BEHAVIOURAL BONE-CONDUCTION RESPONSES OF INFANTS 7-30 MONTHS OF AGE TO WARBLED-TONE STIMULI.

by

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Abstract

The purpose of the present study is to obtain behavioural bone-conduction thresholds of infants 7-15 and 18-30 months of age using a clinical visual reinforcement audiometry (VRA) protocol to determine whether frequency-dependent patterns exist. Assessment of bone-conduction hearing is an essential component of an audiological test battery because it provides the information necessary to differentiate between sensorineural, conductive and mixed hearing losses. Many studies investigated the maturation of air- and/or bone-conduction thresholds in infants using objective physiological measures, such as the auditory brainstem response (ABR) and the auditory steady-state response (ASSR), reporting infant-adult differences in air- and bone-conduction hearing sensitivities. Also, frequency-dependent differences have been reported where air-conduction thresholds are better in the high- compared to low-frequencies while bone-conduction thresholds are better in the low- compared to high-frequencies. These differences reveal a low-frequency "maturational" air-bone gap, which reflects a stimulus calibration issue rather than a conductive pathology. Only one published study has reported behavioural bone-conduction thresholds for infants (Gravel, 1989). However, maturational changes in bone-conduction hearing sensitivity have not been directly investigated using behavioural methods. The present study behaviourally assesses bone-conduction thresholds across frequency (500, 1000, 2000 and 4000 Hz) using a clinical VRA protocol for normal-hearing infants 7-15 and 18-30 months of age. It is hypothesized that the frequency-dependent differences identified for infants using objective techniques will be comparable to the results obtained behaviourally. Therefore, it is expected that all infants tested will have better low- compared to high-frequency thresholds which will become more adult-like with age. Results of this study indicated that, when measured behaviourally, infant's show frequency-dependent bone-conduction thresholds

where their responses at 500 and 1000 Hz are significantly better than those at 2000 and 4000 Hz. Compared to previously documented air-conduction thresholds of infants using similar VRA techniques, there is a difference between air- and bone-conduction thresholds in the low-frequencies. However, thresholds obtained from the younger group of infants (mean age of 10.6 months) were not significantly different from those obtained from the older group of infants (mean age of 23.0 months) at any frequency, suggesting minimal maturational changes in bone-conduction hearing sensitivity between these groups.

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List of Abbreviations

ABR – Auditory Brain Response

ANOVA - Analysis of Variance

ASSR – Auditory Steady State Response

BOA – Behavioural Observation Audiometry

COR – Conditioned Orientation Reflex

DPOAE – Distortion Product Otoacoustic Emissions

MRL – Minimal Response Level

OAE – Otoacoustic Emissions

PCA – Post-conceptional Age

SPL – Sound Pressure Level

TEOAE – Transient Evoked Otoacoustic Emissions

VRA – Visual Reinforcement Audiometry

RETSPL – Reference equivalent sound pressure level

RETFL - reference equivalent threshold force level

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CHAPTER 1: Literature Review: Maturation of Bone-Conduction Hearing Sensitivity

1.1 Introduction

Assessment of bone-conduction hearing is an essential component of an audiological test battery because it provides the information necessary to differentiate between sensorineural, conductive and mixed hearing losses (Wright & Cannella, 1969). Bone-conduction hearing need not be assessed unless air-conduction thresholds are elevated. When air- and bone-conduction thresholds are elevated, a sensorineural component is present. When the difference between air- and bone-conduction thresholds are 10 dB or greater, a conductive component is present. A mixed hearing loss is characterized by the presence of both a sensorineural and conductive component. Bone-conduction hearing in adults is well understood; however, further investigation is required to expand on our limited knowledge of bone-conduction hearing in infants. A number of studies have investigated the maturation of bone-conduction thresholds in infants using physiological measures, such as the auditory brainstem response (ABR) (e.g., Cone-Wesson & Ramirez, 1997; Foxe & Stapells, 1993; Stapells & Ruben, 1989) and the auditory steady-state response (ASSR) (e.g., Small & Stapells, 2006; 2008a). In these studies, infant-adult differences in bone-conduction hearing were reported. In particular, they showed frequency-dependent differences in bone-conduction hearing sensitivity in infants which differ from adults. Only one published study has reported behavioural bone-conduction thresholds, and only for one group of infants (Gravel, 1989). Maturational changes in bone-conduction hearing sensitivity have not been directly investigated using behavioural methods. The purpose of the present study is to obtain behavioural bone-conduction thresholds of infants at different ages to determine whether frequency-dependent patterns also exist.

For several decades it has been understood that normal hearing sensitivity from 500-4000 Hz is required throughout infancy for the development of normal speech and language abilities, (e.g., Ling, 1976; Paul & Quigley, 1987). Although not all speech sounds fit into this frequency range (i.e., some speech sounds are lower than 500 Hz or higher than 4000 Hz), these frequencies are considered the most important for understanding speech (e.g., Landier, 1998; Ling, 1976; Paul & Quigley, 1987). In order to identify children with hearing loss, a current focus of Canadian healthcare systems is to implement universal newborn hearing screening (UNHS) programs. Provincial programs have been implemented in British Columbia, Ontario, New Brunswick, and will soon be available in Quebec (as of 2010). Their goal is to screen the hearing of all children before one month of age, to audiologically assess children who are at risk for hearing loss by three months of age and to provide appropriate intervention by six months of age (B.C. Early Hearing Program, 2008; Joint Committee on Infant Hearing, 2007; Hyde, 2005). Because infants under six months of age cannot provide reliable behavioural responses to sounds, physiological measures, such as otoacoustic emissions (OAEs) and ABRs, are used to assess the integrity of the cochlea and the auditory system. The identification of hearing loss and provision of intervention services early in life are expected to minimize the detrimental effects of hearing loss on speech and language development.

Not all hearing losses are diagnosed by three months of age for a variety of reasons: some infants are difficult to test, the tests may not be sensitive to milder hearing losses, and some hearing losses are progressive in nature. Also, some infants inevitably miss the hearing screening because they were not born in a hospital or because they were born out of province. At any time, infants may be brought to a hearing clinic because of hearing-related concerns, such as ear infections, lack of responsiveness to sounds or language delays. In general, 20-30 percent of hearing-impaired infants do not present with hearing loss at birth, but acquire their hearing loss during childhood (Durieux-Smith, Seewald & Hyde, 1999). In order to ensure that progressive, late-onset and acquired hearing losses are identified as early as possible, it is necessary for UNHS programs to include a system of follow-up monitoring throughout infancy and early childhood, which typically continue until the child reaches three-to-five years of age (Joint Committee on Infant Hearing, 2007). These monitoring programs are assigned to infants who have been identified with hearing loss as well as to those who present with middle-ear infections and/or risk factors for progressive hearing loss. Because many of these infants are older than six months of age, there must be appropriate diagnostic methods to evaluate their auditory system.

Infants mature rapidly during the first few years of life. Therefore, depending on their age and level of development, different testing methods, both physiological and behavioural are available to assess their hearing sensitivity (Moore, Wilson and Thompson, 1977; Nozza & Wilson, 1984; Small & Stapells, 2006, 2008a). Specifically, behavioural methods of threshold assessment are not appropriate for infants under six months of age (Joint Committee on Infant Hearing, 2007; Moore et al., 1977). Although some studies claim that reliable behavioural responses can be elicited from infants as young as five months of age (Moore et al., 1977), other studies have been unsuccessful in obtaining reliable behavioural responses from infants under six months of age, even when using more interesting stimuli and more engaging reinforcement (e.g., Delaroche, Thiebault & Dauman, 2004; Massie, Dillon, Ching & Birtles, 2006). Therefore, infants younger than six months of age are more reliably and efficiently assessed using physiological techniques, such as the ABR or ASSR. ABRs are used clinically to identify hearing loss in infants at birth and can be reliably recorded in infants as young as 29 weeks post-conception (Ponton, Moore, Eggermont, Wu & Huang, 1994). ASSRs are also effective in identifying both air and bone-conduction thresholds in infants, but are not yet widely implemented in clinics (Cone-Wesson, Dowell, Tomlin, Rance & Ming, 2002a; Kumar, Sinha &

Bhat, 2008; Rance, Tomlin & Rickards, 2006; Stapells, 2009). Even though the ABR, which was first discussed by Jewett, Romano and Williston in the 1970s, is a widely accepted proxy gold standard physiologic measure of neonatal hearing assessment and screening (Joint Committee on Infant Hearing, 2007; Stapells, 2000; Stapells, Herdman, Small, Dimitrijevic & Hatton, 2005), it is not always the most ideal diagnostic assessment technique, especially for older children.

By approximately six months of age, infants begin to localize, with a head turn, towards a sound source (Ewing & Ewing, 1944; Murphy, 1962). These infants can be assessed behaviourally, which is preferable to physiological assessment methods because of the shorter testing time required, less invasive procedures, and results that are observable and easily related to the parents. Behavioural testing methods also have the advantage of testing the entire auditory system including higher-up auditory perception and responsiveness, whereas ABRs and ASSRs only assess the integrity of the auditory system up to the level of the auditory brainstem (Hashimoto, Ishiyama, Yoshimoto & Nemoto, 1981; Møller, 1981; Møller & Jannetta, 1981; Møller, Jannetta & Møller, 1981). Children older than six months of age are typically only referred for physiological testing if behavioural assessment is not possible, or if confirmation of results is desired. Therefore, a behavioural testing technique known as visual reinforcement audiometry (VRA), which was first described by Suzuki and Ogiba (1961), is the recognized gold standard for the hearing assessment of infants 6-30 months of age (Delaroche et al., 2004; Moore et al., 1977). VRA uses a visual stimulus to reward an infant's appropriate auditory localization response (Moore et al., 1977; Suzuki & Ogiba, 1961). Infant behavioural responses are easily affected by non-sensory factors, such as attention, stimulus-type and reinforcers, which will be reviewed later. Therefore, the measurable responses obtained from infants are commonly referred to as minimum response levels (MRLs), rather than thresholds (Diefendorf & & Gravel, 1996).

The following sections provide an overview of the literature related to the present study. The first three sections discuss the physiological and behavioural measurements of infant hearing. The subsequent section will discuss the current knowledge surrounding bone-conduction hearing and its mechanisms in infants and adults. The final section discusses our knowledge of the maturation of air- and bone-conduction hearing thresholds.

1.2 Behavioural Assessment of Infant Hearing

Traditional behavioural methods for audiological assessment are not appropriate for all infants and young children due to their age, motor function, lack of attention, and their inability to understand and follow verbal and/or demonstrated instructions. As a result, a variety of techniques have been used in research to identify behavioural audiometric MRLs for infants and young children. Some of these techniques include behavioural observation audiometry (BOA), observer-based psychoacoustic procedures (OPP), visual reinforcement audiometry (VRA) and play audiometry. Once a child has surpassed the need for play audiometry, a standard behavioural assessment protocol can be followed. The uses of BOA, OPP, VRA and play audiometry in the hearing assessments of infants and young children will be discussed briefly in the following section. VRA will be discussed in more detail, as it is the test of interest in the present study.

1.2.1 Behavioural Observation Audiometry (BOA)

BOA involves careful observation of an infant's behaviour in the presence and absence of acoustic stimuli (Thompson & Weber, 1974; Widen, 1993). The observer looks for a change in behaviour accompanying onset of the stimulus, suggesting that the infant has heard the sound. Some changes in behaviour that may be observed include sucking, eye movement, eye widening, startle, and reduced breathing. The responses vary depending on the child's age, development, interest and state of arousal. Unfortunately, BOA observations are very subjective because there is no consistent BOA response that will be seen in all infants and the observer's expectations and knowledge of the stimulus may affect their decision about whether a response was present (Widen, 1993). Studies by Gans and Flexer (1982) and Ling, Ling and Doehring (1970) determined that a "blind" BOA observer, who is unaware of stimulus presentation, tends to provide more false-positive responses compared to observers who are aware of the stimulus. They concluded that awareness of the stimulus makes an observer less likely to see a response during silent control trials than during stimulus presentation trials (Gans & Flexer, 1982; Ling et al., 1970).

Another issue with BOA is that it primarily elicits supra-threshold responses to auditory stimuli (Thompson & Weber, 1974). BOA cannot be expected to obtain infant thresholds as infants will generally not respond in an observable manner to auditory stimuli at their threshold level. Consequently, BOA tends to measure and infant's responsiveness to sound rather than their sensitivity to sound (Widen, 1993).

Infants' preferences also affect their responses. For example, most infants respond to softer stimulus levels in response to speech compared to tonal stimuli (Hoversten & Moncur, 1969; Northern & Downs; 1991; Thompson & Thompson, 1972). Infants' responses depend on stimulus characteristics including frequency, bandwidth, intensity and meaningfulness to the child, although there is no way to guarantee a reliable response (Widen, 1993). Infants' responses also depend on the age of the child. With maturation, infants respond at progressively lower stimulus levels (Thompson & Weber, 1974). For instance, 90% of three-to-five month-old infants respond to speech sounds at 90 dB SPL, while 90% of six-to-eleven month-old infants respond at 60 dB SPL and 90% of 18-to-23 month-old infants respond at 40 dB SPL (Figure 1.1). At any age, BOA measures only elicit responses from 10% of infants at levels as low as 10-20 dB SPL, even though physiological studies show that normal-hearing infants can hear at this level (Thompson & Weber, 1974).

