RADBOUD UNIVERSITY

MASTER THESIS

Frequency specificity of the auditory brainstem response versus cortical auditory steady-state responses using chirp stimuli

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Abstract

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by Leonie Vonk

The auditory brainstem response and the auditory steady-state response are objective methods to estimate hearing loss. Level-specific CE chirps are new stimuli for these methods, that compensate for the cochlear travelling wave delay. The purpose was to investigate the thresholds as obtained by these objective methods compared to subjective threshold, using these stimuli. Participants were normal hearing adults (42 ears), infants with hearing loss (90 ears) and adults with steeply sloping hearing loss (2 ears). The objective and subjective thresholds correlated well. For air conduction, the objective thresholds for the 500 and 1000 Hz conditions were higher than the subjective thresholds. These findings did not replicate for bone conduction. Correction factors for the objective responses are suggested. On top of that, there was a latency shift in wave V for the 500 Hz AC condition.

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Chapter 1

Introduction

Good hearing is very important for proper native language acquisition (Schaerlaekens, 2008, pp 77-78). Because of this, infants need to be screened on hearing problems as early as possible. The sooner hearing loss is found, the sooner something can be done to secure a future for the child in which they can communicate. Solutions range from hearing aids or cochlear implants to family members learning sign language.

As infants cannot reliably take part in subjective audiometry, a number of objective measurements have been developed. These objective measures focus on the auditory brainstem responses. There are different methods and different stimuli, which all have their benefits and disadvantages. This study will compare two objective methods, using a relatively new stimulus: the level specific narrowband CE-chirp.

This study consists of three parts. First, it will be verified whether different sound transducers deliver the same results in terms of latency of wave V of the auditory brainstem response. Second, hearing thresholds will be obtained with two different objective measurements, using air-conduction as well as bone-conduction. Finally, the frequency specificity of the narrowband CE-chirp stimuli will be investigated. To achieve this, objective hearing thresholds will be compared in patients with a steeply sloping audiogram.

In this introduction, a short overview of the auditory system will be given. The different objective measurements using auditory evoked potentials, and the stimuli that are used for these assessments will be described.

1.1 Anatomy of the ear

The ear is divided into three parts: The outer ear, the middle ear, and the inner ear. This can be seen in figure 1.1.

The outer ear consists of the auricle, the ear canal and the tympanic membrane. The middle ear begins on the other side of the tympanic membrane. The middle ear is composed of the tympanic cavity and the ossicles. The inner ear consists of the cochlea and the vestibular system.

The middle ear is separated from the outer ear by the ear drum. The ear drum or tympanic membrane is a thin, flexible membrane which vibrates easily. Attached to the ear drum are the ossicles: the malleus, the incus, and the stapes. The function of the ossicles is to lower the air to fluid impedance, by acting as a lever. This is because the inner ear is filled with fluid endolymph.

The cochlea is located in the inner ear and is embedded in the mastoid. It consists of three canals: the scala tympani, the scala vestibuli and the scala media. The first two are filled with perilymph, the latter with endolymph. The basilar membrane is located in the scala media. Attached to the basilar membrane are inner en outer hair cells. When these are stimulated, the spiral ganglion cells fire. The basilar membrane is tonotopically organized, with the high frequencies at the base and the lower frequencies at the apex of the cochlea (McFarland, 2009).

The vestibular system is also found in the inner ear. This system consists of the three semicircular canals, which measure rotational movements of the head and the two otoliths, which measure horizontal and vertical linear acceleration.

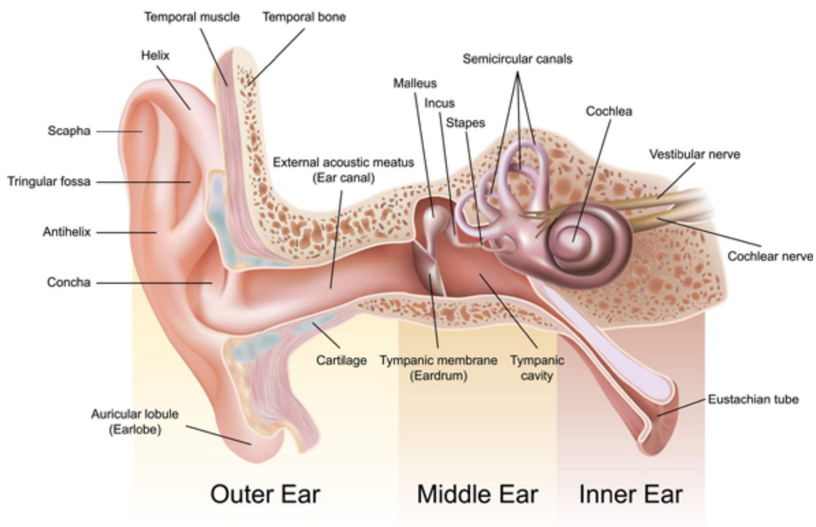


FIGURE 1.1: Anatomy of the ear, with the three parts (outer, middle, inner) indicated. Retrieved from http://www.audiologyspecialists.com/anatomy-of-the-ear.

1.1.1 Air conduction

Air conduction (AC) is the "usual" way of hearing. When a sound wave travels through the air, it passes along the ear canal. The tympanic membrane vibrates along with the sound waves and moves the ossicles. The third of the ossicles, the stapes, vibrates on the oval window and brings the fluid inside the cochlea in motion. This causes a mechanical traveling wave along the basilar membrane. The hair cells are stimulated by this wave and fire. The auditory nerve carries the signal to the brain: a sound is heard.

1.1.2 Bone conduction

As described, the cochlea can be stimulated by the sound waves traveling through air through the outer and middle ear. Another way is to stimulate the cochlea directly is via bone conduction (BC). This is possible because the cochlea is embedded in the mastoid part of the temporal bone.

A bone conduction device is a small vibrating block which can be placed on either the mastoid or the forehead. The sound waves produced by the bone conductor travel through the bone and to the cochlea. This way, the ear canal and the ossicles are bypassed.

This makes bone conduction a valuable way to get insight in hearing loss. The difference between air and bone thresholds is called the "air-bone gap". If the air conduction threshold is much higher than the bone conduction threshold, there could be a problem in the ear canal (a blockage) or a dysfunction of the ossicles. If the bone conduction threshold is in the normal range, it means the cochlea works normally (Carhart and Hayes, 1949; Hood, 1960).

When a sound of 50 dB HL is presented to a normal hearing right ear by air conduction, it will be heard ipsilaterally at 50 dB HL. However, it will also be heard contralaterally through vibration of the skull, only at a lower intensity. This is called the intra-aural attenuation. For air conduction, this attenuation can be 40 to 80 dB, depending on the person (Hood, 1960; British Society of Audiology, 2011). When stimulating ipsilaterally by bone conduction however, the attenuation to the contralateral ear is much lower and varies from 0 to 20 dB. Thus, the sound will arrive at the contralateral cochlea at almost the same intensity. Because of this, it cannot be determined which cochlea is measured. To counter this problem, the contralateral ear should always be masked with noise (Hood, 1960; British Society of Audiology, 2011; American Speech-Language-Hearing Association, 2005).

In this experiment, masking will be used by delivering narrow band noise with an insert earphone or over-the-ear headphones to the contralateral ear.

Bone conduction can give valuable information about the type of hearing loss.

1.2 Hearing loss

There are two major types of hearing loss. Conduction loss is a loss caused by a defect in the chain of the sound transduction to the cochlea. There is no defect in the cochlea. Perception loss or sensorineural hearing loss is a loss caused by a defect in the cochlea. There can also be a mixed type of loss.

Hearing loss does not have to be the same in every frequency. A perception loss could for example only affect the base of the cochlea, resulting in a high-frequency loss. There are people with steeply sloping hearing losses. This means that there is a large difference in threshold between two adjacent frequencies.

The definition of steeply sloping or ski slope hearing loss differs across literature. Liu and Xu (1994) defined gently sloping hearing loss as a difference of 10 to 24 dB HL and sharply sloping hearing loss as a difference larger than 25 dB HL. However, Ballay et al. (2005) defined steeply sloping loss as a difference of 20 dB of bigger between two adjacent test frequencies. In addition, McDermott et al. (1998) had two groups of participants with steeply sloping loss. The first group had a difference of more than 50 dB and the other group 41-50 dB difference between adjacent test frequencies.

1.3 Auditory Evoked Potentials

There are different objective ways to measure hearing loss. These all make use of auditory evoked potentials.

When a sound above threshold is presented to the ear, the hair cells in the cochlea fire. These signals are carried on to the brain by the auditory nerve as electrical potentials. These electrical activities in the brain in response to sound are called auditory evoked potentials (Picton et al., 1974). These can be measured through an electroencephalogram (EEG). The EEG records the electrical potentials through the scalp.

The auditory evoked responses can be divided in three parts. The auditory brainstem response (ABR) is the first and therefore fastest response. It occurs within 10 ms of the stimulus. Second comes the middle latency response, which occurs in 10 to 50 ms after the stimulus. Even later is the long latency response, which occurs between 50 and 300 ms after the stimulus (Picton et al., 1974; Hall, 1992). Figure 1.2 shows these different parts.

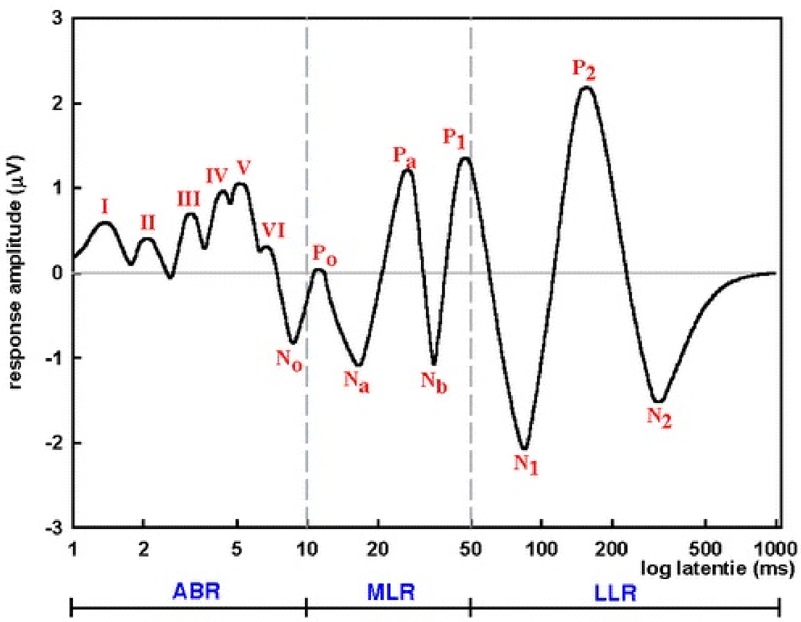


FIGURE 1.2: The different parts of the auditory evoked potentials. Retrieved from http://www.audiologieboek.nl/htm/hfd4/4-5-1.htm

Evoked potentials can be transient, through one stimulus, or steady-state, through a continuous stimulus. This has to do with the stimulus rate. The transient response is up to 50 Hz rate. After that, the peak responses cannot be seen as separate any more, because the stimuli are so fast the responses melt into each other. This kind of response is the steady state response.

1.4 Objective Audiometry

Infants and children cannot always reliably take part in subjective audiometry. Because of this, ways have been found to measure the hearing of infants in an objective way. There are two methods of obtaining the threshold. The ABR uses the transient AEP response, the ASSR uses the steady state AEP.

