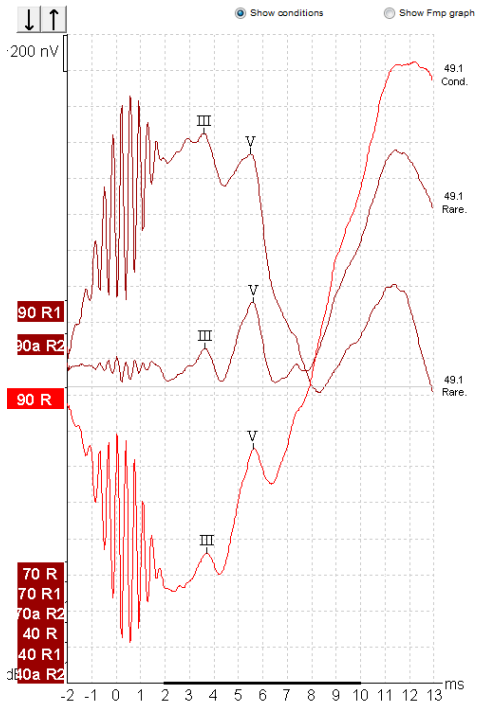
Appendix XI – Screenshots AC NB 4k LS CE-chirp influenced by electrical artifact



Electrical artefact for the AC NB 4k LS CE-chirp at 40 dB nHL



Electrical artefact for the AC NB 4k LS CE-chirp at 70 dB nHL



Electrical artefact for the AC NB 4k LS CE-chirp at 90 dB nHL.

Appendix XII – Relationship between the present study and the area of language and speech pathology

The present study involves an evaluation of a new stimulus for air- and bone-conducted Brainstem Evoked Response Audiometry (BERA). BERA is an objective measure of hearing functioning that is often used in the assessment of hearing loss in infants under six months of age. For this age group, subjective measures are not feasible. BERA is a suitable alternative, since auditory brainstem response (ABR) measurements do not require an active response from the patient. Therefore, ABRs can even be recorded in newborns and hearing functioning can thus be evaluated at a very young age. This early evaluation of functioning is critical for the spoken language development of the child. To develop a spoken language, an infant needs access to auditory input. By assessing hearing functioning within the first months of an infant life, hearing aid provision, and potentially cochlear implantation, can be advanced substantially. This has a significantly positive influence on spoken language acquisition.

The LS CE-chirp stimulus that has been evaluated in the present study consists of a broadband and four narrowband versions. These narrowband versions of the LS CE-chirp allow for the collection of frequency-specific BERAs. By collecting BERAs at the four narrowband centre frequencies, i.e. 500, 1000, 2000 and 4000 Hz, clinicians can determine hearing threshold for specific frequency-bands. This information is highly valuable in the adjustment of hearing aids. The same holds for bone-conduction ABR. By comparing air- and bone-conduction ABR, the nature of the suspected hearing loss of an infant can be examined (as has been elaborated upon in section 8). This information can then be used for optimal hearing aid adjustment for the individual infant, which, in turn, optimizes the access to auditory input, including language.

To conclude, proper assessment and treatment of restrictions in hearing functioning is crucial for the development of a child. Clinicians attempt to determine the optimal adjustment of hearing aids for each individual patient as quickly as possible in order to attain optimal access to auditory input and thus language input. The smaller the period of language input deprivation, the better the prognosis of language and speech development of the patient.