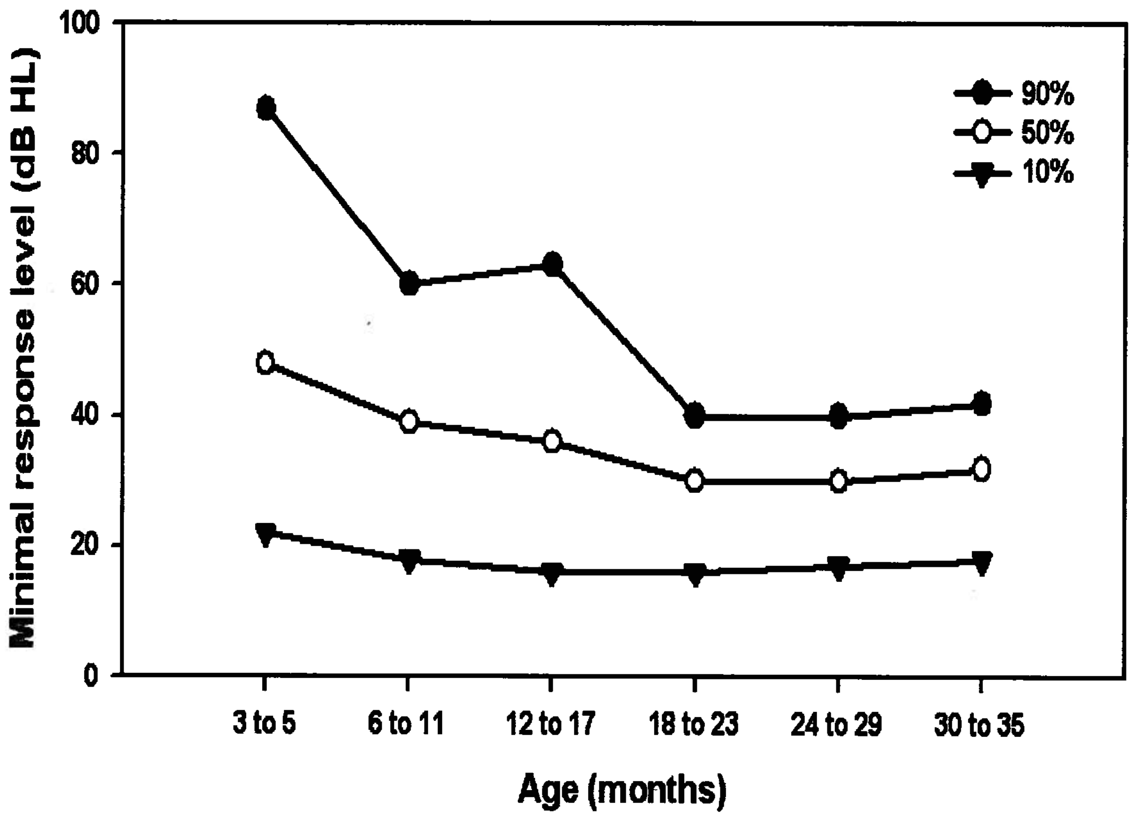

Figure 1.1 Intra-subject variability in BOA analysis as a function of age in response to speech or a complex noise signal. Adapted from Thompson and Weber (1974).

Overall, BOA is limited by infant behavioural responsiveness to soft sounds as well as by infant habituation to test stimuli and is generally not considered an accurate measure of threshold responses, limiting its clinical use (Widen, 1993). BOA is used as a last resort for behavioural assessment of individuals who cannot respond to play or VRA assessment techniques. It is primarily used in the assessment of infants from birth through six months of age who are too young for VRA and on whom reliable ABRs cannot be completed. However, it is also used for developmentally delayed and difficult-to-test children where VRA results cannot be obtained. Because BOA provides a measure of higher-order auditory processing and responsiveness, Madell (2008a) suggests that BOA has some potential for use in infant hearing assessments, but only when it is used in conjunction with other auditory assessment techniques.

1.2.2 Observer-Based Psychoacoustic Procedures (OPP)

Because BOA is considered a poor assessment method for infants, and infants younger than six months of age cannot be reliably assessed using VRA, OPP has been developed to behaviourally assess infants two weeks through two years of age (Bernstein & Gravel, 1992; Trehub & Schneider, 1986; Trehub, Schneider, Thorpe & Judge, 1991; Werner-Olsho, Koch, Halpin & Carter, 1987). Unlike VRA, OPP does not require a specific head-turn response. Instead, it accepts any response, such as eyebrow movement or sucking, from the infant that indicates a sound has been heard.

OPP uses an automated system to present auditory stimuli to the infant's ears, which the observer cannot hear. The observer is expected to make a force-choice judgment whether the infant heard a sound or not (Werner-Olsho et al., 1987). If a correct judgment is made, a visual reinforcer is activated in the test booth. The assumption is that if the observer can reliably identify the presence of a stimulus, then the infant was able to provide sufficient cues indicating a sound was heard (Werner-Olsho et al., 1987). Although OPP can be used to assess infants across a wider age range than other behavioural methods, it can be easily influenced by observer bias, attention and habituation and is not widely used in clinics (Werner-Olsho et al., 1987).

1.2.3 Visual Reinforcement Audiometry (VRA)

The use of behavioural conditioning to obtain auditory thresholds was first described by Suzuki and Ogiba (1960) who termed it the conditioned orientation reflex (COR). On average, by six months of age infants have sufficient muscular strength and head-and-neck control to turn their head (Gravel & Traquina, 1992; Suzuki & Ogiba, 1960), allowing them to localize towards a sound source with a head-turn response (Ewing & Ewing, 1944; Murphy, 1962). As a result, infants six months of age and older can also be conditioned to turn their head reliably to sounds by pairing the presentation of an auditory stimulus with an attractive reinforcing stimulus (Gravel & Traquina, 1992; Suzuki & Ogiba, 1960). The reinforcer is expected to preserve the head-turn response for about 30-40 trials within each test session (Suzuki & Ogiba, 1960). In 1969, Liden and Kankkunen slightly modified this procedure and re-termed it VRA. The VRA task requires that an attractive visual reinforcer be paired with an audible acoustic stimulus in order to encourage a child to predictively respond to audible sounds. In general, VRA uses an operant conditioning procedure to effectively pair a visual reward with an infant's reflexive head-turn response to auditory stimuli.

In 1977, Moore, Wilson and Thompson suggested that the hearing sensitivity of infants younger than six months of age cannot be reliably assessed using VRA. Some researchers have attempted to use a more interactive VRA test protocol to achieve reliable responses from infants four-to-six months of age by replacing the video or mechanical toy reinforcer with dramatic social reinforcement following the infant's conditioned response to auditory stimuli (Delaroche et al., 2004). However, they were still unable to obtain reliable responses for more than half of the infants they tested, suggesting that VRA procedures have limited use in obtaining reliable responses from infants under six months of age (Delaroche et al., 2004).

In the mid-70s, VRA began to be used to test ear-specific air- and bone-conduction thresholds of infants at least six months of age from 500-4000 Hz. Additional studies have shown a good viability and reliability of the results (Delaroche, 1989; Delaroche et al., 2004; Portmann & Delaroche, 1986, 1991). Therefore, infants six months of age or older are clinically assessed behaviourally, and then only referred for physiological assessment if behavioural testing is not possible, or if confirmation of the results is desired. Children older than 30 months of age tend to lose interest in the conditioned task and reinforcer and stop reliably responding to VRA (Moore & Wilson, 1978; Moore, Thompson & Folsom, 1992; Suzuki & Ogiba, 1961). Therefore, VRA testing is primarily used to assess air- and bone-conduction hearing in infants 6-30 months of age.

Many factors influence the reliability and success of VRA assessments. The factors which are specific to bone-conduction testing, such as placement of the bone-oscillator and coupling method, will be discussed later. Other factors involved in VRA assessments that can significantly influence the measurable outcome include the type of reinforcer, attention, state of arousal/alertness, behaviour, habituation, and type of stimulus. Although these factors may affect the measured MRL, they do not affect an infant's cochlear sensitivity (i.e., thresholds). Therefore, a clinician must recognize these factors and their impact on threshold versus MRL measurements during infant auditory assessments. The following sections outline these factors.

Type of Reinforcer

The type of reinforcer is important as it must be interesting enough for the child to effectively "reward" their head-turn. A variety of toys and videos are available to be used as reinforcers. Moore, Thompson and Thompson (1975) and Moore and et al. (1977) determined that complex visual reinforcers are better at holding a child's attention and accomplishing localization compared to simple reinforcers (Figure 1.2). They determined that the best reinforcers are those that are novel and interesting, such as brightly illuminated mechanical toys (Moore et al., 1975). Many studies have found that novel reinforcers help to maintain an infant's responses, and may succeed in renewing an infant's interest in the VRA task, should it be lost (Bond, 1972; Lipsitt & Werner, 1981; Primus & Thompson; 1985). Novelty can be enhanced by the use of multiple reinforcers during VRA assessments, including different mechanical toys and video reinforcers (Diefendorf & Gravel, 1996).

Studies by Schmida, Peterson and Tharpe (2003) and Lowery, Hapsburg, Plyler and Johnstone (2009) compared video reinforcement to conventional mechanical-toy reinforcement. Schmida et al. (2003) found that video-reinforcement elicited more head-turn responses for children 6-24 months of age. Lowery and colleagues (2009), however, found that young infants, 6-17 months of age, respond equally well when reinforced by video or conventional mechanical-toys (Lowery et al., 2009). These findings support Madell's (2008b) conclusion that both types of reinforcers are useful in VRA assessments, but that a video may hold an older infant's attention longer, whereas either reinforcer is effective when assessing a younger infant.

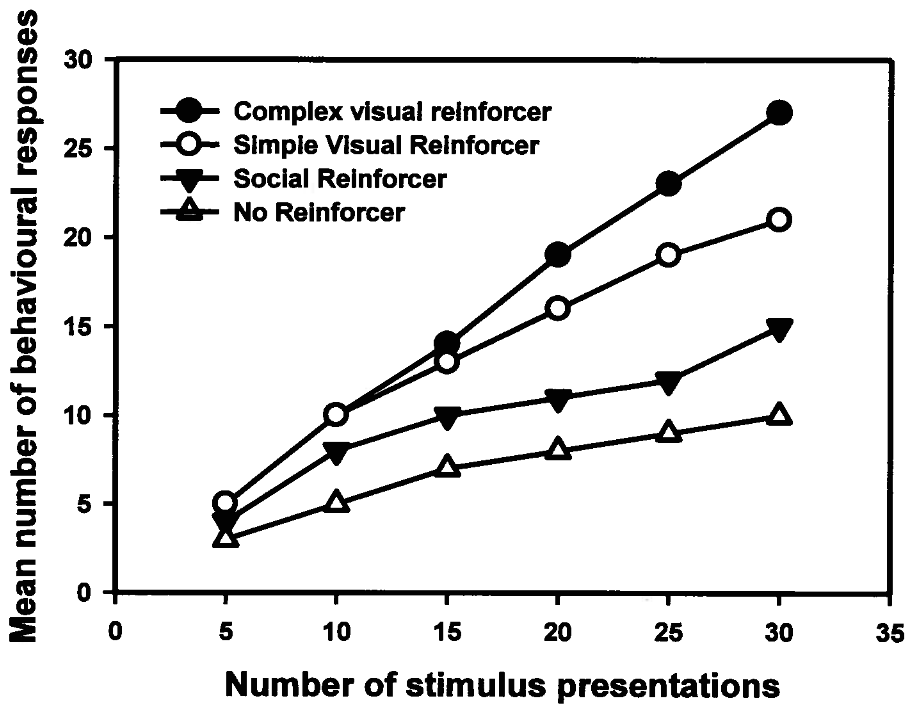

Figure 1.2 Effect of reinforcer complexity on the number of responses obtained during VRA conditioning of infants under 12 mo of age. Adapted from Moore et al. (1975).

Attention; State of Arousal/Alertness; Behaviour

Infant subjects are particularly difficult to test because their attention, state of arousal and behavioural cooperativeness during testing varies both between subjects and in the same subject throughout the testing period. These factors affect how easily and reliably responses can be obtained through VRA testing (Parry, Hacking, Bamford & Day, 2003). In the worst cases, it becomes impossible to obtain reliable responses. If a child is fussy, tired or unfocussed, they will not be paying attention to the auditory stimulus, may not turn to look for the signal, or lose interest in the VRA task very quickly. Sometimes a child can be brought into a cooperative testing state by using a more interesting stimulus (e.g., speech), an interesting reinforcer, or a different transducer (e.g., soundfield speakers, headphones). However, it is possible that the child is simply not able to be assessed on that day.

Variability in attention, state of arousal and behaviour in an individual child are responsible for the assumption that VRA testing can only definitively elicit MRLs rather than thresholds. Sometimes an infant's MRL may, in fact, be their threshold; however, it is essentially impossible to determine if this is the case.

Habituation

As test-time increases, infants become less interested in the task and the reinforcer. Behaviourally, Eisenberg (1965) and Eisenberg, Hunter, Griffin & Coursin (1964) found that all infants habituate to the continued presentation of stimuli, meaning their behavioural responses over many trials will essentially become extinct. Generally, it is expected that more mature neurological systems, such as those in older infants and children, will habituate faster than the less mature, infant-like, systems (Mencher, Mencher & Rohland, 1985). As a result, young infants provide between 30-40 head-turn responses before habituation occurs while the number of elicited head-turns tends to decrease with age (Suzuki & Ogiba, 1960). In order to effectively assess a child in a single session, their tendency to habituate must be monitored, particularly considering the child's age in anticipating the number of cooperative head-turn responses to be expected. Sometimes, changing the stimulus or reinforcer will hold the child's attention for longer periods, allowing for the elicitation of more head-turn responses.