1.4.1 Auditory Brainstem Response

The auditory brainstem response (ABR) is a transient auditory evoked response (Picton et al., 1977). It is analysed in the temporal domain. As seen, the ABR is the earliest potential in response to an auditory stimulus. The ABR has a typical morphology, which is shown below in figure 1.3. Peaks or waves can be identified in the response. Each wave corresponds with the firing of neurons in specific nuclei in the auditory pathway. Peak I and II come from the auditory nerve, III comes from the nucleus cochlears. IV finds its origin in the olive complex and V in the lateral lemniscus (brain stem) (Hall, 1992). If wave V is seen in the response, it can be said that the sound is heard (Sohmer and Feinmesser, 1967).

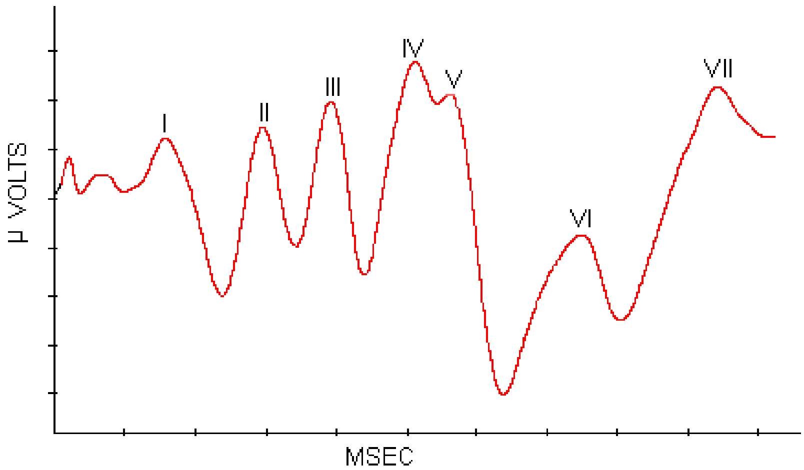


FIGURE 1.3: A typical ABR of an adult with normal auditory function. Retrieved from `http://firstyears.org/c3/c3.htm`, April 13, 2017.

The waves not only occur in a fixed order, they also occur at a fixed latency, corresponding to the intensity of the stimulus. The lower the intensity, the later the latency. When the intensity is higher, the neurons fire more rapidly, which in turn means the synaptic transmission is faster. This results in a shorter latency. The relationship between latency and intensity can be described with a formula, called the latency-intensity curve (Picton et al., 1977; Serpanos et al., 1997).

To observe the ABR, an electroencephalogram is used. The recommended setup is to place electrodes on the vertex and on the mastoid, with the ground electrode on the forehead (Newborn Hearing Screening Program, 2014). Because the response is very small (+/- $200nV$), at least 1000 to 2000 averages are needed to get a clear response. It is important that the participant sleeps or lays very still to minimize noise.

There are a number of parameters that influence the ABR. Gender is an important factor. Males typically have longer latencies than females. This is due to males having a bigger cochlea, resulting in a longer times for the traveling wave. For the same reason, head size influences the ABR. However, females and males with the same head size still differ in latencies. On top of that, the ABR differs with age (Mitchell et al., 1989).

Hearing loss affects the morphology of the ABR, too. (Don and Eggermont, 1978; Don et al., 1979; Mitchell et al., 1989)

Finally, tinnitus influences the ABR in terms of latency and reproducibility. The latency times are longer and the responses do not reproduce well (Kehrle et al., 2008; Ikner and Hassen, 1990).

ABR is a valuable way to obtain objective information about hearing loss in children (Abramovich et al., 1987). The ABR threshold correlates well with the subjective pure tone threshold, as shown by several studies (Schoonhoven et al., 2000; Stapells and Oates, 1997).

The most widely used stimulus to evoke the ABR is the click. The other different stimuli are described in section 1.5.

1.4.2 Auditory Steady State Response

The auditory steady state response (ASSR) is another way to objectively determine the hearing threshold. Unlike ABR, ASSR relies on a statistical method to determine whether a response is present or not. The response is analysed in the frequency domain, as opposed to the temporal domain as is the case with ABR. ASSR has shown to be a reliable method of estimating the hearing threshold, in both adults and children (François et al., 2016; Kandogan and Dalgic, 2013; Lee et al., 2015).

In ASSR, the stimuli are modulated in amplitude and frequency. Stimuli can be tone bursts, clicks or (narrowband) chirps, among others. Recent research has shown a strong correlation between thresholds obtained with ASSR using tone burst stimuli and with ASSR using chirp stimuli (Michel and Jørgensen, 2017).

The detection of the response takes place in the spectral domain. There is a carrier wave of the test frequency (0.5, 1, 2 or 4 kHz CE-chirps). This carrier wave is modulated in amplitude. The system records the response to this stimulus and Fourier transforms the response to a spectrum. If the sound is heard, the response is seen in the spectrum as harmonics of the modulation rate. If the modulation rate is for example 90 Hz, then harmonics will occur at 90, 180, 270 Hz, etc. in the spectrum. If these harmonics in the response differ significantly from the noise in the spectrum, the ASSR system returns that the sound is detected (Beck et al., 2007). The way this spectrum could look like can be seen in figure 1.4.

To detect the response effectively, the modulation rate is adjusted according to the state of the participant. When participants are asleep, a rate of above 70 Hz can be used, whereas are rate of 40 Hz works better for awake

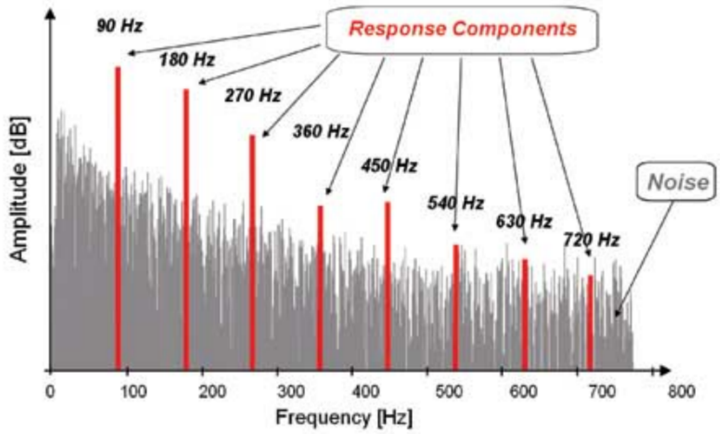


FIGURE 1.4: A Fourier transformation of an ASSR, showing the detection. Retrieved from Beck et al. (2007), July 14, 2017

participants (Cohen et al., 1991; Newborn Hearing Screening Program, 2009). The InterAcoustics Eclipse system, which is used in the present study, uses a 90 Hz modulation rate for participants who are asleep

A big advantage of ASSR is that the stimuli of different frequencies can be presented simultaneously, limiting the test time enormously. The different frequency stimuli are all modulated at a slightly different rate. In this way, the response can be tracked back to the initial stimulus using the harmonics.

1.4.3 Comparing ASSR and ABR

Both ASSR and ABR are reliable methods to get information about the hearing threshold. However, both have their advantages and disadvantages.

Frank et al. (2017) compared the air conduction in ASSR and ABR for the 500 Hz frequency using different chirps. Stürzebecher et al. (2006) reports that both the ASSR and ABR are less reliable in the 500 Hz frequency than for the other frequencies. same. The 500 Hz ASSR is not possible for bone conduction in the Eclipse system. This low frequency inaccuracy could be caused by a polarity effect in the ABR.

Xu et al. (2014) report: "The use of a chirp-ABR testing ensures higher sensitivity and accuracy than that of auditory steady-state evoked response (ASSR) for measuring frequency-specific thresholds in young children."

A disadvantage of both methods is that the participant has to sleep or be calm, to minimize noise.

It is difficult to perform ASSR in people with steeply sloping hearing loss. This is because the presented simultaneous stimuli cannot differ more than 20 dB from each other, as the lower intensities could be masked by the high intensities. ASSR can still be performed, but the different frequencies should be presented separately. The advantage of shorter testing time is then nullified, however.

There is some literature on bone conduction. Small and Stapells (2006) report that the ASSR bone conductions thresholds of adults were very different from those of infants. This should be kept in mind, as one of the test groups in this study will consist of adults. The BC ASSR is reliable in children with conduction loss, but maybe not so in children with a sensorineural hearing loss (Ismaila et al., 2016). It also seems to be reliable in adults (Ishida et al., 2011).

Even if ASSR is a better method than ABR for estimating the hearing threshold, the ABR will still be used to assess the latency of the ABR waves (François et al., 2016).

1.5 Stimuli

1.5.1 Non frequency specific stimuli

Click

The click is the most widely used stimulus for evoking the ABR. The click is a short (100 ms) broadband pulse. When a click stimulus is presented to the ear, there is almost simultaneous firing of all the hair cells along the basilar membrane. Because of this, there is the neural synchrony that is needed to get a clear response (Stapells and Oates, 1997; Picton et al., 1994; Don et al., 2009).

The assumption was long that the response to a click consisted of all frequency areas in the cochlea, because it is a broadband stimulus. A limitation of the click, however, is that the ABR thresholds as measured by clicks correlate best with the pure tone threshold of 1000-4000 Hz, but not with the 500 Hz pure tone threshold. This is because the click stimulates mostly the higher frequency areas of the basilar membrane. These are found at the base of the cochlea. Because the sound wave has to travel along the membrane before reaching the apex, it takes longer for the lower frequencies to fire. This results in a response that consists mostly of the higher frequency firing. There are ways to compensate for this problem.

One solution is the stacked ABR. To do this, click stimuli with high pass noise are presented, with different cut-off frequencies. This way, there are narrowband responses belonging to all different frequency areas of the cochlea. These have different latencies, depending on the place in the cochlea. The narrowband responses are then shifted to all fall on the same latency and summed. The summed response is generally larger than the "normal" click ABR (Don et al., 1997, 2009).

Stacked ABR compensates for the travelling wave using the output. We can also compensate using the input: use a different stimulus, i.e. the chirp.

Broadband chirp

To compensate for the cochlear traveling wave delay (CTWD) of the basilar membrane, the chirp stimulus was developed. The chirp stimulus is a broadband stimulus, just like the click. The difference is that the lower frequencies start earlier than the higher frequencies. This is because the higher frequencies are at the base of the basilar membrane and therefore fire first. The wave arrives later at the apex, where the lower frequencies are located, therefore those will fire later. The delay of the chirp is the inverse of the travelling wave delay in the cochlea. In this way, all the hair cells will fire simultaneously. This leads to a response that is not only larger (Dau et al., 2000), but also visible after fewer sweeps compared to the click.

There are different delay models for the chirp. The standard equation to describe the chirp is:

$$\tau = k \cdot f^{-d} \tag{1.1}$$

In this equation, τ is the latency in seconds, f is the frequency in Hertz. k and d are constants. Their value differs between models. (Elberling et al., 2007).

(Elberling et al., 2007) discussed different chirp designs. One chirp was based on a cochlea model (De Boer, 1980; Fobel and Dau, 2004). Fobel and Dau (2004) also constructed a chirp based on oto-acoustic emissions. The second chirp was based on tone burst evoked ABR. The third chirp was based on narrowband ABR.

These chirps only compensate for the time delay of the cochlea, but not for the delay caused by different intensity levels. Elberling and Don (2010) designed a level specific chirp, which compensates for the intensity delay.

Elberling et al. (2010) evaluated again different chirps. Shorter chirps showed better results at high frequencies and longer chirps at lower frequencies.

The InterAcoustics Eclipse EP25 System ®, which is used in the present study, is equipped with the level specific CE-chirp.

1.5.2 Frequency specific stimuli

In the previous section (1.5), the stimuli for getting broadband information are described. However, frequency specific information is needed. Hearing is not the same in every frequency, and there may be a larger loss in the higher frequencies than in the lower frequencies, for example. There are a number of ways to get this frequency specific information. Frequency specific methods usually focus on four frequencies: 500, 1000, 2000 and 4000 Hz. These are the frequencies that are found in speech and are therefore especially important. The different methods will be discussed below.

Masking

One way to get frequency specific information is to mask the frequencies that will not be assessed. A click is used together with masking of the unwanted frequencies.

Don and Eggermont (1978) made use of high-pass noise to mask the frequencies that are not wanted in the response. The nerves in the hair cells that respond to frequencies below the high pass noise do not contribute to the response in this way. Thus, the response only comes from the unmasked part of the cochlea (Don et al., 1979). They used different cut-off frequencies of the noise.

Van Zanten and Brocaar (1984) used a click stimulus with notched noise to obtain a frequency ABR.

Tone pip

The tone pip or tone burst is a stimulus developed to get a frequency specific ABR. Tone bursts consist of a rise, a plateau, and a fall. This can be seen in figure 1.5.

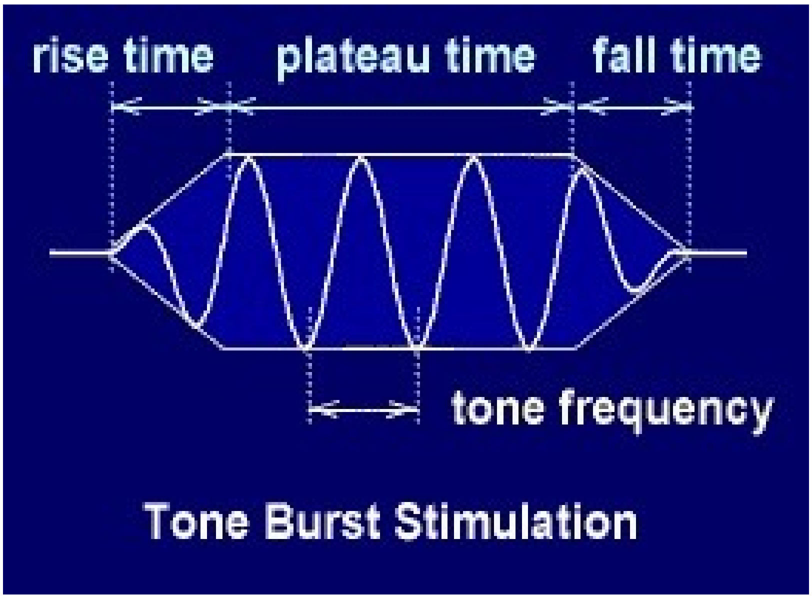


FIGURE 1.5: The composition of a tone pip. Retrieved from http://m.blog.daum.net/inbio880/16091429, July 24, 2017

Tone pip responses are found to correlate well with the pure tone threshold. Dagna et al. (2014) found a high correlation with the pure tone for the 1 kHz tone pip. Gorga et al. (2006) also found the tone pip responses to correlate well with the pure tone threshold.

Kileny (1981) investigated the frequency specificity of the tone pip as compared to clicks masked with white noise. Their results indicated that the reponse is derived from the same place on the basilar membrane, and thus stimulates the same frequency area. Both correlated well with the subjective threshold.

A disadvantage of the tone pip is that the response amplitude is smaller than when stimulating with the click (Cobb and Stuart, 2016; Ferm et al., 2013). This is because a smaller area of the basilar membrane is stimulated. The smaller response results in a longer test time. This is undesirable when testing young children and babies, because they can wake up anytime. The test time should thus be as short as possible.

On top of that, the morphology of the response differs for each frequency, because of the different traveling times per frequency.

Another disadvantage of the tone pip is that it loses its frequency specificity when conducting via bone.

Because of these disadvantages, we will use a different, relatively new stimulus: the narrowband CE-chirp.

Narrowband chirps

Narrowband chirps (NB CE-chirps) are developed around 4 frequencies: 0.5 kHz, 1 kHz, 2 kHz and 4 kHz.

These are developed around the same principle as the broadband chirp: the lower frequencies start before the higher frequency. The response amplitude is larger than that of the tone pips (Ferm et al., 2013; Elberling and Don, 2010; Wegner and Dau, 2002; Cobb and Stuart, 2016). This is because the neural synchrony is higher, just like in the broadband chirp.

The decomposition of the NB chirps from the broadband chirp is shown in figure 1.6.

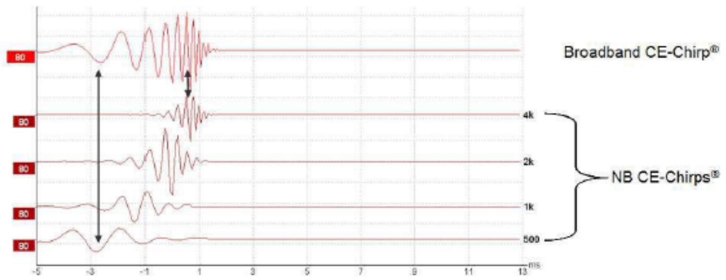


FIGURE 1.6: The decomposition of the BB chirp into the NB chirps.

Little is known about the "real" frequency specificity of the NB-chirps. This could be evaluated by testing patients with a steeply sloping hearing loss. The threshold could for example be 60 dB vs 20 dB on two adjacent test frequencies. The test with the NB-chirp should accurately reflect that loss. There should not be smearing between frequencies. In this study, patients with a ski slope hearing loss will be tested to investigate this.

(Xu et al., 2014) found a good correlation with behavioral thresholds for (different) NB-chirps.

1.5.3 Comparison with ASSR

As seen, the ASSR always assesses four frequencies. There has been a lot of research in the correlation between frequency specific ABR and ASSR.

Michel and Jørgensen (2017) compares the ASSR with tone pip and with CE chirps.

There seems to be more on the ASSR using NB chirps than on ABR. See for example Lee et al. (2015); Stapells (2011); Seidel et al. (2015); Venail et al. (2015). There is also little on the bone conduction thresholds.

The NB-chirp could be useful for bone conduction, as using tone pips is not possible for bone conduction ABR.

1.6 Stimulus parameters

1.6.1 Transducer

For air conduction, headphones or insert earphones are used. The standard headphones are the TDH-39 headphones.

These have their own advantages and disadvantages.

An advantage of the inserts is the small or absent stimulus artefact. Another advantage is the maximum exclusion of ambience sound, because the inserts block the whole ear canal (provided the inserts are inserted correctly) (Clemis et al., 1986).

A disadvantage of the headphones is the stimulus artefact.

Another way of transducing is via bone conduction. A vibrating conductor is placed on the mastoid or the forehead, where the sound is conducted via the bone to the cochlea. A bone conductor that is widely used is the B-71 bone conductor. Recently a new version, the B-81 has been developed. The conductor is held in place with a metal band, in order to exert the same pressure in each participant (about 5 Newton).

1.6.2 Stimulus rate

The Newborn Hearing Screening Program (2014) has suggested stimulus rates for the air and bone conduction. These can be seen in table 1.1 below.

TABLE 1.1: Recommended stimulus rates for AC and BC ABR.

Stimulus	AC rate	BC rate
500 Hz	37.1/s	19.1/s
1000 Hz	39.1/s	19.1/s
2000 Hz	45.1/s	19.1/s
4000 Hz	49.1/s	19.1/s

The stimulus rate for air conduction is about two times higher than recommended for bone conduction. Because of this, the bone conduction test takes more time. Only one ear was tested in the bone conduction condition, to limit the test time.

1.6.3 Stimulus level

The intensity of the stimulus has a number of effects on the response. Firstly, the higher the intensity, the clearer the waveforms can be seen in the response.

Secondly, the latency of the waves gets longer when the intensity gets lower. This follows a certain pattern, called the latency-intensity function (Serpanos et al., 1997; Picton et al., 1977). There are normative data for these functions (Beattie, 1998). Delayed waves could be caused by certain pathologies, such as a vestibular schwannoma. The slope of click evoked ABR also seems to be related to certain types of hearing losses (Gorga et al., 1985).

1.6.4 Stimulus polarity

The stimulus polarity refers to the movement of the transducer membrane when producing the stimulus. The membrane can first move outward and then inward. This causes a high pressure followed by a low pressure. This is called rarefaction polarity. In contrast, the membrane can move inward first and then outward, causing a low air pressure first and then a high pressure. This is called condensation polarity. These two polarities can also be alternated (Hall, 1992).

The NSHP (Newborn Hearing Screening Program, 2014) recommends using alternating stimulus polarity. Alternating the polarities has the advantage of negating the stimulus artefact. However, alternating polarity can smear the response, especially in low frequencies. The cause of this is that the different polarities can result in different latencies of wave V (Klaassen, 2016; De Lima et al., 2008). The trend seems to be that wave V comes earlier with rarefaction stimuli than with condensation stimuli. This effect can be seen clearly in figure 1.7. If these responses would be averaged, wave V would disappear completely.

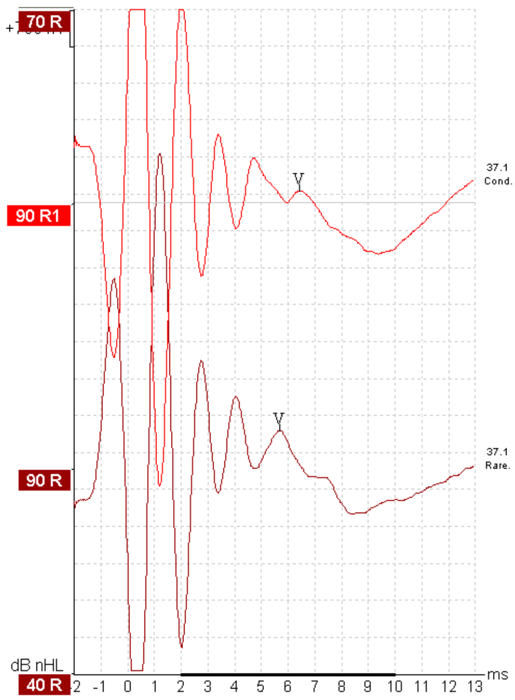


FIGURE 1.7: Responses of a male participant to a 90dB 500 Hz NB-chirp, using a headphone transducer. The upper curve is the response to the condensation chirp, the lower the response to the rarefaction chirp.

The stimulus artefact is large because of the use of headphones. As seen, when using inserts the artefact is smaller. This rises the question if the shift in latency is caused by this artefact or if it is found in the neural response. These effects of polarity in combination with transducer effects will be studied in experiment 1.

1.7 Present study

1.7.1 Aim of the study

The aim of this study is threefold. The first aim is to compare the responses to insert earphones to the responses to headphones. Stimulus artefact would theoretically be significantly reduced when using insert earphones compared to headphones. In headphones, the latency of the waves can be influenced by different stimulus polarity (Klaassen, 2016). It is not known if this is also the case for the insert earphones. Thus, the aim is to compare the insert data to the headphone data.

The second aim is to determine the reliability of the threshold as measured by ABR and ASSR with both air- and bone conduction, compared to the behavioral thresholds.

The third aim of the study is to get more insight in the frequency specificity of the narrowband chirps. This is done by testing people with a steeply sloping hearing loss.