Type of Stimulus

When assessing infants, it is important to use stimuli that are interesting. In general, a more complex stimulus tends to be more interesting, and more likely to hold a child's attention. The most commonly used stimuli include: music, noise-makers, narrowband noise, warbled-tones[1], pulsed pure-tones, and pure-tones. However, not all stimuli are equal. Use of particular stimuli is a balancing act between holding the child's attention and the frequency-specificity of the stimulus to make the responses most accurate for assessing hearing sensitivity at discrete frequencies. Ideally, a clinician wants threshold responses to pure-tone stimuli, as is the standard for adult hearing assessments. However, using pure-tone stimuli to condition a child is more difficult than using a more interesting narrow-band noise or warbled-tone stimulus (Eisenberg et al., 1964).

Studies assessing adult behavioural thresholds have compared the use of pure tones and warbled tones (Morgan, Dirks & Bower,1979) as well as pulsed tones and warbled tones (Luts & Wouters, 2004) and have found no statistically or clinically significant differences in the thresholds obtained. A more recent behavioural study also found that the use of warbled tones, pulsed-tones and warbled-pulsed tones do not elicit different threshold responses from adults (Franklin, Johnson, Smith-Olinde & Nicholson, 2009). Therefore, any of these stimuli can be considered equally effective in eliciting adult thresholds. However, for infant assessments, many VRA studies have suggested that the frequency and bandwidth of a stimulus affect how easily an

[1] Warbled-tones, also known as frequency-modulated tones, are tones whose frequency varies several times per second over a small frequency range (Reilly, 1958). Warbled-tones are typically modulated to +5% of the center frequency at a rate of 5 Hz, although some variation exists between different equipment (Staab & Rintelmann, 1972). These tones are most commonly used in sound field testing to avoid the problems cause by pure tone standing waves. Warbled-tones have been used in ear-specific threshold testing for infants and young children for the past several decades (Langenbeck, 1965).

infant can be conditioned (Diefendorf & Gravel, 1996; Eisenberg, 1965; Eisenberg et al., 1964; Gravel, 2000; Hoversten & Moncur, 1969; Moore et al., 1975; Shaw & Nikolopoulos, 2004). Studies that compare different stimuli suggest that infants preferentially respond to speech and broad-band stimuli compared to frequency-specific tones (i.e., pure tones) (Thompson & Thompson, 1972). Other studies on infant speech preferences suggest that infants also preferentially respond to high-frequency speech sounds (e.g., infant-directed speech) (Fernald, 1985; Fernald & Kuhl, 1987; Panneton-Cooper, Berman & Staska, 1997; Pegg, Werker & McLeod, 1992). Because of infant preferences, clinical VRA protocols typically use mid-frequency stimuli (i.e., 1, 2, or 4 kHz) during initial conditioning trials to elicit reliable head-turn responses (Day, Bamford, Parry, Shepherd & Quigley, 2000).

Stimulus frequency and bandwidth can also affect the MRLs obtained during infant assessments (McConnell & Ward, 1967). Specifically, infants of all ages tend to respond better to speech stimuli and broadband noises (i.e., noisemakers) compared to frequency-specific warbled-tones or pure-tones (Figure 1.3). However, speech and broadband-noises are more familiar sounds to an infant and stimulate a larger region of the cochlea compared to a warbled- or pure-tone stimulus (McConnell & Ward, 1967; Thompson & Thompson, 1972). Therefore, it is not surprising that broadband and speech stimuli would elicit better MRLs during infant assessments (McConnell & Ward, 1967). Because infants are thought to preferentially respond to high-frequency sounds such as infant-directed speech, it is conceivable that they will also respond more preferentially (i.e., closer to their true threshold) in response to high-frequency stimuli, and potentially have more elevated MRLs in response to low-frequency stimuli, although no studies have directly investigated this claim.

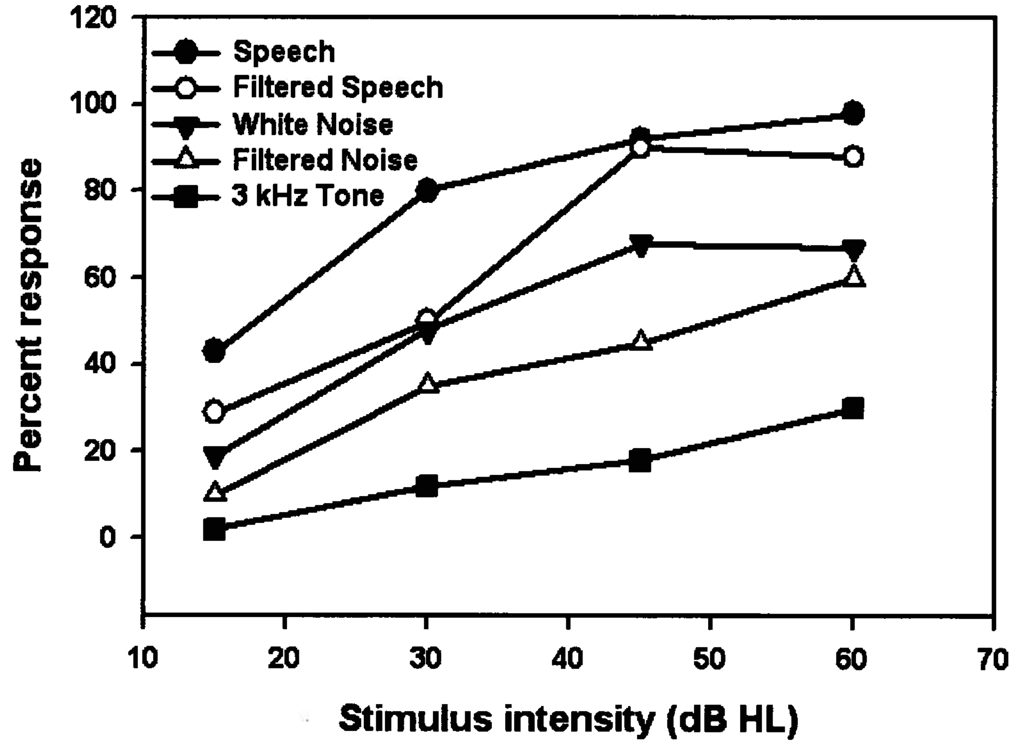

Figure 1.3 Percent of responses obtained from normal-hearing infants 7-12 months of age as a function of stimulus intensity. Adapted from Thompson and Thompson (1972).

Thompson and Folsom's (1985) study compared infant MRLs to three high-frequency auditory signals that differed primarily in frequency bandwidth: 2000 Hz warbled-tone, 2000 Hz pulsed tone-burst, and a high-pass complex noise between 2000 and 4000 Hz. They determined that there were no significant differences in infant MRLs obtained from these stimuli, suggesting that clinicians can use auditory signals that have a high degree of frequency specificity (i.e., warbled-tones or pulsed pure-tones) without compromising their ability to obtain reliable MRLs (Thompson & Folsom, 1985). Thompson and Folsom (1985) did not find that their subjects' responsiveness diminished as testing continued. However, they note that their conclusions can only apply to infants and young children who are capable of being conditioned and who do not habituate rapidly to VRA.

1.2.4 Play Audiometry

Play audiometry is an assessment method using another conditioning task that requires a young child to cooperate in performing an activity in response to auditory stimuli. It requires that the child have the cognitive skills to follow spoken and demonstrated instructions. Typically, play audiometry can be successfully used in the hearing assessment of children at a cognitive age of approximately 30 months or older, and allows clinicians to obtain threshold responses, rather than MRLs (Madell, 2008c). In order to obtain all the necessary testing information, play tasks can be modified and switched frequently to hold a child's attention for longer periods of time (Madell, 2008c). However, play audiometry is not typically used to assess the hearing of children younger than 30 months of age as they do not possess the cognitive skills necessary to reliably follow task instructions. Because infants under 30 months of age are the cohort of interest in the present study, the specifics of play audiometry will not be discussed further.

1.3 Physiological Assessment of Hearing in Infants

Although assessing infant hearing abilities behaviourally is ideal, it is not always a feasible option. Children with a developmental level younger than that of infants six months of age are less likely to elicit reliable behavioural responses during testing either due to limitations in developmental cognitive ability, lack of interest, or a lack of muscular neck control, which is required for adequate head turns (Delaroche et al., 2004; Gravel & Traquina, 1992; Suzuki & Ogiba, 1960). The use of BOA in these situations is not considered a clinically reliable testing technique, especially when attempting to obtain thresholds (Thompson and Weber 1974; Widen, 1993). Because it is important to detect hearing loss in young infants, other reliable techniques must be used to provide a measure of auditory integrity (Joint Committee on Infant Hearing, 2007). Physiological measures are used because they do not require behavioural cooperation and can be implemented across all ages, regardless of an individual's developmental level. To date, there are primarily two physiological measures that are used to assess hearing sensitivities: the auditory brainstem response (ABR) and the auditory steady-state response (ASSR). These physiological responses measure the integrity of the auditory pathway including primarily the cochlea, auditory nerve and brainstem, but do not assess higher-order processing abilities. ABRs reliably estimate the frequency-specific thresholds in infants and adults (Stapells, 2000b). However, even though ASSR have been found reliable for estimating the behavioural and ABR audiogram (Dimitrijevic et al., 2002; Steuve & O'Rourke, 2003; Tlumak, Rubinstein & Durrant, 2007), they are still being investigated for their use in the diagnosis of hearing loss (Small & Stapells, 2008a).

1.3.1 Auditory Brainstem Response (ABR)

Clinically, brief-tone threshold-ABRs are currently the method of choice for assessing frequency-specific hearing sensitivities of infants younger than six months of age as well as for special populations. They provide results with reasonable accuracy for both adults and infants when individuals cannot be behaviourally tested (Stapells, 2000a; Stapells, 2000b; Stapells, Gravel & Martin, 1995; Stapells, Picton, Durieux-Smith, Edward & Moran, 1990). ABRs are performed on sleeping individuals. They assess the integrity of the auditory pathway up to the level of the generator which is reflected by the presence of specific ABR waves, as shown in Table 1 (Hashimoto, Ishiyama, Yoshimoto & Nemoto, 1981; Starr & Hamilton, 1976). For example, the presence of wave V would indicate a functional auditory pathway up to the level of the inferior colliculus. ABRs estimate frequency-specific thresholds by testing each ear and each frequency of interest separately. As such, the assessment procedure is quite slow, requiring multiple recordings to be independently made and compared at each frequency. Interpretation of the ABR requires a skilled professional to subjectively compare replicated responses (Stapells, 2000a). However, this potentially results in significant tester bias, along with unreliable interpretations depending on the experience of the clinician.

Table 1.1 ABR Waves and their neural generators (Hashimoto, Ishiyama, Yoshimoto & Nemoto, 1981; Møller, 1981; Møller & Jannetta, 1981; Møller, Jannetta & Møller, 1981).

WAVE	GENERATOR
Cochlear Microphonic	Cochlea
Wave I	Cochlear nerve exiting the cochlea
Wave II	Cochlear nerve entering the brainstem
Wave III	Cochlear Nucleus
Wave IV	Superior Olivary Complex; Cochlear Nucleus; Lateral Lemniscus
Wave V	Inferior Colliculus

There has been a significant amount of research done on the use of ABRs in both air- and bone-conduction threshold assessments throughout infancy and into adulthood (e.g., Edwards, Durieux-Smith & Picton, 1985; Foxe & Stapells, 1993; Stapells & Ruben, 1989; Stuart et al., 1996; Yang, Rupert & Moushegian, 1987). This research has identified infant-adult differences in interaural attenuation, ipsilateral/contralateral recordings (i.e., recordings measured on the same/opposite side of the head as the bone-oscillator, respectively), latencies and thresholds. The use of two-channel recordings of ABR responses in infants helps clinicians determine from which cochlea a response to a bone-conducted tone originates (Foxe & Stapells, 1993; Stapells

& Ruben, 1989; Stuart et al., 1996). As a result of skull immaturities, infants show up to 25 dB interaural attenuation of bone-conducted stimuli across the head (Small & Stapells, 2008a; Yang et al., 1987). As their skulls mature, this interaural attenuation decreases, being largest in newborns, smaller in 12 month-old infants, and smallest in adults (Yang et al., 1987). Infants and young children's ABR responses also show waves V with later latencies and smaller amplitudes in contralateral recordings compared to the latencies and amplitudes of ipsilateral recordings (Foxe & Stapells, 1993; Stapells & Ruben, 1989). Because similar ipsilateral/contralateral findings have been observed in response to air-conducted stimuli (Edwards, et al., 1985; Stapells & Mosseri, 1991), the cause of these differences is attributed to both developmental changes in skull structure, resulting in interaural attenuation, as well as neurophysiological differences in the structure and positioning of neural generators, which also contribute to ipsilateral/contralateral asymmetries.

Overall, ABRs have been the gold standard for estimating neonatal hearing sensitivities and screening infant hearing for many years (Cox, 1984; Galambos, Hicks & Wilson, 1984; Joint Committee on Infant Hearing, 2007; Kenworthy, 1990; Stapells, 1989; Durieux-Smith, Picton, Bernard, MacMurray & Goodman, 1991). Because the present study focuses on infant behavioural MRLs, the trends and infant-adult differences in ABR thresholds and latencies will be discussed later in detail. However, infant-adult differences in interaural attenuation and ipsilateral/contralateral recordings will not be discussed further.