1.7.2 Research questions

The research questions that belong to these aims are the following:

1. Transducer effects
   (a) Do the average wave V latencies differ significantly between transducers in normal hearing participants?
   (b) Do the average wave V latencies differ significantly between polarities in normal hearing participants?
2. Electrophysiological vs. behavioral assessment
   (a) Do the AC thresholds as measured by the ABR, ASSR, and PTA differ significantly from each other?
   (b) Do the BC thresholds as measured by the ABR, ASSR, and PTA differ significantly from each other?
   (c) Do the thresholds as measured by the ABR, ASSR, and PTA correlate significantly with each other?
3. Frequency specificity of the NB CE-chirps
   (a) Does the treshold as measured by the ABR differ significantly from the subjective treshold in patients with a steeply sloping hearing loss?
   (b) Does the threshold as measured by the ASSR differ significantly from the subjective htreshold in patients with a steeply sloping hearing loss?

1.7.3 Clinical Relevance

ABR and ASSR are used in testing children and infants. Improving these methods means that hearing loss can be detected earlier. On top of that, thresholds measured could be more frequency specific.

Electrophysiological responses to both air conduction and bone conduction need to be investigated, as the air-bone gap provides useful information about the type of hearing loss.

Chapter 2

Experiment 1: Transducer effects

2.1 Introduction

First an experiment was carried out to verify the use of insert earphones. Insert earphones consist of a generator box and tubing, on which the earplugs go. The earplugs sit inside the meatus. The sound is generated in the box and then travels through the tube into the ear. This means there is a delay between generating the sound and the participant actually receiving the stimulus. The insert phones are calibrated to deliver the stimulus at the ear at the same time as the headphones would.

Inserts are preferred over headphones, because of the large stimulus artefact headphones can generate. The artefact is especially large at high intensities (Hall, 1992). This artefact can mask wave I in the response (De Lima et al., 2008), which is undesirable. The artefact is smaller when using inserts, because the generator box is further away from the electrodes. Because of this, we will use inserts in the second experiment.

To get rid of the artefact, one can choose for alternating polarity of the stimulus, as seen in the introduction. However, alternating polarity should be used with caution, because the difference between the wave V latency response on rarefaction and condensation can be large. When this is the case, alternating polarity can smear the response or even lead to an invisible response (Fowler et al., 2002; Maurer, 1985; Schwartz et al., 1990). Rarefaction polarity clicks have been used for clinical application, because they lead to a shorter latency and a bigger amplitude of wave V (Hall, 1992; Stockard et al., 1979). However, Fowler et al. (2002) found no diagnostic advantage of one polarity over the other.

In figure 2.1 can be seen how the wave V latency shifts when using different polarities.

Maurer (1985) also found the shorter latencies when using rarefaction polarity. The stimuli they used were tone pips.

Another study (Schwartz et al., 1990) used rarefaction and condensation clicks to investigate the effect of polarity on latency. They found a bigger amplitude of wave V for the rarefaction clicks. On top of that, there was a trend of shorter latencies in wave I and V for rarefaction.

De Lima et al. (2008) found the same effect of polarity on the ABR. Stimulation was a click in insert earphones. The latencies of wave V were shorter in the rarefaction polarity compared to condensation and alternating polarity.

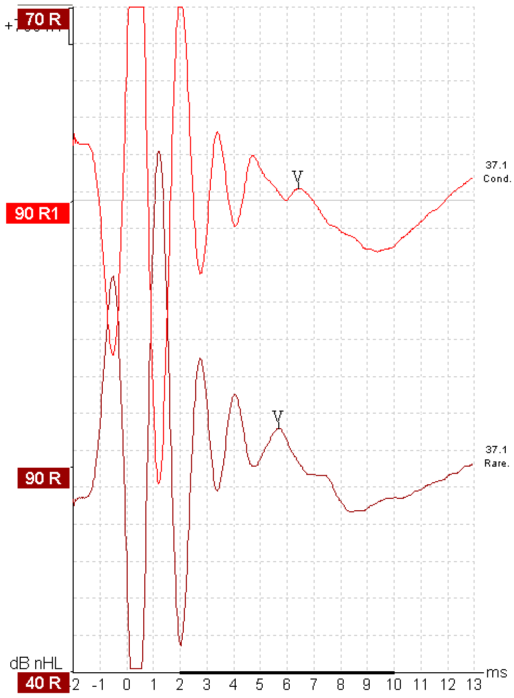


FIGURE 2.1: Responses of a male participant to a 90dB 500 Hz NB-chirp stimulus, presented trough TDH-39 headphones. The upper curve is the response to the condensation chirp, the lower the response to the rarefaction chirp.

Don et al. (1996) used rarefaction and condensation clicks. They found a trend towards shorter latency to rarefaction clicks. The majority of participants had a significant difference between latency to rarefaction and to condensation. They also reported a larger amplitude of wave V to rarefaction. However, there was a great variability between participants.

Like Don et al. (1996), Schwartz et al. (1990) found a shorter latency to rarefaction clicks along with an increased amplitude.

So, some studies have shown that rarefaction leads to shorter wave V latency, but some studies show no difference in polarities.

There are a number of causes for this latency shift.

The first main cause is found in the cochlea. The basilar membrane only stimulates hair cells when the wave goes upward. When stimulated with a rarefaction stimulus, the wave goes first upward and then downward to go upward again. To a condensation stimulus, the wave goes downward first. Because of this, the firing to a condensation stimulus will be a half period later. This also explains why the polarity effect seems more clear in the lower frequencies: the lower the frequency, the bigger the period and thus, the bigger the distance between rarefaction and condensation (Don et al., 1996).

The second cause is greater variablity between participants for the lower frequencies (Don et al., 1996; Schwartz et al., 1990; Fowler et al., 2002).

These earlier studies all used clicks or tone bursts. In the present study, the stimuli presented will be CE-chirps. It is not known whether a polarity effect exists when using the chirp. Only one thesis used chirps. Klaassen

(2016) found a difference in wave V latency for rarefaction and condensation polarity too, when stimulating with headphones: the latency was shorter for the rarefaction chirps.

Moreover, only one study discussed used insert earphones to look into polarity effects. Because of this, we will also investigate the effects of the transducer used.

Considering these findings, a first experiment will be carried out. In this experiment the latencies of wave V will be compared between inserts and headphones, in both the rarefaction and the condensation polarity. The latencies will also be compared between the two polarities.

The research questions are as follows:

1. Do the average wave V latencies differ significantly between inserts and headphones in normal hearing participants?
2. Do the average wave V latencies differ significantly between rarefaction polarity and condensation polarity in normal hearing participants?

The first hypothesis is that there will be no latency difference between the insert earphones and the headphones, for the length of the probe tube is compensating for the travelling time of the acoustic stimulus.

De Lima et al. (2008) used insert earphones and found a shorter wave V latency to rarefaction polarity. Thus, hypothesised is that the inserts will show the same polarity effects.

2.1.1 Method

Materials

The headphones used were the Telephonics TDH-39 headphones. The inserts used were the E-A-RTONE™ 3M insert earphones. The ABR recordings were done with the InterAcoustics Eclipse EP25 System ®.

Participants

Ten healthy, normal hearing participants took part in the experiment. Their mean age was 23, ranging from 21 tot 26 years old. Three were male, seven were female. One ear was tested for each participant. Participants were informed about the procedure prior to testing and all of them signed their informed consent.

Procedure

Patients were instructed to lie down on a comfortable bed. They were encouraged to relax and sleep if possible. The recordings took place in a soundproof room.

All participants received both the headphones and inserts condition, in a random order. Due to limited time, the participants did not receive all of the narrowband chirps. One half got the broadband chirp, the 1000 Hz NB chirp and the 4000 Hz chirp. The other half received the broadband chirp too, the 500 Hz and the 2000 Hz NB chirp. All the stimuli were presented at three different intensities: 40, 70, and 90 dB. The order of the intensities was randomised. Finally, each condition was carried out once with condensation polarity, and once with rarefaction polarity. Only one ear was stimulated, to shorten the test time. The other ear was masked with white noise. The masking was 10 dB when stimulating at 40 dB, 40 dB when stimulating at 70 dB, and 60 dB when stimulating at 90 dB.

Two channel ABR recordings were made using four disposable electrodes, which were placed according to the 10-20 International Electrode system (Jasper, 1958). The ground electrode was placed on the forehead (Fp_z), a non-inverting electrode on the vertex (C_z), and two inverting electrodes on the left and right mastoid (M_1 and M_2). Before applying the electrodes, the skin was cleaned with alcohol containing disinfectant and scrubbed with Nuprep Skin Prep Gel. The electrodes were applied with Ten20 conductive paste and secured with tape. Impedance was below 3 kΩ, and the inter-electrode impedance was below 3 kΩ, too.

Following the Newborn Hearing Screening Protocol (Newborn Hearing Screening Program, 2014), the stimulus rate for the different stimuli was as follows:

TABLE 2.1: Stimulus rates

Stimulus	Rate
500 Hz	37.1/s
1000 Hz	39.1/s
2000 Hz	45.1/s
4000 Hz	49.1/s
Broadband	39.1/s

The band-pass filter of the EEG was between 33 and 3000 Hz. The rejection level was $\pm$ 40 μV. The number of stimuli per polarity and per intensity was at least 2000: 1000 and another 1000 to check reproducibility. Typically for the Eclipse system, Bayesian weighting and "minimize interference" settings were switched on to optimize recording. The response confidence was 99% (Fmp $\geq$ 3.1).

2.1.2 Analysis

Analyses were carried out using IBM SPSS Statistics version 22. The mean latencies of wave V were compared for the headphones and the inserts condition. This was done for each intensity and each frequency. Comparisons were done using a repeated measures ANOVA.

The mean latencies of wave V were also compared between condensation and rarefaction polarity, again for each intensity and frequency.

However, after the comparisons between polarity, the effects were not as expected. This is likely because of individual variations in latency of wave V.

When averaging the latencies between different people, the means of the rarefaction and condensation may not differ anymore, where they did differ in the different participants individually. Because of this, difference scores were calculated. Another repeated measures ANOVA was carried out to assess the difference scores.

There were three difference scores for each condition. The first one was the difference between the two condensation responses. The second one was the difference between the two rarefaction responses. The third one was the difference between the merged condensation response (so, the two condensation responses summed) and the merged rarefaction response.

The difference between the two responses with the same polarity should be low, because the responses reproduce well. The difference between the two merged responses with different polarity could be bigger, especially for the lower frequencies. The difference between rarefaction and condensation should thus differ significantly from the difference within a polarity.

2.2 Results

2.2.1 Transducer

Two repeated measures ANOVAs were carried out. One to assess the absolute latencies and one to assess the difference scores. This results are summarised in table 2.2 below.

TABLE 2.2: Transducer effects. */**/*** means a significant difference between transducers for the respective condition.

Frequency	Intensity	Con	Rar	Sum
500	90	***		
	70			
	40			
1000	90			
	70			*
	40			
2000	90			
	70			
	40			
4000	90			
	70		**	
	40			
BB	90	**		***
	70		***	*
	40	***	***	***

Significance levels: * $p < .05$, ** $p < .01$

There were no significant effects of transducer in terms of the difference scores. Thus, the difference between measurements were the same across transducers.

However, there were some differences in the absolute latencies of the transducers. There seemed to be a trend, where the latencies of the inserts were shorter than those of the headphones. The absolute latency results can be seen in figures 2.2, 2.3 and 2.4.
Full results are listed below. When no significant effect was found, the result for the respective condition was not described.

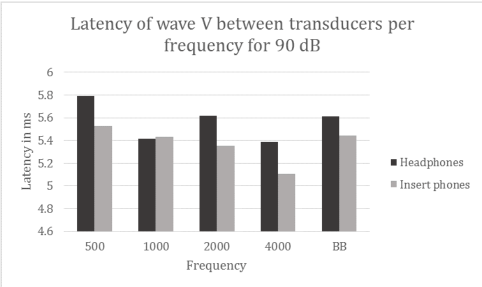


FIGURE 2.2: Latency of wave V compared between transducers, for the 90 dB condition

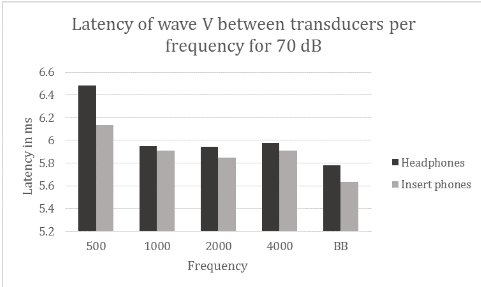


FIGURE 2.3: Latency of wave V compared between transducers, for the 70 dB condition

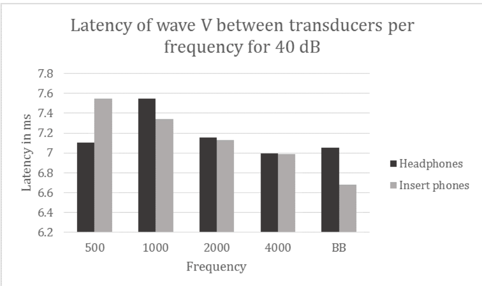


FIGURE 2.4: Latency of wave V compared between transducers, for the 40 dB condition

500 Hz
There was a significant effect of transducer for the 500 Hz, 90 dB, condensation condition, $F(1,3) = 1016.8, p < .001$, partial $\eta^2 = .997$. Wave V came on average earlier when using the inserts ($M = 5.563ms, SD = .187$) than when using the headphones ($M = 6.237$ ms, $SD = .183$).

1000 Hz
The 1000 Hz, 70 dB, condensation and rarefaction averaged condition showed a significant effect of transducer, $F(1,2) = 25.964, p = .036$, partial $\eta^2 = .928$. The latency of wave V was shorter when using insert earphones ($M = 6.021, SD = .275$) than when using headphones, $M = 6.253$ ms, $SD = .230$.

2000 Hz
No significant effects.

4000 Hz
The next effect of transducer was found in the condition 70 dB rarefaction on 4000 Hz. A significant main effect of transducer was found, $F(1,4) = 22.194, p = .009$, partial $\eta^2 = .847$. The wave V latencies of the headphones were on average later ($M = 6.006$ ms, $SD = .083$) than those of the inserts ($M = 5.823$ ms,$SD = .082$).

Broadband
For the broadband condition, there were multiple significant effects of transducer.

For the 90 dB condition with rarefaction and condensation summed, there was a significant main effect of transducer, $F(1,9) = 55.337, p < .001$, partial $\eta^2 = .860$. The insert phones delivered a significant shorter latency ($M = 5.444$ ms, $SD = .082$) than the headphones ($M = 5.611$ ms, $SD = .078$).

The 90 dB condition was also significant for the condensation condition. There was a significant main effect of transducer, $F(1,9) = 15.274, p = .004$, partial $\eta^2 = .629$. There was a main effect of condition too, $F(2,9) = 8.737, p = .002$, partial $\eta^2 = .493$. Post-hoc pairwise comparisons showed that the wave V latencies were on average earlier with the inserts ($M = 5.471$ ms, $SD = .093$) compared to the headphones ($M = 5.687$ ms, $SD = .082$). Post-hoc pairwise comparisons showed that the first condensation measure ($M = 5.555$ ms, $SD = .080$) differed significantly from the second $M = 5.607$ ms, $SD = .085, p = .026$.

The next effects were found for 70 dB rarefaction. The assumption of sphericity was violated for condition ($W = .167, p = .001$) and for transducer*condition ($W = .003, p < .001$). $\varepsilon < .75$, therefore a Greenhouse-Geisser adjustment was used.

There was a significant main effect of transducer, $F(1,9) = 27.937, p = .001$, partial $\eta^2 = .756$. The interaction effect of transducer*condition was significant too, $F(1.002, 9.015) = 6.055, p = .036$, partial $\eta^2 = .402$. The wave V latencies were on average earlier when using the inserts ($M = 5.580$ ms, $SD = .091$) compared to the headphones ($M = 5.786$ ms, $SD = .093$).

All the 40 dB conditions (rarefaction, condensation, condensation + rarefaction) showed significant effects of transducer.

Condensation plus rarefaction: There was a significant effect of transducer, $F(1,8) = 28.962, p = .001$, partial $\eta^2 .784$. The insert earphones resulted in a shorter latency of wave V ($M = 6.655$ ms, $SD = .130$) compared to the latency when stimulating with headphones ($M = 6.986$ ms, $SD = .158$).

Condensation: A significant main effect of transducer was found, $F(1,8) = 29.135, p = .001$, partial $\eta^2 = .785$. The latency of wave V was longer for the headphones ($M = 6.986$ ms, $SD = .151$) than for the inserts ($M = 6.680$ ms, $SD = .132$).

Rarefaction: There was a significant main effect of transducer, $F(1,9) = 26.189, p = .001$, partial $\eta^2 = .744$. The mean latency of wave V when stimulating with the inserts was 6.695 ms ($SD = .131$), which was .331 ms shorter than when using the headphones ($M = 7.025$ ms, $SD = .153$).

2.2.2 Polarity

A repeated measures ANOVA was carried out to assess the difference scores in terms of polarity. The results are shown in figures 2.5a to 2.5f and described below.

500 Hz
There was a significant effect of condition for the 90 Hz intensity, $F(2,4) = 56.338$, $p = .001$, partial $\eta^2 = .966$. Pairwise comparisons with Bonferroni correction showed the following. The difference in latency between condensation and rarefaction was significantly higher ($M = .583$ ms, $SD = .025$,$p = .042$) than the difference between the two condensation measures, $M = .133$ ms, $SD = .033$. The con-rar difference was also higher than the difference between the two rarefaction responses, $M = .073$ ms, $SD = .033$, $p = .007$.

No significant effect of transducer was found, which means that the effect of polarity was the same between transducers.

A significant effect of condition was found for the 70 Hz intensity too, $F(2,4) = 62.574$, $p = .001$, partial $\eta^2 = .969$.

Pairwise comparisons showed a significant difference between the con-rar and the con-con condition, $p = .052$. There was a significant difference between the con-rar and the rar-rar condition, too, $p = .040$.

There was only one valid case for the 40 Hz intensity. It was therefore not included in the analysis.

1000 Hz
No significant effects.

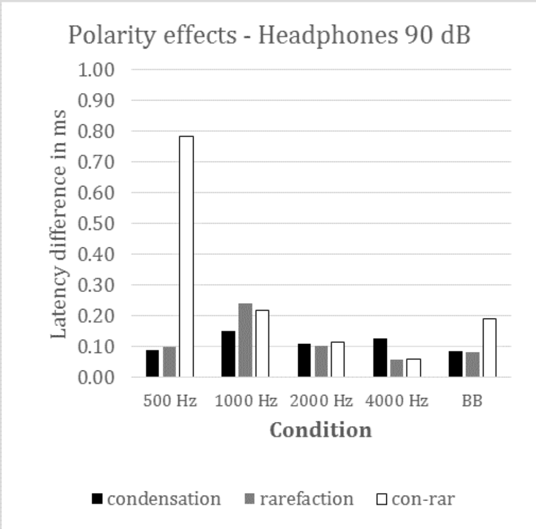
2000 Hz
There was a significant effect of condition for the 40 Hz intensity, $F(2,8) = 20.834$, $p = .00$, partial $\eta^2 = .839$.

The mean difference between condensation and rarefaction was .238 ms ($SD = .010$) , which was significantly higher than the mean difference between the two rarefaction responses ($M = .090$ ms, $SD = .016$, $p = .006$).

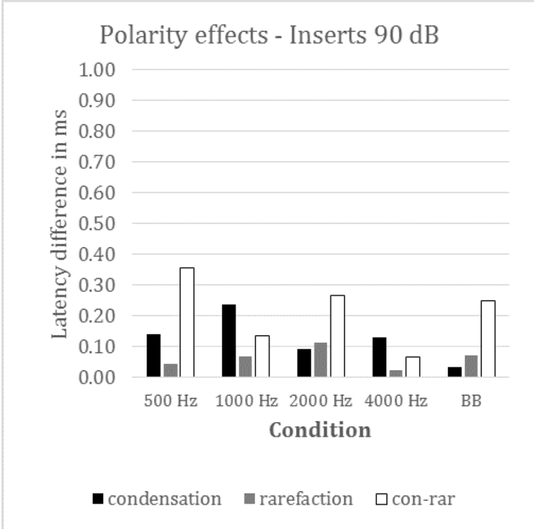
4000 Hz
No significant effects.

Broadband
The 90 dB intensity showed the following effects.

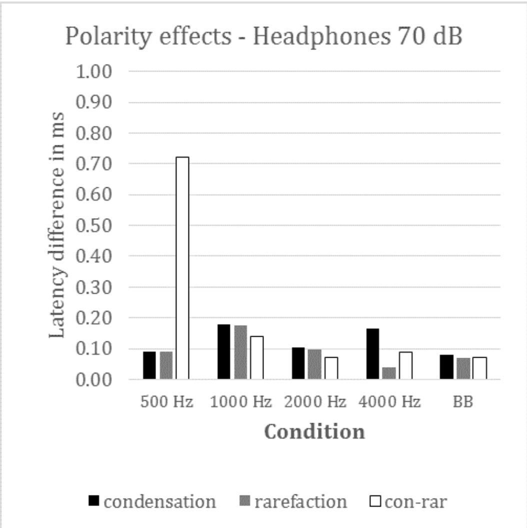
The assumption of sphericity was violated, $W = .394$, $p = .024$. Because $\varepsilon < .75$, a Greenhouse-Geisser adjustment was used for the degrees of freedom.



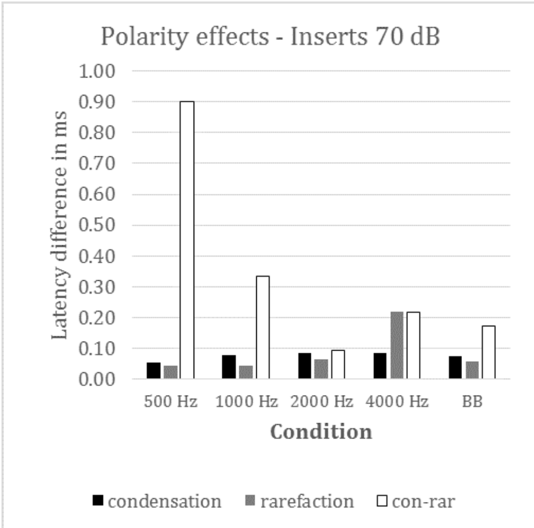
(A) Polarity effects for the 90 dB headphones condition.



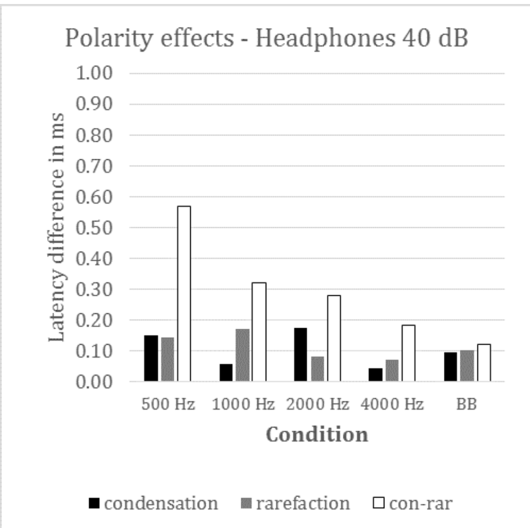
(B) Polarity effects for the 90 dB inserts condition.