1.3.2 Auditory Steady-State Responses (ASSR)

ASSRs are periodic electrical responses recorded from the brain in response to auditory stimuli (Maiste & Picton, 1989; Stapells, Linden, Suffield, Hamel & Picton, 1984). ASSRs are used both as an alternative to ABR measures as well as sometimes being used in conjunction with ABR measures. Either brief-tones or continuous stimuli are amplitude and/or frequency modulated to elicit this neural electroencephalogram (EEG) response, estimating hearing sensitivity (Picton, Skinner, Champagne, Kellett & Maiste, 1987; Kuwada & Batra, 1986). In 1981, Galambos, Makeig and Talmachoff suggested that a 40-Hz ASSR response could identify hearing sensitivity just above behavioural thresholds in adults. Similarly, ASSRs using more rapid stimulus rates (greater than 70-Hz) are best used to record responses from infants and young children (Lins et al., 1996; Rickards et al., 1994; Savio, Cardenas, Perez-Abalo, Gonzalez & Valdes, 2001). As a result, extensive research has been done using 80-Hz ASSR responses to assess the frequency-specific hearing sensitivity of infants (Cone-Wesson et al., 2002b; John et al., 2004; Levi et al., 1995; Lins et al. 1996; Rance & Tomlin, 2006; Rickards et al., 1994; Savio et al., 2001; Swanepoel, Ebrahim, Friedland, Swanepol & Pottas, 2008; reviewed in Tlumak et al., 2007). Similar to the ABR, the 80-Hz ASSR is suspected to be generated primarily in the auditory brainstem. As a result, it also assesses the integrity of the auditory nerve and brainstem structures (Herdman et al., 2002; Kuwada et al., 2002).

Although ASSRs are not yet widely used clinically, they do present some benefits over ABRs. ASSRs can test both ears and multiple frequencies simultaneously with significantly shorter test time, which is particularly important for infants who may not sleep for long periods (Hatton, 2008; Herdman & Stapells, 2001, 2003; John, Purcell, Dimitrijevic & Picton, 2002; Luts, Desloovere, Kumar, Vandermeersch & Wouters., 2004; Picton, Dimitrijevic & Purcell, 2003). Also, ASSR responses are objectively interpreted using statistical tests, unlike ABRs which are subjectively interpreted by clinicians. Overall, ASSRs and ABRs have both been found to be an efficient and reliable measure for estimating physiological hearing sensitivity in normal hearing individuals (Cone-Wesson et al., 2002a; Kumar, Sinha & Bhat, 2008; Picton et al., 2003; Rance et al., 2006).

Similar to the results of ABR studies, ASSRs also show infant-adult differences in interaural attenuation, ipsilateral/contralateral recordings and thresholds. Again, contralateral recordings of ASSRs to bone-conduction signals elicit poorer thresholds and appear smaller in amplitude compared to ipsilateral recordings (Small & Stapells, 2008b). These ipsilateral/contralateral asymmetries are larger and observed more often in infants compared to adults. Small and Stapells (2008b) also found that infants have an interaural attenuation of at least 10 to 30 dB in response to bone-conducted ASSR stimuli, independent of frequency. As was the case for ABR results (Yang et al., 1987), this interaural attenuation is not present in adults. Although these asymmetries can be useful in interpreting ASSR assessments, they will not be discussed further. However, the trends and infant-adult differences observed in ASSR thresholds will be discussed later in detail.

1.4 Hearing Screening in Infants

1.4.1 Otoacoustic Emissions

In order to accurately investigate normal hearing thresholds in infants and toddlers, there must be an objective way to screen for normal hearing. Physiological measures, including ABRs, ASSRs and OAEs can all be used as effective screening tools. ABRs and ASSRs require the use of scalp electrodes to measure the brainstem activity of sleeping infants. They are very useful in diagnostic testing to accurately determine air- and bone-conducted hearing sensitivities of infants of all ages. However, testing for brainstem responses requires children to be asleep, involves a more complex set-up (i.e., obtaining good contact of scalp electrodes) and is time consuming. OAEs, however, can be used as an excellent screening tool to identify infants who are at risk for hearing loss (Norton et al., 2000). OAE screeners require less time and cooperation from an infant compared to diagnostic OAEs, while still maintaining sufficient test specificity. Although OAE measures do not provide specific information about the status of the outer- or middle-ear, we typically expect OAEs to be absent in the presence of occluding cerumen, middle-ear fluid or ossicular dysfunction (Chang, Vohr, Norton & Lekas, 1993; Filipo et al., 2007). However, the presence of OAEs cannot rule out the existence of a mild conductive or sensorineural pathology of 30 dB or greater in infants 8-12 months of age (Norton et al., 2000).

Transient-evoked otoacoustic emission (TEOAEs) and distortion-product otoacoustic emissions (DPOAEs) can be measured in nearly all ears that have normal cochlear hearing, as long as they also have clear ear canals and normal middle-ear functioning (Lonsbury-Martin et al., 1990a; 1990b). However, TEOAEs and DPOAEs arise from two fundamentally different mechanisms: linear auditory reflections and non-linear distortions (reviewed in Shera, 2004). Low-intensity TEOAEs result primarily from linear auditory reflections following a transient or brief auditory stimulus (Kemp, 1978; reviewed in Shera, 2004), whereas high-intensity TEOAEs and DPOAEs result from a combination of these linear auditory reflections along with non-linear distortions, where a new auditory emission is produced and reflected after the presentation of two auditory stimuli (Knight & Kemp, 2001; Konrad-Martin, Neely, Keefe, Dorn & Gorga, 2001; reviewed in Shera, 2004). The presence of both TEOAEs and DPOAEs indicate functional outer hair cells, although their mechanisms of action differ (reviewed in Shera, 2004). However, studies that have compared the functionality of using TEOAEs and DPOAEs in hearing screenings have found both TEOAEs and DPOAEs to be clinically acceptable hearing screening tests (Norton et al., 2000).

1.4.2 Acoustic Immittance

Tympanometry is a quick, non-invasive and inexpensive method clinically used to examine middle-ear function. Because tympanometry is based on measures of tympanic membrane mobility it provides no information regarding cochlear sensitivity, higher-order functioning of the auditory system, or the degree of hearing loss in the presence of auditory pathology (Feldman, 1977). Acoustic reflex measurements, however, require the contribution of the stapedius muscle reflex, providing some information about middle-ear status, cochlear sensitivity, auditory nerve and lower brainstem functioning (Feldman, 1977). Acoustic reflex measurements allow for inferences to be made regarding sensorineural and conductive pathologies, but do not provide information regarding the degree of pathology indicated (Feldman, 1977). In order to ensure a participant can be included as a "normal-hearing" subject in research, their cochlear functioning must be identified as "normal". However, because some individuals will not pass the TEOAE screening, even in the presence of normal cochlear functioning, tympanometry can be conducted to at least rule out the presence of outer and middle-ear pathology (Joint Committee on Infant Hearing, 2007). Because the present study assesses cochlear function through bone-conduction hearing, the relationship between middle-ear status and bone-conduction hearing thresholds will be discussed next.

1.5 Bone-Conduction Hearing

1.5.1 Impact of Middle-Ear Status on Bone-Conduction Hearing

Bone-conduction hearing thresholds are expected to represent the hearing sensitivity of the cochlea, bypassing the outer- and middle-ear. However, in the presence of middle-ear pathology, some studies suggest that bone-conduction thresholds are affected. For instance, mass-loading of the tympanic membrane lowers the resonant frequency and increases the relative velocity of the stapes at the oval window, potentially altering bone-conduction thresholds without affecting actual cochlear sensitivity (Decraemer, Khanna & Funnell, 1994; Huizing, 1960; Kirikae, 1959; Stenfelt & Goode, 2005; Stenfelt, Hakansson & Tjellstrom, 2000; Stenfelt, Hato & Goode, 2002). In addition, ossification of middle-ear ossicles, as seen in otosclerotic ears, can affect the bone-conduction thresholds, particularly at 2000 Hz (Awengen, 1993; Carhart, 1962; Yazki, Sazgar, Motiee & Ashtiani, 2009).

Contrary to early studies which suggested that the mobility of the round window is of paramount importance to basilar membrane mobility and therefore bone-conduction hearing (Hulka, 1941; Huizing 1964; Palva & Ojala, 1955), Tonndorf (1966, 1968, 1972) used animal studies to show that distortion of the otic capsule is more important. This implies that otitis media with effusion should have minimal effect on bone-conduction hearing thresholds. Gravel (1989) and Fria, Cantekin and Eichler (1985) both support this finding, showing that infants who tested positive for otitis media with effusion also presented with normal bone-conduction hearing sensitivity. In these studies, infants with middle-ear pathology show similar or slightly improved (by no more than 5-10 dB) bone-conduction thresholds compared to infants with no middle-ear pathology. Milner, Weller and Brenman (1983) investigated the impact of otitis media on bone-conduction hearing thresholds in adults, finding that high-frequency thresholds (2000 and 4000 Hz) worsened slightly with no changes observed in the low frequencies. They suggested that the worsening of high-frequency hearing sensitivity could be due to long-term chronic middle-ear pathology, causing permanent sensorineural damage, which is unlikely to be observed when evaluating infant bone-conduction sensitivities.

Overall, there is limited knowledge regarding the effects of middle-ear pathology on bone-conduction thresholds. However, most research suggests that the involvement of the middle ear is minimal with regard to bone-conduction hearing sensitivity in unoccluded ears (reviewed in Stenfelt & Goode, 2005).

1.5.2 Factors Affecting Bone-Conduction Threshold Estimation

Although bone-conduction testing has been used clinically for decades, there are certain factors that need to be considered, particularly when testing bone-conduction hearing in infants. First, the method of coupling the bone-oscillator to the skull must be considered as an infant may not tolerate all types of headbands. Having different options available can greatly improve the chances of obtaining reliable behavioural responses. Second, the comfort of the bone-oscillator must be balanced against the provision of a sufficient amount of force against the infant's head. If sufficient force is not provided, the estimated threshold or MRL will not be accurate. Finally, understanding the best locations on the skull for placement of the bone-oscillator is also necessary in order to obtain the best, and most accurate bone-conduction MRLs.

Bone-Oscillator Coupling Method

The steel headband maintains a constant force on the oscillator, although individual head size may cause this force to vary slightly (approximately 450-550g). Larger heads also tend to cause slightly more force to be applied by the oscillator against the skull (Harrell, 2002; Wilber, 1979). Because infant head sizes are often smaller than adult and child head sizes, judgement must be used to ensure sufficient force is being provided by the oscillator on the infant skull using the child-size steel headband.

Using an elastic band to couple the bone-oscillator to the infant's head is feasible, particularly for research, because a known constant force can be applied on the oscillator and verified by a spring scale measurement (Yang & Stuart, 1990). However, this verification step is often omitted in clinical practice. The force applied by an elastic band is dependent on how tightly it is pulled around the child's head. Therefore, the elastic band should always be applied by a trained individual to ensure that it provides a sufficient amount of force on the oscillator while causing minimal discomfort or causing the oscillator to slip out from beneath it (Small, Hatton & Stapells, 2007).

For infants who are unwilling to wear the metal or elastic headband for the duration of the test, the hand-held coupling method is another option. In the past, some studies have discouraged its use because of the potential for variability in the placement location and force applied to the oscillator during testing, (Stuart et al., 1990; Yang, Stuart, Stenstrom & Hollett, 1991) and the assumed dampening of the oscillator's response due to hand pressure on its superior surface (Wilber, 1979). However, a study by Small et al. (2007) found that a trained individual can hand-hold the oscillator on a sleeping infant's or adult's head with constant and sufficient force, eliciting comparable results to the use of an elastic band. However, care must be taken in behavioural assessments using the hand-held coupling method, particularly avoiding regular removal of the oscillator from the head, as the infant may otherwise begin to pair the presence of the reinforcer with the contact of the oscillator. As a result, the hand-held coupling method is acceptable in behavioural testing only if the bone-oscillator can be held with a constant pressure against the child's head without being removed between stimulus presentations.

Overall, it is important to keep the coupling force as consistent as possible while minimizing discomfort in infant assessments. This can be accomplished equally well by the steel headband, elastic band or hand-held coupling method. In behavioural testing, priority should be given to both the steel and elastic headbands over the use of the hand-held coupling method, as is done in current VRA protocols (B.C. Early Hearing Program, 2008).

Bone-Oscillator Coupling Force

Many studies have been used to investigate the necessary bone-oscillator coupling force for both infant and adult populations (Dirks, 1964; Harris, Haines & Myers, 1953; Konig, 1957; Whittle, 1965; Lau, 1986; Yang et al., 1991). In general, increasing the force of the vibrator on the adult head reduces the amount of energy that is required to obtain thresholds (Dirks, 1964). Harris et al. (1953) determined that these changes occur with increasing force from 100 to 400 g, with little change in thresholds when the force is increased above 400 g. Konig (1957), however, observed threshold changes with increased coupling force up to 750 g. Whittle (1965) suggests that inter-subject variability may account for some of these differences. However, none of these studies assessed the bone-oscillator coupling force for infants. Because the physiology of infant skulls differs from adults (Anson & Donaldson, 1981; Eby & Nadol, 1986), it is possible that the required bone-oscillator coupling force differs as well. An ABR study by Yang et al. (1991)

found that providing a force of 225 or 325 g tended to produce less efficient transmission of bone-conducted sounds to the cochlea, compared to coupling forces of 425 and 525 g. They determined that increasing the coupling force will improve wave V latencies of the ABR response up to the point where sufficient force (i.e., 400-450 g) is being applied. Once this sufficient force has been reached, wave V latencies will not improve with additional force (Yang et al., 1991). Although latency responses cannot be directly related to thresholds, similar trends are observed where increasing the coupling force of the bone-oscillator results in measurable changes up to approximately 400 g against both infant and adult heads, after which minimal changes are observed with increasing force.

Additional factors to be considered for infant behavioural testing are the potential to cause discomfort, affecting test reliability (Lau, 1986) and the likelihood that the bone-oscillator will be displaced with head movement because of a weak or excessive coupling force (Yang et al., 1991). Therefore, the oscillator's coupling force must be balanced by comfort to maintain the infant's cooperation as well as ensuring that its position on the head is maintained.