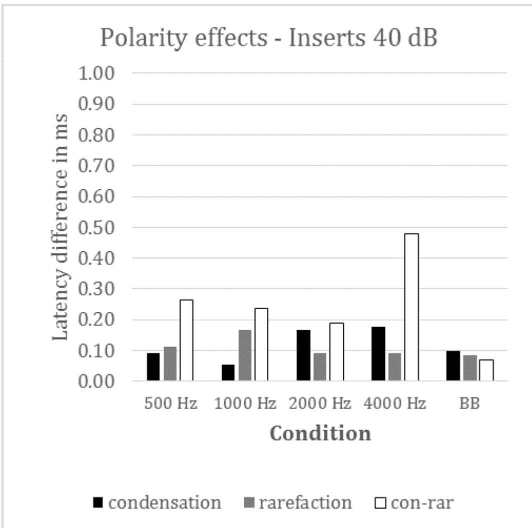
(C) Polarity effects for the 70 dB headphones condition.



(D) Polarity effects for the 70 dB inserts condition.



(E) Polarity effects for the 40 dB headphones condition.



(F) Polarity effects for the 40 dB inserts condition.

FIGURE 2.5: Polarity effects.

There was a significant effect of condition, $F(1.245, 11.207) = 12.992$, $p = .003$, partial $\eta^2 = .591$.

Pairwise comparisons with Bonferroni correction showed that the difference between rar and con was significantly larger ($M = .222$ ms, $SD = .040$) than the differences between con ($M = .062$ ms, $SD = .011$, $p = .017$) and between rars ($M = .081$, $SD = .017$, $p = .008$)

2.3 Discussion

It was hypothesised that no differences would be found between the inserts and headphones. However, we found some significant differences. Those differences did not seem to be limited to a certain condition. What we did see, was the difference going in only one direction. The latency of wave V was consistently shorter to stimuli delivered with the insert earphones.

The system has to compensate for the travelling time of the acoustic stimulus through the insert tubes. So, the shorter wave V latency to the inserts could be caused by wrong calibration of the insert earphones.

However, when looking at the difference in latency scores across transducers, no significant effect was found. This means both transducers vary in the same way in latency. This is desirable, because

The second hypothesis was that there would be an effect of polarity, especially in the lower frequencies (500 and 1000 Hz). If this effect is caused by the artefact generated by the headphones, it should only be seen in the headphones and not in the insert condition. However, the 4000 Hz inserts condition showed a significant effect of polarity on 90 dB. This could mean that the polarity shift is not caused by the headphone artefact. The expectation was that the polarity effect can be seen in the lower frequencies, because a shift of one period for 4000 Hz means a shift of only 1/4000 s, which is .25 ms.

There are some limitations to be noted. Each narrowband chirp has only five data points or less. For the 500 Hz condition, there were especially a lot of missing values. Because of this, not all findings are reliable.

The aim of this experiment was to verify the use of insert earphones, in terms of delivering the same wave V latencies as the headphones. We want to use the insert earphones in the second experiment, because of the advantages over the headphones.

A big advantage of using the inserts is the smaller or absent stimulus artefact due to the sound generator being far away from the electrodes. Because of the small artefact, the responses to the lower frequencies were easier to interpret.

If the polarity effect would be caused by the artefact, it should not be seen when using the inserts. However, there is also a polarity effect found to the insert earphones. This means the polarity effect has more likely a neural cause, rather than the shift being caused by the large artefact, because in the latter case the shift should not be seen when using insert earphones.

Another advantage is the blocking of ambient noise (Clemis et al., 1986).

A disadvantage of the insert is that they are hard to put in correctly. On top of that, infants/small children is even harder. Moreover, earwax can block the inserts, causing a higher threshold than is the actual case. In adults, inserts can be taken out and put in again when a blockage is suspected. In infants however, one has to be careful not to wake them up, because test time is precious and they may not fall asleep again.

The insert phones will be used in the second experiment, for the smaller or absent artefact makes interpretation of the waveforms easier. The shorter latency times and the 500 Hz latency shift should be kept in mind, however.

Alternating polarity should not be used, because of the reported shift in latency to different polarities. When averaging the shifted waves, the response could become unclear.

2.4 Conclusion

Participants showed a shorter wave V latency to stimuli delivered with insert earphones, compared to headphones. Only a few differences were significant. This difference could be caused by insufficient compensation of the Eclipse system for the travelling time of the acoustic stimulus. Because the latency difference scores did not differ significantly across transducers, this does not seem to be a large problem.

As expected, a polarity effect was found for low frequencies to the headphones. The same effect was found for the insert phones. This means the polarity effect is not just caused by the stimulus artefact of the headphones, but has a neural origin.

A big advantage of the insert phones is the absence of a stimulus artfact. Because of this, the responses are more clear, especially in the lower frequencies and higher intensities.

Chapter 3

Experiment 2: Electrophysiological and behavioral thresholds

3.1 Introduction

To investigate the correlation and differences between the objective and subjective thresholds, a second experiment was carried out.

The correlation between ABR and ASSR responses and subjective thresholds has been well established (Lee et al., 2015; Stapells, 2011; Seidel et al., 2015; Venail et al., 2015; Xu et al., 2014).

However, there is little information on ASSR using the CE-chirp. As for bone conduction results, no consequent results are found.

Both infants and adults will be investigated in this experiment. The adults will be normal hearing participants, as control group. The infants all had hearing loss, with different severity. It is interesting to see if the results differ for the infants because of the hearing loss. Secondly, the objective methods are primarily used in infants who probably have some degree of hearing loss. Because of this, the correlations should be good for this group.

3.2 Method

3.2.1 Participants

There were two groups of participants. The first group consisted of children with hearing loss. These children were patients whose data was collected for hearing screening. This data was already available, with permission to use this data. This experiment was carried out to add more data: the second group of participants consisted of normal hearing adults.

The first group consisted of 45 infants (90 ears). The second group consisted of 29 adults (42 ears).

3.2.2 Materials

The pure tone audiometer used was the InterAcoustics AD629. The air conduction thresholds were obtained using the TDH-39 supra-aural headphones. The bone conductor used was the RadioEar B-81, with a metal headband delivering 5.4 Newtons of force. For masking during bone conduction, the TDH-39 was used.

The ABR and ASSR recordings were done with the InterAcoustics Eclipse EP25 System®. The insert earphones used for the air conduction and for masking for the bone conduction, were the E-A-RTONE™ 3M insert earphones. The bone conductor used was the RadioEar B-81, with a metal headband delivering 5.4 Newtons of force to the skull.

3.2.3 Procedure

The participants received only the bone conduction or only the air conduction condition for ABR/ASSR recordings, to keep the test time limited. Both ears were tested if possible.

Pure tone audiometry

First, all participants underwent pure tone audiometry (PTA). This had two reasons. Firstly, to verify if the normal hearing group had normal hearing. Secondly, to obtain an audiogram to compare the ABR and the ASSR thresholds to. Their thresholds were obtained for four frequencies: 500, 1000, 2000 and 4000 Hz. The pure tone subjective thresholds were obtained according to the guidelines of the American Speech-Language-Hearing Association (2005).

For the air conduction threshold, the two steps up/one step down paradigm was used, starting at 50 dB. The order of the frequencies tested was: 1000, 2000, 4000, 1000 again and finally 500 Hz.

For the participants tested with bone conduction, the air conduction thresholds were measured first according to the above paradigm.

Then the bone conduction threshold was determined. The bone conductor was placed on the mastoid at the side of the worst ear. The contralateral ear was masked with narrowband noise, 20 dB above the air conduction threshold. The masking was done with the TDH-39 headphones.

The procedure of determining the threshold was the same as for the air conduction.

ABR and ASSR

Objective thresholds were obtained using two methods: The ASSR and the ABR. The order in which the participants received these methods was randomised between participants. The objective thresholds were obtained over the four same frequencies as the PTA: 500, 1000, 2000 and 4000 Hz. In ASSR, these four frequencies are presented simultaneously. For the ABR, the order of the four NB CE-chirps was randomised.

Air conduction

Participants got insert earphones in both ears. The non-test ear was masked with white noise, 30 dB HL below the test intensity. Both ears were tested.

The ABR preparation and parameter settings were the same as in the first experiment. For this procedure, see section 2.1.1.

The starting intensity in the ASSR was 50 dB for every frequency. When the stimulus was detected, 10 dB down until threshold was reached. If the threshold was not found, 5 dB up again. Threshold was determined as the lowest intensity that could still be heard.

The starting intensity for the ABR was 70 dB. On 70 dB, both a condensation stimulus and a rarefaction stimulus were presented. Whichever delivered the clearest response, was used to go further to threshold. From 70 dB the intensity went down to 50 dB and then to 30 dB. If 30 dB still gave a clear response, then 10 dB. In this way, the threshold was found the fastest.

When one ear was stimulated, the non-test ear was masked with white noise. The intensity of the masking was -30 dB, e.g. when stimulating at 70 dB, the other ear was masked with 40 dB white noise.

Bone conduction
The bone conductor was placed on the same mastoid as in the PTA. An insert earphone was put in the non-test ear, for masking. In the bone conduction condition, only one ear was tested. This was because of limited time and the uncomfortable bone conductor.

The ABR preparation and parameter settings were the same as in the first experiment. For this procedure, see section 2.1.1.

The starting intensity for the ASSR was 30 dB, as stiimulus artefact was too large at higher intensities. The non-test ear was masked with 50 dB white noise.

The starting intensity for the ABR was 30 or 40 dB, depending on the frequency. 4000 and 500 Hz started on 30dB, 1000 and 2000 at 40 dB. This was because of the artefact. At least 1000 responses were obtained. The non-test ear was masked with white noise, 10 dB above the test intensity. When the test intensity was 20 dB for example, the non-test ear was masked with 30 dB.

3.2.4 Analysis

The mean threshold difference was calculated for each frequency. This mean threshold was calculated for the PTA-ABR, ABR-ASSR, and PTA-ASSR. The analyses were done over these difference scores. Both correlations and ANOVAs were carried out to compare the thresholds. IBM SPSS Statistics version 22 was used for the analyses.

3.3 Results

3.3.1 Correlations

Correlations with pearsons R were carried out on the raw threshold scores. Below, the results are summarised in table 3.1.

TABLE 3.1: Air conduction correlation coefficients.

Group	Frequency	PTA-ABR	N	PTA-ASSR	N	ABR-ASSR	N
Normal hearing adults	500	.143	23	-.177	24	-.168	21
	1000	-.167	26	.065	24	.096	24
	2000	.529**	26	.435*	24	.328	24
	4000	.481*	26	.347	24	.460*	24
Infants	500	n/a	0	n/a	0	.965***	10
	1000	n/a	0	n/a	0	.940***	35
	2000	n/a	0	n/a	0	.955***	72
	4000	n/a	0	n/a	0	.945***	42
Groups together	500	n/a	0	n/a	0	.797***	31
	1000	n/a	0	n/a	0	.919***	59
	2000	n/a	0	n/a	0	.951***	96
	4000	n/a	0	n/a	0	.944***	66

Significance levels: * $p < .05$, ** $p < .01$, *** $p < .001$

Air conduction

Firstly, both participant groups were put together. Correlations were calculated between the PTA, the ABR, and the ASSR threshold. This was done for each test frequency.

The 500 Hz condition showed a significant positive correlation between the ABR thresholds and the ASSR thresholds, $r = .797$, $p < .001$. There was no significant correlation between the PTA and ASSR or PTA and ABR.