Bone-Oscillator Placement

Because of the nature of bone-conducted sound, auditory stimulation can be elicited by the vibration of different cranial bones. The main locations suggested for the placement of the bone-oscillator are on the frontal and the temporal bones of the skull. Although early studies have suggested that responses for frontal-bone placement are less affected by middle-ear status (Dirks & Malmquist, 1969; Goodhill, Dirks, & Malmquist, 1970; Studebaker, 1962), frontal-bone placement tends to elicit poorer thresholds and longer latencies compared to temporal-bone placements, particularly in infants (Corliss, Smith & Magruder, 1961; Khanna, Tonndorf & Queller, 1976; Small et al., 2007; Stenfelt & Goode, 2005; von Békésy, 1960; Yang et al., 1987).

Similar results have been found for occipital- compared to temporal-bone placements (Yang et al., 1987). In general, for infants, increasing the distance between the bone-oscillator and the cochlea effectively increases the latency of wave V (Stuart et al., 1990; Yang et al., 1987). Small et al. (2007) have also investigated differences in bone-conduction placement at different locations on the temporal bone: high temporal-bone and low-temporal bone (i.e., mastoid). They found no significant difference between signal attenuation and thresholds measured at either location. As a result, for infant hearing assessments, it is most effective to place the bone-oscillator anywhere on the temporal bone rather than on any other cranial bone, as bone-conducted stimulation of the temporal bone provides the least signal attenuation and the best thresholds.

1.5.3 Mechanisms of Bone-Conduction Hearing

To date, our understanding of the mechanisms that explain bone-conduction hearing is limited, particularly in infants. In 1932, von Békésy first questioned whether bone-conducted hearing resulted from cochlear stimulation. Through his and others' research, air-conducted tones were cancelled out by bone-conducted tones of opposite phase from 100 to 15,000 Hz and over an intensity range of 40-70 dB HL (Khanna et al., 1976; Lowy, 1942; von Békésy 1932; Wever & Lawrence, 1954). Similarities in traveling wave mechanics (von Békésy, 1955), cochlear microphonics (Wever & Bray, 1936) and laser doppler vibrometry (Stenfelt & Hakansson, 2002) elicited by both air- and bone-conducted tones also support von Békésy's original hypothesis that the bone-conduction mechanism results from cochlear stimulation.

Although many studies have identified similarities between the mechanisms of air- and bone-conduction, differences also exist. For instance, a residual second harmonic exists following the cancellation of air- and bone-conducted stimuli (Khanna et al., 1976), the loudness growth of air- and bone-conducted tones differ (Stenfelt & Hakansson, 2002), and OAEs amplitudes are smaller when elicited by bone-conduction (Rossi, Solero, Rolando & Olina, 1988). Air-conduction ABR latencies have also been shown to be longer than bone-conduction ABR latencies (e.g., Beattie, 1998). The most likely explanation for these differences is that the pathways taken by air- and bone-conducted sound to the cochlea differ, with the final excitation pattern of the basilar membrane in the cochlea remaining the same (Stenfelt & Goode, 2005; Stenfelt & Hakansson, 2002).

Throughout history, researchers have devised theories to explain the physiology behind the mechanisms that differ between air- and bone-conduction responses. Many researchers including Zwislocki (1953), Tonndorf (1962) and Stenfelt and Goode (2005) have created theoretical models of air- and bone-conduction basilar membrane motion. Some researchers suggest that the only contributing factor to bone-conduction hearing is the impact of skull vibrations on cochlear fluids (Allen & Fernandez, 1960). Other researchers argue that more than one factor contributes to the mechanism of bone-conduction hearing (Brinkman, Marres & Tolk, 1965; Tonndorf, 1962). The majority of current research supports that the mechanisms underlying bone-conduction hearing are not explained by any single pathway (Stenfelt & Goode, 2005). However, it is very difficult to distinguish between the different contributors, leaving the mechanisms of bone-conduction hearing not fully understood.

Three Pathways of Bone-Conduction Hearing

Historically, it was believed that "inertial", "compressional", and "osseotympanic" pathways sufficiently accounted for the transmission of bone-conducted sound (Barany, 1938; Kirikae, 1959; Wever & Lawrence, 1954). The "inertial" pathway suggests that bone-conduction vibrations elicit movement from all skull bones including the bone surrounding the cochlea and the middle-ear ossicles. This theory assumes that there is an inertial lag between the motion of the ossicles and the cochlea, causing them not to vibrate synchronously (Barany, 1938). The lack of synchronicity results in a relative motion of the stapes at the oval window, causing cochlear fluid displacement and stimulation of the basilar membrane, particularly for the transmission of low-frequency sounds (Barany, 1938; Kirikae, 1959; Stenfelt & Goode, 2005; Wever & Lawrence, 1954). The "compressional" pathway proposes that bone-vibrations radiate towards the cochlea, distorting the shape of the cochlea (Hood, 1962). This also displaces the cochlear fluids, causing the propagation of the traveling wave along the basilar membrane. The compressional pathway is proposed to be especially efficient at propagating waves in response to high-frequency stimuli (Stenfelt & Goode, 2005). Finally, the "osseotympanic" pathway proposes that some energy from a bone-conducted sound follows the same pathway as does the energy from an air-conducted sound. Therefore, energy from bone-vibrations will be transmitted into the ear canal and radiated through the tympanic membrane and middle ear, stimulating the cochlea via the air-conduction pathway (Stenfelt & Goode, 2005).

Current Theory of Bone-Conduction Hearing

Although these three pathways outline the basic contributors to cochlear stimulation through bone-conduction, further research has since been completed that both challenges and improves our knowledge about factors contributing to bone-conduction hearing. Recently, Stenfelt and Goode (2005) have identified five different components, which they feel contribute most significantly to the bone-conduction mechanism, as shown in Figure 1.4: sound radiated in the ear canal; middle-ear cavity radiation; inertia of the cochlear fluids; compression of the cochlear walls; and pressure transmission through cerebrospinal fluid.

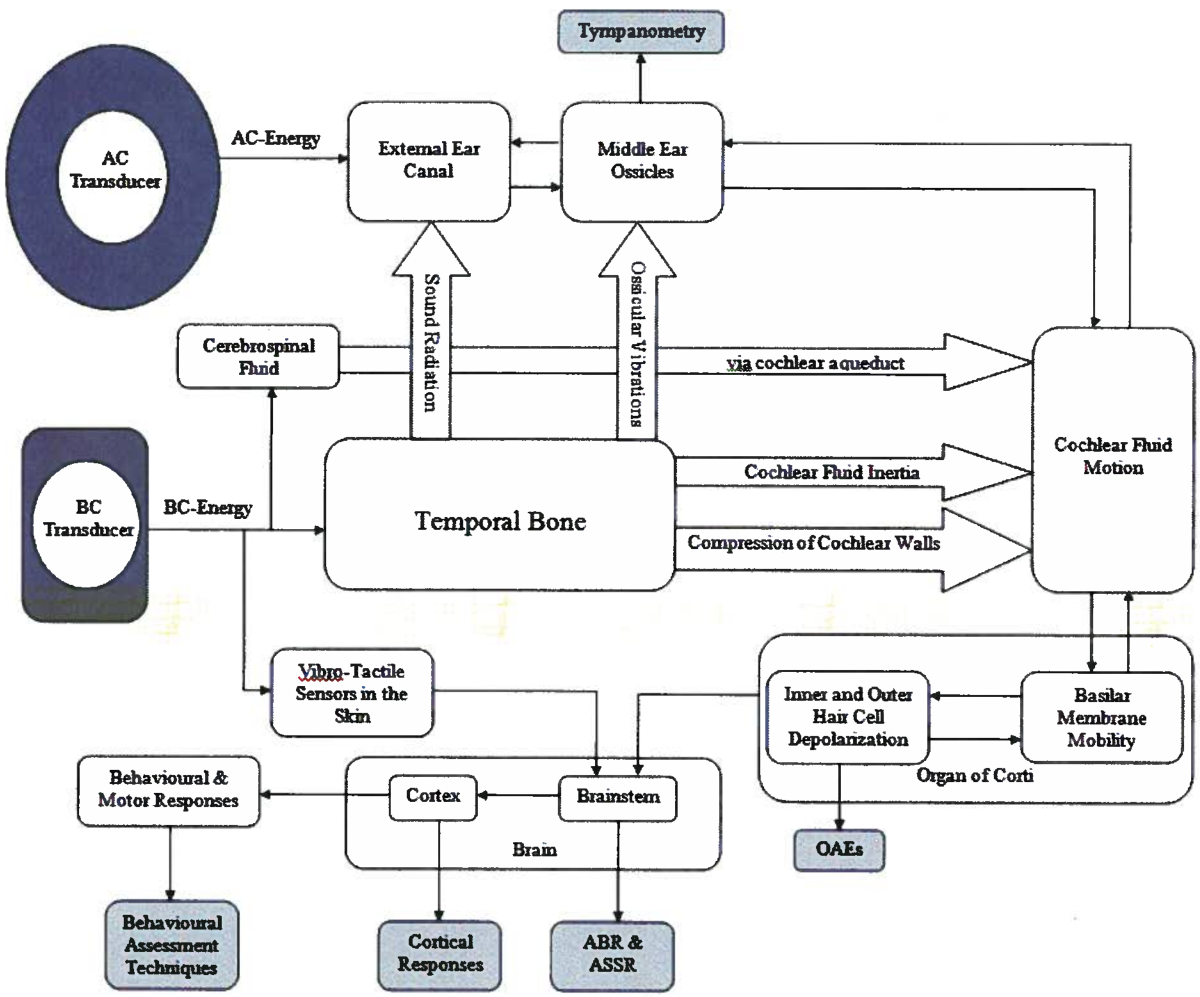

Figure 1.4 Diagram of air- and bone-conduction auditory pathways. All auditory, vestibular and tactile input is integrated in the brain. The methods used to assess different parts of the auditory system are shown in shaded boxes, next to the highest-order structure that they assess. Adapted from Stenfelt and Goode (2005).

Although these five distinct pathways have been outlined, Stenfelt and Goode (2005) suggest that only a few components significantly contribute to bone-conduction hearing at any given time. For example, studies that investigated hyper-sensitivity to bone-conducted sound suggest that that cochlear fluid inertia is likely the most important contributor to low-frequency bone-conduction hearing in unoccluded adult ears (Kucuk et al., 1991; Rosowski, Songer, Nakajima, Brinsko & Merchant, 2004; Stenfelt & Goode, 2005; Yoshida & Uemura, 1991). However, in occluded adult ears, sound radiated in the ear canal has contributed more significantly to bone-conduction hearing, particularly in the low-frequencies (Huizing, 1960; Stenfelt & Goode, 2005; Stenfelt, Wild, Hato & Goode, 2003; Tonndorf, 1966). This causes an enhanced sensitivity to low-frequency sounds, known as the "occlusion effect". Although other transmission pathways may not be the main contributor to bone-conduction hearing under specific conditions, they may continue to show minor contributions to the bone-conduction mechanism (reviewed in Stenfelt & Goode, 2005).

Although it is accepted that many factors contribute to bone-conduction hearing, the majority of studies have been completed on adult subjects, not infants. Substantial immaturities exist in infant neural development as well as in the size and structure of the infant skull, middle ear and ear canal compared to adults, which will be discussed later. Because of this maturation, the mechanical properties contributing to bone-conduction hearing may differ between infants and adults. In support of this claim, no occlusion effect is observable in young infants, suggesting different contributions of bone-conduction mechanisms compared to adults (Small et al., 2007). However, further investigations are needed in this area of research.

1.6 Maturation of Hearing Sensitivity

Because infants are not born with adult-like hearing sensitivities, it is necessary to understand how infant thresholds mature. It is also necessary to compare the maturational effects of air- and bone-conduction hearing sensitivity to determine the efficacy of using an air-bone gap to diagnose a conductive hearing loss in infants of different ages. For adults, air- and bone-conduction hearing sensitivities across frequencies differ when measured in dB SPL and dB re: 1 μN, respectively. The use of hearing level (dB HL) has become the standard to account for these differences in hearing sensitivities across frequency. Reference equivalent sound pressure level (RETSPL) and reference equivalent force level (RETFL) conversion factors have been created to convert the air- and bone-conduction thresholds of normal-hearing adults, respectively, to a baseline of 0 dB HL. As a result, there is no air-bone gap or frequency-dependent differences in the hearing sensitivities of normal-hearing adults in dB HL. This allows for the presence of an air-bone gap to indicate a conductive component to a hearing loss. Behavioural assessment of infants is also measured using this dB HL scale with the same RETSPL and RETFL conversion factors and the same criteria for air-bone gap identification. However, recent physiological studies have shown distinct frequency-dependent differences in both air- and bone-conduction hearing sensitivities in dB HL for infants compared to adults. These differences may affect the diagnostic value of an air-bone gap for identification of a conductive hearing loss. This section will discuss the maturational trends observed in infancy by both behavioural and physiological studies for air- and bone-conduction hearing.

1.6.1 Maturation of Air-Conduction Hearing

Physiological (ABR and ASSR) Thresholds

Over the past three decades, many studies have reported ABR and ASSR thresholds of infants and adults across frequency. A meta-analysis of 32 air-conduction tone-evoked ABR studies of infants, children and adults with normal hearing or sensorineural hearing loss (Stapells, 2000b) revealed that air-conduction tone-evoked ABR thresholds were able to accurately predict behavioural thresholds in normal-hearing and hearing-impaired individuals of all ages. Similarly, studies that directly compared frequency-specific ABR and ASSR responses in the same individuals also showed similar results (Steuve & O'Rourke, 2003; Vander Werff, Brown, Gienapp & Schmidt, 2002). A second meta-analysis was conducted by Tlumak et al. (2007) for 56 published air-conduction ASSR studies. This meta-analysis concluded that air-conduction ASSRs also accurately predict behavioural air-conduction thresholds in normal hearing and hearing-impaired individuals over six years of age. However, Johnson and Brown (2005) note that the ASSR may more accurately estimate behavioural thresholds for individuals with steeply sloping audiograms. Additional air-conduction studies have also shown that frequency-specific ASSRs can accurately estimate behavioural thresholds in infants (e.g., Cone-Wesson et al., 2002a,b; Luts, Desloovere & Wooters, 2006; Han, Mo, Liu, Chen & Huang, 2006; Rance & Rickards, 2002; Rance et al., 2006). However, Rance et al. (2006) suggest that even though behavioural thresholds can be accurately estimated by ASSRs, the ASSRs are more affected by maturational development and are more variable across individuals compared to tone-evoked ABRs. They therefore conclude that frequency-specific ABRs still offer a more reliable estimation of hearing sensitivity for the neonatal population (Rance et al., 2006).

Based on most of these studies, similar trends in hearing sensitivity and frequency-specific maturation of auditory responses have been observed using behavioural and physiological techniques. Studies that have investigated the maturation of infant air-conduction hearing have shown that ABR thresholds at all frequencies improve with age (Stapells, 2000b), but that high-frequency thresholds tend to improve earlier in life than low-frequency thresholds (Balfour, Pillon & Gaskin, 1998; Klein, 1984; Sininger, Abdala & Cone-Wesson, 1997; Werner, Folsom & Mancl, 1994). Klein (1984) studied the hearing sensitivities of infants 2 through 28 weeks of age to show the maturation of their ABR thresholds. The findings show an improvement in hearing sensitivity at both 500 and 4000 Hz with increasing age, improving more at 4000 Hz. Therefore, high-frequency air-conduction thresholds improve earlier than low-frequency air-conduction thresholds (Klein, 1984). Although other ABR studies did not investigate the maturation of infant thresholds directly, they did find similar improvements in hearing sensitivities with increasing frequency (0.5, 2 and 4 kHz) for infants of different ages (Balfour et al., 1998; Sininger et al., 1997; Stapells et al., 1995; Swanepoel et al., 2008). In summary, infants show frequency-dependent differences in their air-conduction ABR thresholds where high-frequency thresholds are significantly better than low-frequency thresholds, particularly for older infants (e.g., Balfour et al., 1998).

Recent ASSR investigations have also shown similar trends in the frequency-specific maturation of hearing sensitivities (Picton et al., 2003; Savio et al., 2001; Rance et al., 2006). Rance et al. (2006) studied ASSR compared to ABR hearing thresholds in infants 2, 4 and 6 weeks of age at 500 and 4000 Hz. They found similar threshold trends for both ABR and ASSR measures, showing significantly better thresholds at 4000 Hz compared to 500 Hz. Other studies have supported this finding, showing elevated ASSR thresholds at 500 Hz, consistent with previous air-conduction data on neonatal and infant subjects (Lins et al., 1996; Rance & Rickards, 2002; Savio et al., 2001; Van Maanen & Stapells, 2009). Overall, most air-conduction ASSR studies have reported that estimated thresholds at 500 Hz are at least 5-10 dB poorer than those at 4000 Hz (Cone-Wesson et al., 2002b; Lins et al., 1996; Luts & Wouters, 2004; Picton et al., 1998; Picton, Dimitrijevic, Perez-Abalo & Van Roon, 2005; Swanepoel et al., 2008)

Although a couple studies on adult hearing sensitivities (Gorga, Stern, Ross & Nagler, 1988; Stapells et al., 1990) have shown some improvement in air-conduction hearing sensitivity with increasing frequency, similar to the trends observed for older infants, this finding is not consistent across studies (reviewed in Stapells, 2000b; reviewed in Tlumak, 2007). Rather, most studies which investigated adult thresholds found minimal differences across frequency (.5, 1, 2 and 4 kHz); and even in the cases when slight differences are observed, they do not follow the same frequency-dependent pattern as is observed in infant thresholds (Gorga et al., 1988, 1993; Klein, 1984; Kodera, Yamane, Yamada & Suzuki, 1977; Purdy, Houghton, Keith & Greville, 1989; Stapells et al., 1990; Suzuki, Hirai & Horiuchi, 1977, 1981; Werner-Olsho et al., 1993).

Behavioural MRLs

Many behavioural studies have also assessed infant air-conduction hearing sensitivity. Some have used BOA while others have used VRA or other OPP procedures. Across these studies, there is large variation in age of participant, stimulus type, stimulus duration and transducer type used. Each of these variables can affect the MRLs obtained. However, despite these differences, similar trends can be seen across studies with progressively improving hearing sensitivity as the child matures from birth to adulthood (Note: these studies did not account for SPL differences in the ear canal).

Eisele, Berry and Shriner (1975) and Weir (1979) studied infants one-to-nine days old, observing their motor responses to auditory stimuli. The MRLs obtained from these neonates were 59-80 dB SPL, depending on the frequency tested. Comparatively, studies of infants 1-1.5 months of age showed a considerable improvement in MRLs to 40-64 dB SPL (Werner & Gillenwater, 1990; Hoversten & Moncur, 1969; Trehub et al., 1991; Werner & Mancl, 1993). Progressive improvement continues to be observed in infants three months of age (i.e., MRLs at 26-47 dB SPL) (Werner-Olsho, Folsom & Mancl, 1993), and even small improvements in infants' MRLs up to 6-12 month of age (i.e., MRLs 12-38 dB SPL) (Bargones, Werner & Marean, 1995; Berg & Smith, 1983; Moore & Wilson, 1978; Nozza, 1995; Nozza & Hensen, 1999; Nozza & Wilson, 1984; Parry et al., 2003; Sinnott, Pisoni & Aslin, 1983; Trehub, Schneider & Endman, 1980; Werner-Olsho et al., 1993). These infant response levels closely approach adult sensitivities of 4-30 dB SPL by 12-18 months of age, but are not expected to be fully mature until approximately 10 years of age (Werner, 1996).

In addition to thresholds improving progressively with age, these infant data show some frequency- and age-dependent trends. The youngest infants show very similar responses across frequency (Eisele et al., 1975; Weir, 1979) whereas three month-olds begin to respond better to high- compared to low-frequencies (Werner-Olsho et al., 1993). As infants approach six months of age and beyond, they continue to show improved MRLs in response to high-frequency stimuli, showing better thresholds in the high compared to low frequencies (e.g., Parry et al., 2003).

A VRA study done by Parry et al. (2003) summarizes the frequency-dependent trends seen in infant behavioural responses. They determined air-conduction MRLs of normal-hearing infants 8-12 months of age at 0.5, 1, 2, and 4 kHz, finding that the average MRLs for 500 and

1000 Hz were significantly poorer than the average MRLs at 2000 and 4000 Hz. Compared to adult warbled-tone thresholds (Franklin et al., 2009), Parry and colleagues' (2003) infant MRLs show poorer responses in the low frequencies and better responses in the high frequencies (Figure 1.5) (Parry et al., 2003). The trend seen in these air-conduction responses show the same frequency-dependent trend as physiological air-conduction responses (e.g., Balfour et al., 1998; Stapells et al., 1995), but an opposite frequency-dependent trend compared to physiological bone-conduction responses (e.g., Small & Stapells, 2008a), which will be discussed later.

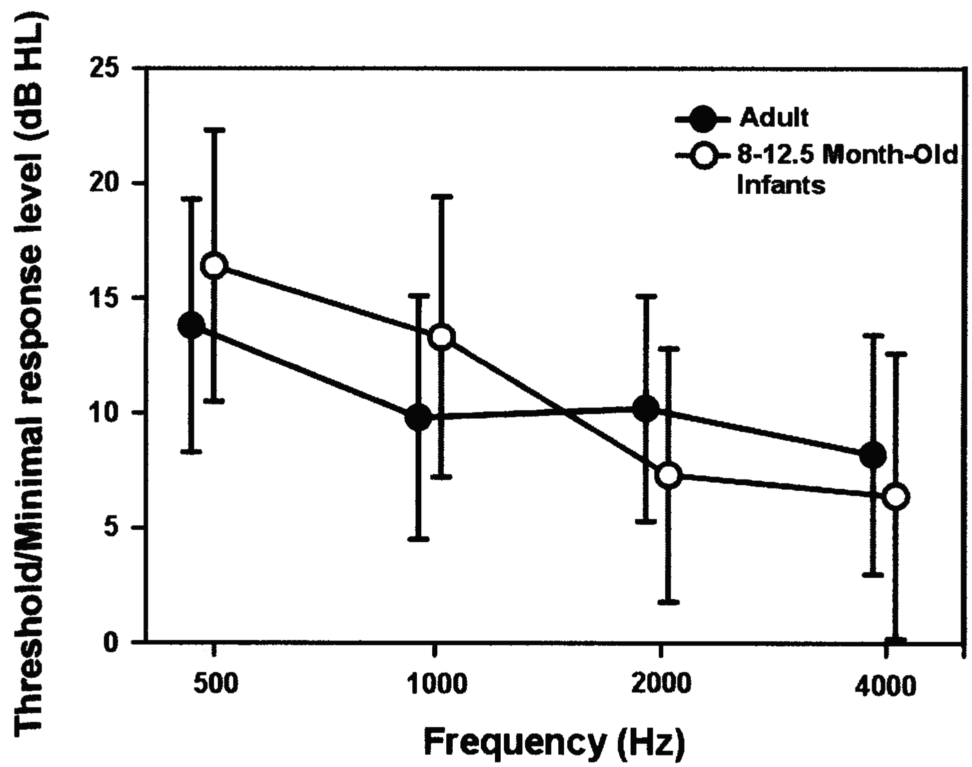

Figure 1.5 Comparison between infant and adult air-conduction hearing sensitivity (dB HL) in response to warbled-tones through insert earphones. Adapted from Franklin et al. (2009) (adult data) and Parry et al. (2003) (infant data).

1.6.2 Maturation of Bone-Conduction Hearing

Assessment of bone-conduction hearing is an integral component of the typical audiometric assessment and is fundamental to the identification of the type of hearing loss (Haughton and Pardoe, 1981). However, only a limited number of bone-conduction maturational studies have been conducted. Studies that investigate the anatomical and physiological development of the auditory system indicate that many changes occur during the first few years of life. Any developmental changes that affect the structure and properties of the outer-, middle- or inner-ear, the skull, its sutures, or neurons also have the potential to affect an individual's bone-conduction hearing. This is because all of these structures potentially contribute to the passage of acoustic energy from its source, the bone oscillator, to the cochlea. In order to properly assess infants, it is necessary to understand the frequency-dependent trends in bone-conduction hearing for normal-hearing infants throughout development.

Physiological ABR and ASSR Threshold

Infant bone-conduction thresholds are not consistent across studies. Cone-Wesson and Ramirez (1997), Gorga et al. (1993), and Stuart, Yang and Green (1994) found that bone-conducted click-ABR thresholds in adults were poorer than those of infants whereas Cornacchia, Martini and Morra (1983) found no difference between the bone-conduction click-ABR thresholds of toddlers and adults. One key difference between these studies is the age of the children tested: although Stuart et al. (1994) tested infants 0-96 days-old, Cornacchia et al. (1983) tested toddlers 16-20 months of age. Essentially, these click-ABR threshold data suggest that there is the potential for age-related, maturational changes in bone-conduction hearing.

Because click-ABR studies are not ideal for the diagnosis of hearing loss at specific frequencies, subsequent studies have attempted to determine the frequency-specific maturational changes of bone-conduction hearing using brief-tones and continuous stimuli. Studies using ABR and ASSR techniques have identified that there are differences in infant's hearing-sensitivity of bone-conducted sound across frequencies and compared to adults (Foxe & Stapells, 1993; Small & Stapells, 2006; Stapells & Ruben, 1989; Swanepoel, et al., 2008). Specifically, studies on infant ASSRs (Small & Stapells, 2006; 2008; Swanepoel et al., 2008) and infant ABRs (Foxe & Stapells, 1993; Stapells & Ruben, 1989) have found that "normal hearing" young infants' bone-conduction thresholds are better in the low compared to high frequencies. Maturation involves a worsening in low-frequency thresholds and an improvement in high-frequency thresholds, to become progressively more adult-like up to 24 months of age (Small & Stapells, 2008a). These trends are opposite from those observed in the maturation of air-conduction responses.

At 500 Hz, both ABR and ASSR studies have found that infant thresholds are significantly better than adult thresholds (Cone-Wesson & Ramirez, 1997; Foxe & Stapells, 1993; Small & Stapells, 2006; 2008; Stapells & Ruben, 1989). ABR thresholds at 500 Hz have been shown to worsen by approximately 20-25 dB from birth to six months of age and continuing to worsen only slightly (by 2-7 dB) beyond six months of age into adulthood (Foxe & Stapells, 1993; Stapells & Ruben, 1989). Similarly, a recent ASSR study by Small and Stapells (2008a) found that young infants (mean age of 4.0 months) have 17-19 dB better bone-conduction thresholds at 500 Hz compared to adults, as shown in Figure 1.67. However, older infants (mean age of 18.2 months) have shown only 8-11 dB better bone-conduction thresholds at this frequency compared to adults (Figure 1.6). Together, these studies show a maturational effect where bone-conduction hearing at 500 Hz worsens with maturation from infancy into adulthood.

Only ASSR studies have compared infant and adult thresholds at 1000 Hz. The same maturational trend was seen for 1000 Hz as for 500 Hz (Figure 1.6). Thresholds worsened from infancy into adulthood, showing the greatest change for infants younger than 11 months of age and only a small change for infants 12-24 months of age into adulthood (Small & Stapells, 2008a). In addition, young infants hearing sensitivity was significantly better at 1000 Hz compared to all other frequencies (0.5, 2 and 4 kHz). Older infants showed a similar trend where hearing sensitivity was significantly better at 1000 Hz compared to 2000 Hz, approached significance compared to 500 Hz, but was not significantly different from 4000 Hz (Figure 1.6), showing some maturational changes between infant groups.