For the 1000 Hz condition, a significant positive correlation was found between the ASSR and the ABR thresholds, $r = .919$, $p < .001$. There were no significant correlations between the PTA and ABR or ASSR.

There was a significant positive correlation between the PTA and ASSR for the 2000 Hz condition, $r = .435$, $p = .034$. This was also the case for the PTA and the ABR, $r = .529$, $p = .005$. Finally, the ABR and ASSR had a positive correlation, too ($r = .955$, $p < .001$).

Finally, the 4000 Hz condition showed the following. There was a significant correlation between the PTA and the ABR,$r = .481$, $p = .013$. This was not the case for the PTA and ASSR ($r = .347$, $p = .096$). However, the ABR and ASSR thresholds did show a significant correlation, $r = .945$, $p < .001$.

Next, the same was done for separate groups. First, the results of the adult group will be discussed. Because there are no PTA data of the infant group, the results for PTA-ABR and PTA-ASSR are the same. Because of this, only the ABR-ASSR correlation will be noted here.

There was no significant correlation between the ABR and the ASSR thresholds for 500, 1000, and 2000 Hz. The 4000 Hz condition showed a significant positive correlation between the ABR and the ASSR, $r = .460$, $p = .024$.

Correlations were also calculated for only the infant group. Here, only the correlations between the ABR and the ASSR were carried out, as there were no PTA data. This showed the following.

For the 500 Hz condition, a significant correlation was found between the ABR and the ASSR, $r = .965$, $p < .001$.

For the 1000 Hz condition, a significant correlation was found between the ABR and the ASSR,$r = .940$, $p < .001$.

For the 2000 Hz condition, a significant correlation was found between the ABR and the ASSR, $r = .955$, $p < .001$.

Finally, the 4000 Hz condition showed a significant correlation between the ABR and the ASSR too, $r = .945$, $p < .001$.

The correlations between the ABR and ASSR are also shown in graphs 3.1 to 3.4 below.

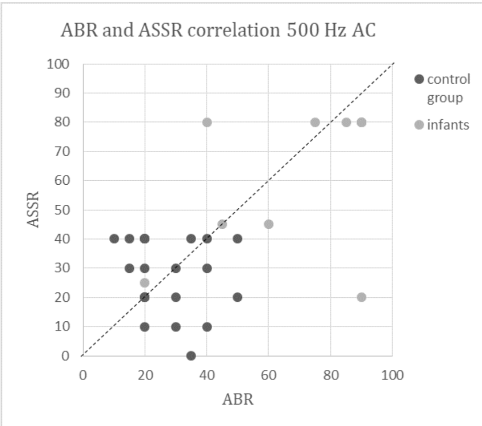


FIGURE 3.1: ABR and ASSR correlations, 500 Hz condition

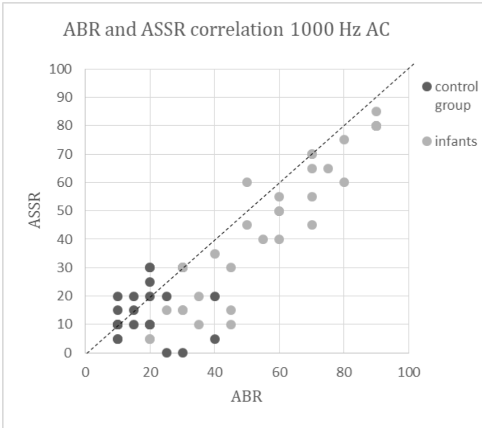


FIGURE 3.2: ABR and ASSR correlations, 1000 Hz condition

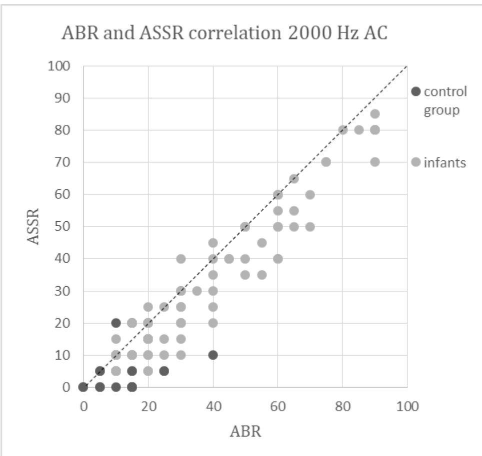


FIGURE 3.3: ABR and ASSR correlations, 2000 Hz condition

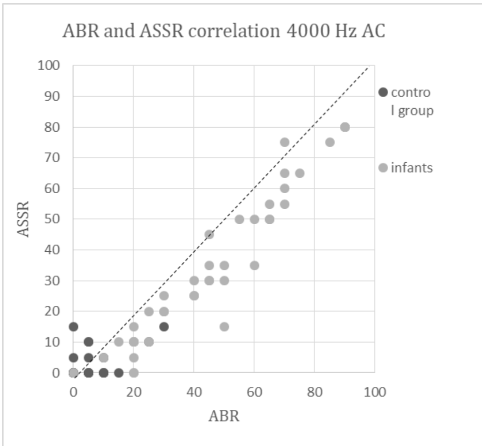


FIGURE 3.4: ABR and ASSR correlations, 4000 Hz condition

Bone conduction

Correlations were also carried out for the bone conduction thresholds. There were only three frequencies, because the ASSR does not record the 500 Hz. Only the control group had enough cases. This showed the following.

For the 1000 Hz condition, a significant correlation was found between the PTA and the ABR threshold, $r = .659$, $p = .020$.

The 2000 Hz condition showed a significant correlation between the PTA and ABR, $r = .515$, $p = .050$.

No correlation was found for the 4000 Hz condition.

The correlation coefficients are summarised in table 3.2 below.

TABLE 3.2: Bone conduction correlation coefficients. The only group here is the normal hearing adult group, as there were no valid cases for the infant group.

	PTA-ABR	N	PTA-ASSR	N	ABR-ASSR	N
500 Hz	.667*	13	n/a	0	n/a	0
1000 Hz	.554*	16	-.136	14	-.184	15
2000 Hz	.539*	16	.556*	15	.070	15
4000 hz	.378	15	.253	15	.559*	14

Significance levels: * $p < .05$, ** $p < .01$

3.3.2 ANOVAs

Repeated measures ANOVAs and one way ANOVAs were carried out to assess the difference scores. First, the repeated measures ANOVA was done to compare the difference scores PTA-ASSR and PTA-ABR (AC and BC). This was done over all frequencies to assess any difference between frequencies. After that, the frequencies were assessed on their own, to investigate if there were any differences between the difference scores.

A significant effect of frequency was found, $F(3, 60) = 15.867$, $p < .001$, partial $\eta^2 = .442$. This means that the differences in thresholds varied along with the frequencies.

Pairwise comparisons showed that only the 500 Hz threshold difference differed significantly from all other frequencies. The mean difference scores and their SD's can be seen in table 3.3. Both ASSR and ABR were on average 18 dB above PTA threshold at 500 Hz test frequency.

TABLE 3.3: Descriptive statistics air conduction: adults

Difference	Frequency in Hz	Mean in dB HL	SD in dB HL	N
PTA vs ABR	500	-18.6	12.0	21
	1000	-12.9	10.9	21
	2000	-10.0	7.4	21
	4000	-7.9	7.7	21
PTA vs ASSR	500	-18.1	14.6	21
	1000	-9.5	9.6	21
	2000	-3.3	7.1	21
	4000	-5.7	6.9	21

A repeated measures ANOVA was carried out to test if the difference between the PTA and the ABR differed from the difference between the PTA and the ASSR AC threshold.

The ABR threshold was on average 18.6 dB higher than the PTA threshold for the 500 Hz frequency. The ASSR threshold was on average 18.1 dB higher than the PTA. These differences did not differ significantly, $p = .908$.

A significant difference was found between the ABR and the ASSR for the 1000 Hz condition. The ABR threshold was on average 13.8 dB ($SD = 10.6$ dB) higher than the PTA, whereas the ASSR was only 9 dB higher ($SD = 9.6$ dB). This difference was not significant, $p = .065$.

For the 2000 Hz condition, the ASSR threshold differed on average 2.9 dB ($SD = 6.9$ dB) from the PTA threshold. This was a significant difference with the ABR difference ($M = -10.6$ dB, $SD = 7.3$ dB), $F(1, 23) = 16.829$, $p < .001$, partial $\eta^2 = .423$.

For the 4000 Hz condition, the ABR threshold was on average 8.5 dB ($SD = 7.7$) higher than the PTA threshold. The ASSR threshold was only 5.8 dB higher than the PTA threshold ($SD = 6.5$). The difference between ABR and ASSR was not significant, $p = .085$.

Second, the same was done for the bone conduction. There was no significant effect of frequency, $p = .369$. The descriptive statistics are summarised in table 3.4. There was also no significant effect of the testtype, $p = .635$.

TABLE 3.4: Descriptive statistics bone conduction (adults)

Difference	Frequency	Mean	SD	N
PTA-ABR	1000	0.4	9.0	13
	2000	-1.9	5.9	13
	4000	-5.0	7.6	13
PTA-ASSR	1000	-1.9	11.5	13
	2000	-4.2	7.8	13
	4000	-3.5	9.9	13
ABR-ASSR	1000	-2.7	12.0	15
	2000	-3.0	10.3	15
	4000	1.4	6.9	14

Finally, a repeated measures ANOVA was carried out to assess difference between the two groups of subjects. After that the group effects were assessed with one way ANOVAS per frequency. The descriptives are shown in table 3.5. The difference between ABR and ASSR thresholds was calculated as ABR threshold - ASSR threshold.

This showed a significant effect of group, $F(1, 27) = 9.211$, $p = .005$, partial $\eta^2 = .254$. The difference between the ABR and ASSR thresholds was on average 8.5 dB larger ($SD = 2.4$) for the children than for the control group ($M = 3.2$, $SD = 1.5$).

This RM ANOVA showed some interaction effects of group * frequency too, but there were many missing values. Thus, to assess the differences between frequencies, separate (between subjects) ANOVAs were carried out for each frequency.

For the 500 Hz condition, the assumption of equality of error variances was violated, $p = .023$.

TABLE 3.5: Descriptive statistics air conduction: ABR and ASSR. The mean is the mean difference in ABR versus ASSR thresholds.

Frequency	Group	Mean in dB HL	SD	N
500	Adults	0.5	18.6	21
	Children	7.0	6.7	10
1000	Adults	4.8	12.1	24
	Children	11.3	9.0	35
2000	Adults	7.7	9.2	24
	Children	6.5	7.2	72
4000	Adults	2.7	7.4	24
	Children	11.2	6.9	42

The difference between ABR and ASSR was .5 dB on average for the normal hearing group ($SD = 18.6$) and 7 dB ($SD = 6.7$) for the children. There was no significant effect of group, $p = .294$.

The 1000 Hz condition showed a significant effect of group, $F(1, 57) = 5.573$, $p = .022$, partial $\eta^2 = .089$.

The difference between the ABR and ASSR threshold was on average higher for the children ($M = 11.3$, $SD = 9.0$) than for the normal hearing adults $M = 4.8$, $SD = 12.1$). The positive difference scores mean that the ASSR threshold was on average lower than the ABR threshold.

The 2000 Hz condition showed no significant difference between groups,$p = .517$.

There was a significant difference between groups for the 4000 Hz condition, $F(1, 64) = 22.049$, $p < .001$, partial $\eta^2 = .256$.