Both ABR and ASSR studies of infants up to six months of age have shown that infants have poorer bone-conduction thresholds at 2000 Hz compared to adults, opposite to the findings for 500 and 1000 Hz (Foxe & Stapells, 1993; Small & Stapells, 2006; Stapells & Ruben, 1989). Small & Stapells (2006) show that bone-conduction thresholds of premature newborn infants are approximately 19 dB HL worse than adults, progressing to being only approximately 8 dB HL worse than adults by 17 weeks of age. However, threshold measures of premature infants are done in hospital rooms with high ambient noise, and may therefore not be as reliable. A more recent ASSR study by Small and Stapells (2008a) has found that, although the hearing sensitivity of young and older infant groups were not significantly different from each other at 2000 Hz, their hearing sensitivity was approximately 6 dB poorer compared to adults' responses at this frequency (Figure 1.6) (Small & Stapells, 2008a). In addition, hearing sensitivity at 2000 Hz was significantly worse compared to all other frequencies for both infant groups (except at 500 Hz for the older infant group). Therefore, with maturation, ABR and ASSR thresholds at 2000 Hz tend to improve with age from infancy into adulthood, opposite to the trend which is seen in the low frequencies.

Because most ABR studies have not included data for bone-conduction hearing at 4000 Hz, only the study by Cone-Wesson and Ramirez (1997) can be used to suggest ABR maturational trends. Their results show minimal differences in bone-conduction hearing sensitivity between newborn infants and adults at 4000 Hz (Cone-Wesson & Ramirez, 1997). Similarly, a recent ASSR study by Small and Stapells (2008a) also showed no maturational effect at 4000 Hz. Overall, their mean 4000 Hz ASSR thresholds did not differ by more than 3 dB across all ages (Figure 1.6) (Small & Stapells, 2008a).

In adults, Small & Stapells (2008a) reported that there are no significant differences in the bone-conduction ASSR thresholds from 1000-4000 Hz, and that thresholds at 500 Hz are worse compared to higher frequencies. Overall, even considering the slight differences that are observed between studies, adults show worse low-frequency thresholds compared to infants (e.g., Picton et al., 2003; Small & Stapells, 2008a).

Because the ASSR study by Small and Stapells (2008a) compares different infant age groups across frequency using the same experimental design, the hypotheses formulated in the present study will be based on their findings, as presented in Figure 1.6. To summarize their results, young infants show better bone-conduction hearing thresholds at 500 and 1000 Hz compared to adults, with worse bone-conduction thresholds at 2000 Hz and similar bone-conduction thresholds at 4000 Hz. These maturational differences in thresholds are seen across all frequencies, except 4000 Hz, until at least 24 months of age.

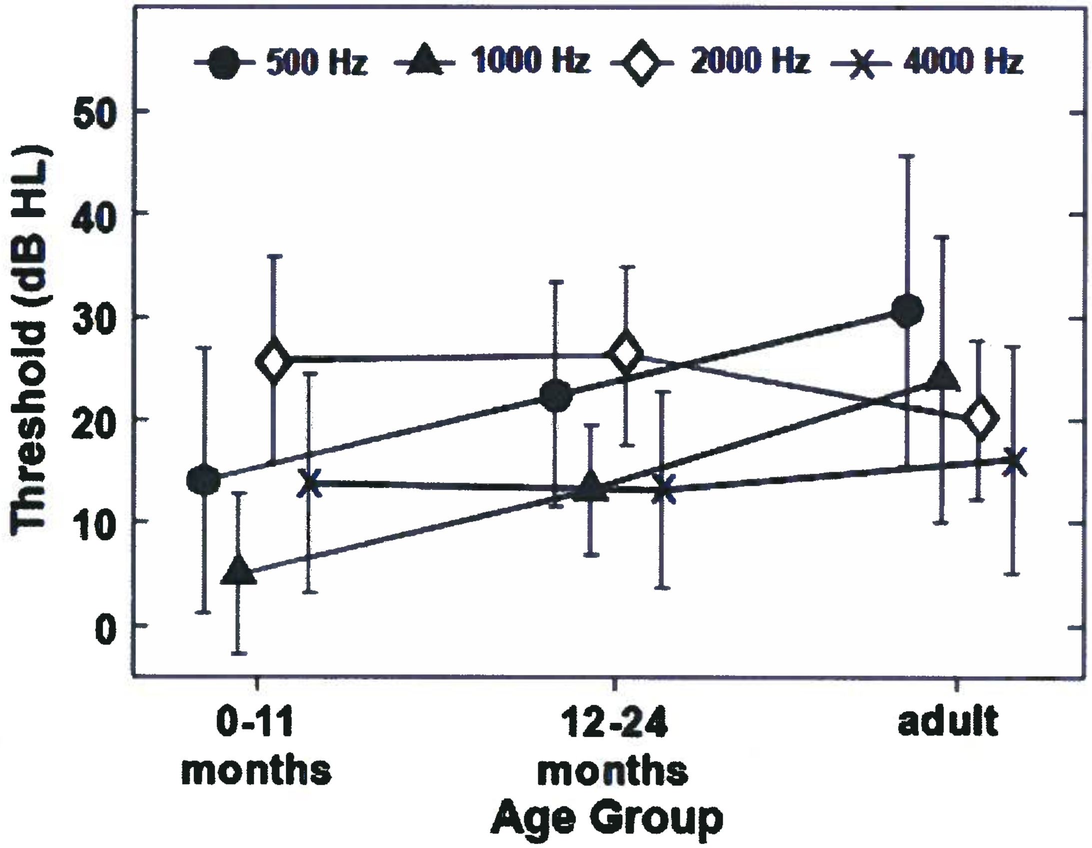

Figure 1.6 Mean bone-conduction ASSR thresholds (+/- 1SD) at each carrier frequency for 35 young infants, 13 older infants and 18 adults with normal hearing (Small & Stapells, 2008a).

In addition to physiological thresholds, infant-adult differences in air-conduction responses exist in ABR wave V latencies. Many infant ABR studies have shown a rapid decrease in wave I, III and V latencies with increasing age (Moore, Perazzo & Braun, 1995; Moore, Ponton, Eggermont, Wu & Huang, 1996; Ponton, Eggermont, Coupland & Winkelaar, 1992, 1993; Ponton et al., 1994; Ponton, Moore & Eggermont, 1996). Specifically, latencies have been found to decrease most rapidly within the first year of life with additional slower decreases in latency up to three-to-five years of age (Moore et al., 1996; Ponton et al., 1992, 1993, 1994, 1996). It has been suggested that these changes in axonal conduction velocity are due to progressive myelination of neural structures along with brainstem growth and improving synaptic efficiency (reviewed in Ponton et al., 1994).

In response to bone-conducted stimuli, the frequency-specific infant-adult differences in wave V latencies are minimal at 2000 Hz. However, infant wave V latencies at 500 Hz are significantly shorter than those of an adult (Foxe & Stapells, 1993; Nousak & Stapells, 1992). This suggests that low-frequency bone-conducted stimuli may be more intense and, therefore, more effectively transmitted to the cochlea in infancy (Nousak & Stapells, 1992). However, changes in latency do not always reflect changes in threshold.

Behavioural MRLs

Although many studies have investigated the effect of certain pathologies, such as otosclerosis on bone-conduction hearing, the maturation of bone-conduction hearing in infancy has not been extensively investigated using behavioural techniques. To date, only one study specifically reported behavioural bone-conduction responses in infancy. A study by Gravel (1989) investigated the ability to use clinical behavioural assessment methods for audiological follow-up in infants 6-12 months of age with middle-ear pathology. Her study was not specifically focussed on bone-conduction hearing sensitivity. However, she graphically reported the bone-conduction MRLs they obtained through VRA assessments. In general, Gravel's (1989) preliminary results appear to show no observable differences in air- or bone-conduction thresholds across frequency and no identifiable difference between air- and bone-conduction thresholds in the normal-hearing infant group, contrary to the maturational trends observed physiologically. Further investigation of the maturation of behavioural bone-conduction hearing sensitivities in infants is needed.

1.6.3 Explanations for Infant-Adult Differences

Many factors have been suggested to account for the infant-adult differences observed in air- and bone-conduction thresholds/MRLs. Some of these are sensory factors, such as middle-ear impedance, skull anatomy and neural processing; others are non-sensory, including attention, habituation, and stimulus/reinforcer factors which were reviewed earlier (Nozza, 1995; Parry et al., 2003). This section focuses on the sensory factors that have been proposed to explain infant-adult maturational changes in hearing sensitivity and briefly outlines the non-sensory contributions to infant-adult differences, which are discussed in more detail throughout this study.

Research using air-conducted stimuli has been primarily used to investigate the contributions of the cochlea and neural structures to the maturation of hearing sensitivity (Ponton et al., 1996; Rance et al., 2006; Sininger et al., 1997). Many studies have found that once an infant reaches term, at approximately at 38-40 weeks post-conceptional age (PCA), the infant cochlea is fully mature in both structure and function (Abdala, 1996, 1998, 2000; Abdala, Sininger, Ekelid & Zeng, 1996; Eggermont, Brown, Ponton & Kimberley, 1996; Brown, Sheppard & Russell, 1995; Bargones & Burns, 1988; Lavigne-Rebillard & Pujol, 1987, 1988; Bredberg, 1968; Pujol, 1985; Tognola et al., 2005). During gestation, the functional components of the cochlea, including the mass and stiffness of the basilar membrane (Harris & Dallos, 1984) as well as the structure of the inner- and outer-hair cells (Davis, 1983; Romand, 1987; Rotteveel et al., 1987), develop and mature affecting cochlear sensitivity. Essentially, early in development, the cochlea matures at the mid-basal turn (i.e., 4000-6000 Hz) and development proceeds towards both the lower and higher frequencies during gestation (Bredberg, 1968; Rübsamen & Lippe, 1998). Recent studies also support these early findings that the infant cochlea is fully mature in both its structure and function by 38 weeks PCA (Abdala & Keefe, 2006; Tognola et al., 2005). Because of this, the maturation of other structures must be responsible for additional infant-adult differences in hearing sensitivity during the first 24 months of life.

Unlike the cochlea, the auditory brainstem is not completely mature until approximately 3-5 years after birth (Moore et al., 1995, 1996; Rance & Tomlin, 2006; Salamy, 1984; Ponton et al., 1992, 1993, 1994, 1996). Myelination at the level of the auditory brainstem begins during gestation (Moore et al., 1995). However, myelination continues until at least one year after birth (Moore et al., 1995). Because ABR and ASSR measures rely on the synchrony of electrical impulses in the cochlear nerve and auditory brainstem, increases in myelination were thought to contribute to the observed decrease in ABR latencies and changes in thresholds observed during maturation. Ponton et al. (1996) proposed a model that attempted to match the development of neuro-anatomical structures within the auditory nerve and brainstem to the maturation of the ABR response. Specifically, this model proposed that, although the auditory nerve and parts of the auditory brainstem mature at different rates and may be fully mature at birth, the entire auditory brainstem is not completely mature until at least 2 years of age (Ponton et al., 1996). This Ponton model suggests that longer interpeak latencies (i.e., wave I-II, III-IV, etc.), as observed in early infancy, may reflect either slower axonal conduction velocities and/or immaturities in synaptic transmission. Conduction velocity may reflect the effect of axonal myelination, as suggested by Moore et al. (1995). However, Ponton's model suggests that axonal conduction velocities are mature by 40 weeks PCA, and that the observed maturation of ABR interpeak intervals throughout the first couple years of life represents the maturation of energy transmission across neural synapses.

Research using both air- and bone-conducted stimuli has studied the maturation of the skull, outer-, and middle-ear and their contributions to infant ABR latencies and thresholds within the first two years of life. The overall size of an infant's skull is much smaller than that of an adult. Throughout the first two years of life, maturation occurs in both the size and density of the mastoid bone (Eby & Nadol, 1986) and in the fusion of skull sutures (Anson & Donaldson, 1981). At birth, an infant's skull bones are connected to each other by flexible cartilaginous sutures that become rigid and calcified during maturation (Anson & Donaldson, 1981). These flexible sutures separate cranial bones from each other, containing bone-conducted energy within the stimulated cranial bone (Stuart, Yang and Stenstrom, 1990). As a result, the energy does not spread as efficiently across flexible cartilaginous sutures as it does across the ossified sutures in adults, potentially contributing to the observed infant-adult differences (Stuart et al., 1990). Also, Foxe and Stapells (1993) have suggested that the smaller temporal bone in infants concentrates the energy of bone-conducted stimuli, resulting in a more intense signal being transmitted to the cochlea. Overall, studies have hypothesized that skull immaturities may enhance the intensity and efficiency of energy transmission to the cochlea, contributing to the observed infant-adult differences in ABR thresholds and latencies (Foxe & Stapells, 1993; Stuart et al., 1990; Sohmer, Freeman, Geal-Dor, Adelman & Savion, 2000; Yang et al., 1987). A recent study by Small and Stapells (2008a) supported this hypothesis by showing frequency-dependent differences in the bone-conduction ASSR thresholds of infants compared to adults. Therefore, the maturation in the size and structure of the infant skull may be a contributing factor to changes in the observed maturation of infant thresholds.

In addition to maturation of the skull, changes have also been observed in the volume, and resonances of the ear canal and middle ear as these structure grow and becomes more calcified, compared to their more cartilaginous composition in early childhood (Bingham, Jenstad & Shahnaz, 2009; Keefe, Bulen, Arehart & Burns, 1993; Keefe & Levi, 1996; Sanford & Feeney, 2008; Shahnaz, Cai & Qi, 2008; Sininger et al., 1997). It is well established that these structural differences result in higher SPLs at the tympanic membrane in infants compared to adults (Kruger & Ruben, 1987). However, even though ear canal and middle-ear changes occur during maturation which potentially affects the level of the stimulus reaching the cochlea, it has been suggested that these changes do not account for infant-adult differences in bone-conduction hearing sensitivity (Rance & Tomlin, 2006; Sininger et al., 1997; Stenfelt & Goode, 2005).