The difference between ABR and ASSR threshold was higher on average for the children $(M = 11.2, SD = 6.9)$ than for the normal hearing adults $(M = 2.7, SD = 7.4)$

3.4 Discussion

Air conduction and bone conduction thresholds were compared between one subjective and two objective methods. Results were obtained for frequency, group, and test method.

The air conduction threshold showed some interesting frequency effects. The difference between the PTA and ABR thresholds and the PTA and ASSR thresholds was on average far larger for the 500 Hz condition than for the other frequencies. The ABR and BERA threshold did correlate well on the 500 Hz. In experiment 1, we already noticed a very flat ABR for the 40 dB 500 Hz, where the subject was normal hearing. There were no frequency effects for the BC condition, however. This could be due to the smaller number of participants.

A striking result was that the difference between ABR and ASSR thresholds was larger for the children on every frequency. Specifically, the ASSR threshold was lower than the ABR threshold. For there were no PTA data for the infants, it is not known whether the ASSR or the ABR would resemble the subjective audiogram more closely. For the adults, the difference between the ABR and ASSR was smaller. However, the ASSR was on average also lower than the ABR. The correlation between the ASSR and ABR was good. Moreover, the ASSR threshold was on average closer to the subjective threshold.

So, the thresholds of the ASSR were lower in both groups, with the ASSR being closer to subjective threshold in the adults. This could mean the ASSR is a better indicator of true threshold in infants too.

An explanation for this difference between adults and infants can be found in the procedure. The ABR is very sensitive to noise. Infants do not always lie still and sleep and this could influence the ABR thresholds. The small responses close to threshold could be snowed under noise. Because the test time is shorter for the ASSR,this is less of a problem there. Besides, headphones were used, which means that waves are not always clearly visible either, because of the stimulus artifact.

TABLE 3.6: Correction factors air conduction (N=24)

Test	Frequency	Correction factor in dB HL
ABR	500	18.6
	1000	12.9
	2000	10.0
	4000	7.9
ASSR	500	18.1
	1000	9.5
	2000	3.3
	4000	5.7

The findings in different tresholds can be translated to correction factors for the thresholds, as seen in table 3.6 above. The correction factors represent the number of dB's that should be subtracted from the objective threshold, to get the subjective threshold. These are based on the adult data (N=24).

It should be noted that the standard deviation was quite high. Thus, there may be some variability in these correction factors. The high standard deviation is also the reason that there are no correction factors for the bone conduction.

The lower thresholds of the ASSR could be due to the subjective interpretation of the ABR. Maybe there is still a wave V, but the interpretor is not sure if it is there or not and does not mark it as a threshold. On the contrary, the ASSR, which works on statistics, will detect the chance that there is a response present between the noise.

One remarkable effect seen between AC and BC is the following: The differences between objective threshold and subjective threshold in BC were larger for the higher frequencies, whereas the differences for the AC were larger for the lower frequencies.

Another reversed result for the BC was found between the ABR and ASSR thresholds. As seen, the ASSR-AC thresholds were on average lower than the ABR-AC thresholds. However, the ASSR-BC thresholds were on average higher than the ABR thresholds.

This could have something to do with the component of vibrating the bone. Lower frequencies could spread more easily because of the longer waves, higher frequency waves may fade away more easily when traveling through the skull. The waves have to travel through the skull because the bone conductor was placed on the opposite side of the test-ear to minimize stimulus artifact. The resonance of the bone is different per person.

The BC ASSR thresholds being higher could be caused by the test procedure. The bone conductor is not very comfortable, and when wearing it most participants could not sleep. Moreover, the ASSR stimuli are less comfortable to listen to than the ABR stimuli. This could cause more noise, which causes a higher threshold.

The large differences seen in the 500 Hz frequency have been established in literature.

One cause which is discussed in chapter 2 is the polarity effect. This polarity effect is largest in the low frequencies. This makes interpretation of the waveforms difficult (De Lima et al., 2008). Wilson et al. (2016) investigated the 500 Hz using ASSR. Their finding was also that the lower frequencies are harder to reliably record using ASSR.

On top of that, there is greater variability between participants for the lower frequencies, which makes interpretation harder too (Don et al., 1996; Schwartz et al., 1990; Fowler et al., 2002).

Rodrigues and Lewis (2014) found a difference between adults and neonates with CE-chirp ASSR. Our findings replicate theirs: the thresholds were higher in the lower frequencies. This could be due to less neural synchronization at 500 Hz.

3.4.1 Frequency specificity of the NB-chirp

A small pilot study was carried out with participants with a ski slope hearing loss. This showed a number of interesting findings. Firstly, the slope was smaller in the objective methods than the subjective slope. The ASSR thresholds were closer to the subjective threshold than the ABR was. This is in line with the results above. Moreover, the 500 Hz threshold was much larger than subjective. This is also in line with the main experiment. For the second participant, the slope as indicated by the ABR even goes the other way around.

NB-chirps do not contain only their frequency (.5k, 1k, 2k, 4k Hz), because their design is based around the idea that lower frequencies start before higher frequencies. This can also be seen in the waveforms, see figure 1.6. Still, they correlate well with thresholds of their respective frequencies (Michel and Jørgensen, 2017).

If the NB-chirps would not be frequency specific enough, the expectation would be that the high end of the slope would be lower when using the chirp. For example, the 1000 Hz threshold of participant 2 could be closer to the 500 Hz threshold. Because, when the 1000 Hz chirp also contains some lower (or higher) frequencies, it may be that the 1000 Hz chirp also stimulates some hair cells belonging to 500 Hz. This could especially be the case when the

1000 Hz nerves are more damaged than the ones that react at 500 Hz. The 1000 Hz threshold would then be closer to the 500 Hz threshold.

This effect could be seen in the ASSR of participant 1, because the threshold at 2000 Hz is lower than the subjective threshold. However, the threshold of the 4000 Hz is much higher than the subjective threshold. This means that the slope is not accurately found.

Participant 2 shows the opposite. The 500 Hz threshold is closer to the 1000 Hz threshold. This could be due to the difficulty of interpretation of the 500 Hz wave, however. The ASSR threshold is closer to the true 500 Hz threshold than the ABR, namely. The 500 Hz condition is known to be less reliable, however (Frank et al., 2017).

So, the expected effect was not found. The frequency specifity may be alright, according to these results and the results of the second experiment. However, the slope using the objective methods did not match the subjective slope.

Objective methods do not (yet) seem to represent a ski slope hearing loss well, but only based on these two cases. This needs to be investigated with more participants with a ski slope loss. This finding does not mean that the NB-chirps are not frequency specific enough, however. The results in normal hearing adults and infants with hearing loss showed a good correlation between ASSR, ABR, and pure tone thresholds.

3.4.2 Clinical implications

ASSR seems to predict the true (subjective) threshold better than the ABR. Besides, the ASSR takes less test time. However, this finding is only for the adults. The ASSR thresholds in the infants were lower, as was the case for the adult group. But since there are no subjective data, it cannot be compared to the true threshold.

Even if ASSR seems to give a better prediction of the true threshold, ABR needs to be used to interpret the waveforms. When using ABR to determine tresholds, the correction factors should be used and improved with more data.

These findings only hold for air conduction. The bone conduction results did not replicate and there were too few data points. Clinical use of bone conduction has the limitation of a large stimulus artifact when stimulating at levels >40 dB HL. For some participants, even 35 dB resulted in too large an artefact. This makes clinical use, where hearing loss may be much higher, difficult (Jeng et al., 2004).

3.5 Conclusion

The AC thresholds as measured by the ABR, ASSR, and PTA differed from each other. The difference was larger for the lower frequencies (500 and 1000 Hz) than for the higher frequencies (2000 and 4000 Hz). A correction factor may be needed for the ABR, for the thresholds are consistently larger than for the ASSR. This is only the case for the children and only for the AC condition.

The suggested correction factors are listed above in table 3.6.

The (AC) ASSR thresholds are closer to the PTA thresholds in adults than the ABR thresholds are. This suggests that the ASSR is a better predictor for the true (subjective) threshold than ABR. On top of that, the ASSR thresholds were consistently lower than the ABR treshold, for the infants too. This may indicate that the ASSR is also a better predictor in infants. However, even if ASSR is a better threshold predictor, ABR still needs to be used. The interpreting of the waves and the latencies can only be done when looking at the ABR.

There were not enough bone conduction data to suggest correction factors. There were also not enough 500 Hz data. The BC thresholds differed significantly in the higher frequencies. The PTA threshold and ABR threshold correlated well, but not for the 4000 Hz. This is the opposite for the AC condition. More BC participants are needed.

Chapter 4

Conclusion

Three experiments on subjective and objective methods of hearing threshold were carried out. The answers on the research questions are summarized below.

1. Transducer effects
   (a) The average wave V latencies did not differ significantly between transducers in normal hearing participants.
   (b) The average wave V latencies differed significantly between polarities in normal hearing participants for the 500 Hz condition.
2. Electrophysiological vs. behavioral assessment
   (a) The AC thresholds as measured by the ABR, ASSR, and PTA differed significantly from each other.
   (b) The BC thresholds as measured by the ABR, ASSR, and PTA did not differ significantly from each other.
   (c) The thresholds as measured by the ABR, ASSR, and PTA correlated significantly with each other, though not for all frequencies.
3. Frequency specificity of the NB CE-chirps
   (a) The treshold as measured by the ABR differed from the subjective treshold in patients with a steeply sloping hearing loss. The slope was not accurately found.
   (b) The threshold as measured by the ASSR differed from the subjective threshold in patients with a steeply sloping hearing loss. The slope was not accurately found.

   In summary, ABR and ASSR work well as objective methods to investigate hearing loss. Especially when looking at air conduction thresholds. The bone conduction thresholds correlated less well with the subjective thresholds. This could be due to the smaller number of participants.

   The 500 Hz condition stays difficult to reliably measure. We saw a shift in latency when using different polarities, independently from the transducer that was used. Moreover, the difference between subjective and objective threshold was the largest at 500 Hz, with the objective threshold being almost 20 dB higher on average. This could mean a difference between a severe and a moderate hearing loss. Two participants with a ski slope loss were tested as a small pilot. The slopes were not accurately found when using the objective methods, but more participants are needed.

There are also a number of suggestions for future studies.

The stimulus rate used for the BC was 19.1 Hz. This is the suggestion of the NHSP (Newborn Hearing Screening Program, 2014), to increase the chance of observing wave I. However, analysing the latencies was not the purpose of this study. Because of this low stimulus rate, the test time was long, and only one ear was tested with BC per participant. Thus, the stimulus rate could have been faster and more BC data could have been obtained. However, when clinically investigating thresholds, one would always also want to assess the latencies and thus use a lower stimulus rate.

The number of participants for the BC condition was quite small because of this. It would also be interesting to see more participants with a ski slope loss, to further investigate the frequency specificity of the NB chirps.

Clinically, correction factors should be used for the ABR based on these results. The correction factor should be subtracted from the threshold found.

TABLE 4.1: Correction factors air conduction (N=24)

Test	Frequency	Correction factor in dB HL
ABR	500	18.6
	1000	12.9
	2000	10.0
	4000	7.9
ASSR	500	18.1
	1000	9.5
	2000	3.3
	4000	5.7

Also, the use of insert earphones for recording the ABR and ASSR is recommended. The first experiment showed a small or absent stimulus artefact. This makes interpretation of the waves easier, especially for larger intensities.

It should be kept in mind that no matter the transducer, there is a latency shift between rarefaction and condensation polarity. This also shows that merging responses of two different latencies is not desirable, for a clear waveform could be lost.

Finally, ASSR thresholds were closer to the subjective thresholds, which suggest ASSR is a better method to estimate the hearing threshold. However, ABR needs to be used to assess the latencies of the waves.

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