An air-conduction ABR study by Sininger et al. (1997) found that the stimulus level in the ear canal that is needed to elicit a threshold was 3 and 24 dB SPL higher at 500 and 4000 Hz, respectively, in infants compared to adults. Similar trends were also observed in an air-conduction ASSR study by Rance and Tomlin (2006). Both of these studies concluded that air-conducted stimuli at the tympanic membrane must be slightly more intense at 500 Hz and much more intense at 4000 Hz to elicit threshold responses in infants compared to adults. Although these studies calibrated the stimuli at the level of the tympanic membrane to account for infant-adult differences in ear-canal resonances, neither study directly accounted for infant-adult differences in the middle-ear (i.e., residual amniotic fluid in the infant middle ear). Sininger et al. (1997) claimed that although the attenuation of sounds through a newborn middle ear can account for some frequency-dependent infant-adult differences in air-conduction thresholds (Keefe et al., 1993), the attenuation is not large enough to account for all these infant-adult differences. Similarly, although Rance and Tomlin (2006) concede that the infant middle ear may subtly attenuate air-conducted sounds, they claim that, based on other studies (Owens, McCoy, Lonsbury-Martin & Martin, 1992; Qui, Stucker & Welsh, 1998), the presence of OAEs negates the contribution of significant middle-ear pathology (i.e., negative middle-ear pressure or resolving middle-ear effusion) to the observed air-conduction thresholds. As a result, both of these studies concluded that most infant-adult differences in air-conduction thresholds result primarily from immaturities in the development at the level of the auditory brainstem, and not as a result of immaturities in the ear canal and middle-ear structures.

Because the primary mechanism underlying bone-conduction hearing in adult unoccluded ears does not involve the osseotympanic pathway (i.e., through the ear canal and middle-ear) (Stenfelt & Goode, 2005), bone-conduction thresholds are even less affected than air-conduction thresholds by ear-canal and middle-ear development. Stapells and Ruben (1989) found better bone-conduction thresholds at 500 Hz in infants compared to adults both for infants with normal hearing and those with conductive losses. This finding supports the conjecture that an osseotympanic pathway is unlikely to contribute to infant bone-conduction hearing.

In adults, occlusion of the ear canal improves low-frequency bone-conduction thresholds (Aazh, Moore, Payvandi & Stenfelt, 2005; Khanna et al., 1976; Killion et al., 1988; Stenfelt et al., 2002; Stone & Moore, 1999; Zwislocki, 1975), termed the "occlusion effect" (Tonndorf, 1966). However, this "occlusion effect" has not been observed in infants in recent ASSR studies (Small et al., 2007; Small & Hu, submitted). Specifically, no more than a 4 dB difference in bone-conduction threshold was observed across all frequencies in infants when their ears were occluded, whereas adults showed up to a 20 dB improvement in their low-frequency thresholds (Dean & Martin, 2000; Small et al., 2007). A recent study by Small and Hu (submitted) also found no improvement in bone-conduction thresholds for occluded ears in younger and older infants. Despite this, they found that the SPL in the occluded infant ear canal increased when a bone-conduction signal was presented at the mastoid, even more so than in an adult ear. As a result, Small and Hu (submitted) concluded that infants only have the "osseo" portion of the osseotympanic pathway (i.e., up to the level of the tympanic membrane) as there is no difference in bone-conduction hearing between occluded and unoccluded infant ears. This absence of an "occlusion effect" in infants demonstrates a significant infant-adult difference in the mechanisms underlying bone-conduction hearing.

In addition to sensory factors contributing to infant-adult differences in hearing sensitivities, non-sensory factors also contribute, particularly when thresholds are measured behaviourally (Nozza, 1995). Nozza's (1995) study suggested that although infant-adult differences in hearing sensitivity are largely due to differences in sensory processing, a portion of the infant-adult differences must also be attributed to other factors, such as the infant's tendencies to behave differently from adults (i.e., attending less well to the stimulus) and their tendencies to habituate to the stimuli (Hogan, 1975). Studies that have attempted to separate the influence of sensory and non-sensory factors on the maturation of hearing sensitivity have been inconclusive. Some studies determined that non-sensory factors could account for only 4 dB of infant-adult differences at 500, 1000, and 2000 Hz, whereas the remaining differences were due to immaturities in peripheral sensitivity and/or sensory processing (Nozza, 1995; Nozza & Hensen, 1999). Other studies have found that peripheral sensitivity is not the primary contributor to the elevated behavioural MRLs (Werner, Folsom & Mancl, 1994; Werner-Olsho et al., 1993). Overall, it is possible that both sensory and non-sensory factors influence the maturation of hearing sensitivity in infancy, but the amount that each of these factors contributes is still unknown.

1.6.4 Implications of the "Maturational" Air-Bone Gap

Further investigation into infant behavioural bone-conduction thresholds is necessary because of its clinical implications for the determination of an air-bone gap. The air-bone gap in adults is the difference between measured air- and bone-conducted thresholds in dB HL. The identification of a "conventional" air-bone gap is used to identify the presence of a conductive hearing loss. However, physiological studies have indicated that normal-hearing infants show poorer air-conduction thresholds and better bone-conduction thresholds in dB HL in the low frequencies compared to adults (Small & Stapells, 2006, 2008a; Vander Werff, Prieve, & Georgantas, 2009). Although Small and Stapells (2008) did not directly compare the air- and bone-conduction ASSR thresholds of infants, they did identify the opposite frequency-dependent trend for infant bone-conduction thresholds compared to what has been found for infant air-conduction thresholds (Van Maanen & Stapells, 2009). A recent tone-evoked ABR study by Vander Werff et al. (2009) compared air- and bone-conduction ABR thresholds in both infants and adults at 500, 2000 and 4000 Hz. They showed that, unlike adults, the relationship between air- and bone-conduction thresholds in infants differed with stimulus frequency. In this study, normal hearing infants showed a mean air-bone gap of 15 dB at 500 Hz, whereas infants who were classified as presenting with a conductive hearing loss showed an even larger mean air-bone gap (Vander Werff et al., 2009). As a result, comparison of air- and bone-conduction physiological thresholds of normal-hearing infants show a "maturational" air-bone gap that reflects a calibration problem, not the presence of an a conductive pathology. Therefore, without adjusting for infant-adult differences in bone-conduction hearing sensitivity, it is incorrect to conclude that the presence of an air-bone gap in infant audiological assessments is sufficient to diagnose a conductive hearing impairment.

1.6.5 Purpose of the Present Study

Because most infants 6-30 months of age are tested clinically using VRA, it is necessary to determine if behavioural testing elicits the same frequency- and age-dependent differences in bone-conduction MRLs for normal-hearing infants, as have been observed physiologically. This study proposes to provide behavioural data on the bone-conduction MRLs of normal-hearing infants 7-30 months of age. These data are important because accurate differential diagnosis of conductive, sensorineural and mixed hearing losses in infants rely on the age- and frequency-dependent comparison of air- and bone-conduction thresholds (Jahrsdoerfer, Yeakley, Hal, Robbins & Gray, 1985; Stapells & Ruben, 1989).

CHAPTER 2: Behavioural Bone-Conduction Responses of Infants 7-30 Months of Age to Warbled-Tone Stimuli

2.1 Introduction

Assessment of bone-conduction hearing is an essential component of an audiological test battery, when air-conduction thresholds are elevated, because it provides the information necessary to differentiate between sensorineural, conductive and mixed hearing losses (Wright & Cannella, 1969). Bone-conduction hearing in adults is well understood; however, further investigation is required to expand on our limited knowledge of bone-conduction hearing in infants. A number of studies have investigated the maturation of bone-conduction thresholds in infants using physiological measures, such as the auditory brainstem response (ABR) (e.g., Cone-Wesson & Ramirez, 1997; Foxe & Stapells, 1993; Stapells & Ruben, 1989) and the auditory steady-state response (ASSR) (e.g., Small & Stapells, 2006; 2008a). These studies report frequency-dependent infant-adult differences in bone-conduction hearing. Only one published study has reported behavioural bone-conduction thresholds for infants, and only did so for one infant age group (Gravel, 1989). Therefore, maturational changes in bone-conduction hearing sensitivity have not been directly investigated using behavioural methods. The purpose of the present study is to obtain behavioural bone-conduction thresholds of infants at different ages to determine whether frequency-dependent patterns, which have been found to exist when infant bone-conduction thresholds are measured physiologically, continue to exist when infant bone-conduction thresholds are measured behaviourally.

Normal hearing sensitivity from 500 through 4000 Hz is essential for normal speech and language development particularly for infants and toddlers (e.g., Ling, 1976; Paul & Quigley, 1987). In order to assess the hearing status of infants, many jurisdictions have implemented universal newborn hearing screening (UNHS) programs which aim to screen the hearing of all infants by one month of age, diagnose a hearing loss by three months of age and provide intervention by six months of age when a hearing loss is diagnosed (Joint Committee on Infant Hearing, 2007; Hyde, 2005; B.C. Early Hearing Program, 2008). Physiological measures such as the auditory brainstem response (ABR) and otoacoustic emissions (OAE) are used to assess the integrity of the cochlea, auditory nerve and brainstem in these UNHS programs. These physiological measures are used because infants younger than six months of age are not old enough to elicit reliable behavioural responses for the estimation of a hearing loss (Cone-Wesson, 2003). Infants identified through UNHS programs with a hearing loss or at high risk for hearing loss are routinely monitored until at least three years of age. Other infants who are not identified through UNHS programs may also be seen clinically after six months of age due to progressive, late-onset, acquired or mild hearing losses. Physiological tests, such as the ABR and auditory steady-state response (ASSR) can be used to assess frequency-specific hearing thresholds of older infants; however, they are more time consuming than behavioural tests and may require sedation (Jerger, Hayes & Jordan, 1980). They also do not measure higher-order neural processing abilities as do assessment tools that require the detection of an active behavioural response to the stimulus. Therefore, infants older than six months of age are mainly assessed physiologically when behavioural responses cannot be reliably obtained or if a confirmation of results is desired. For infants older than six months of age, behavioural methods are the gold standard for assessing hearing sensitivities (Delaroche et al., 2004; Moore et al., 1977). These measures provide a complete assessment of the auditory system and are clinically obtained whenever possible for the estimation of hearing thresholds.

Visual reinforcement audiometry (VRA) is the most common behavioural method of assessment for infants 6-30 months of age, and is used both clinically and in research (Delaroche et al., 2004; Widen, 1993; Widen et al., 2000). VRA procedures use operant conditioning to pair a visual reward with an infant's reflexive head-turn in response to auditory stimuli (Delaroche et al., 2004; Gravel & Traquina, 1992; Liden & Kankkunen, 1969; Moore et al., 1977, 1992; Moore & Wilson, 1978; Portmann & Delaroche, 1986; Suzuki & Ogiba, 1960). The responses obtained in reliable VRA testing reflect an infants' hearing threshold, or may be slightly suprathreshold. Conventionally, the responses obtained through VRA testing are referred to as minimal response levels (MRLs), which reflect the softest sound that reliably elicits the desired behavioural response 50% of the time. Widen et al. (2000) described a clinical VRA protocol that can obtain reliable MRLs for infants 8 to 12 months of age within one testing session. It is this protocol which will be followed in the present study.

With maturation, infant air-conduction thresholds improve with age across all frequencies (500-4000 Hz) (Balfour et al., 1998; Klein, 1984; Sininger et al., 1997; Stapells et al., 1995; Werner et al., 1994). However, most studies show that high-frequency infant thresholds mature earlier in life than low-frequency thresholds, resulting in better high- compared to low-frequency thresholds in infants compared to adults. Maturation of infant bone-conduction hearing, which has only been described in detail based on physiological data, shows better low- and similar high-frequency thresholds compared to adults, opposite to the trends identified for air-conduction maturation. Further research is needed to determine whether a frequency-dependent relationship exists for bone-conduction hearing of younger and older infants when measured behaviourally.

Previous VRA, ABR and ASSR studies have determined that both infant behavioural and physiological thresholds are not mature by two years of age (Balfour et al., 1998; Bargones et al., 1995; Berg & Smith, 1983; Cone-Wesson & Ramirez, 1997; Foxe & Stapells, 1993; Klein, 1984; Moore & Wilson, 1978; Nozza, 1995; Nozza & Hensen, 1999; Nozza & Wilson, 1984; Parry et al., 2003; Sininger et al., 1997; Sinnott et al., 1983; Small & Stapells, 2006, 2008a; Stapells, 2000b; Stapells & Ruben, 1989; Stapells et al., 1995; Trehub et al., 1980; Werner et al., 1994; Werner-Olsho et al., 1993). These studies have also determined that infant hearing thresholds and MRLs show different frequency-dependent trends for both air- and bone-conduction hearing. ABR, ASSR and behavioural measures have all found that low-frequency air-conduction thresholds/MRLs are at least 5-10 dB poorer compared to high-frequencies (Cone-Wesson et al., 2002b; Lins et al., 1996; Luts & Wouters, 2004; Parry et al., 2003; Picton et al., 1998, 2005). Recent infant ASSR studies show the opposite trend for bone-conduction thresholds; low-frequency bone-conduction thresholds are at least 10-20 dB better compared to high-frequencies (Small & Stapells, 2006, 2008a). Gravel (1989) reported the first and only data on infant behavioural bone-conduction MRLs in response to tonal stimuli. This study compared air-conduction MRLs in infants 6-12 months of age in the presence and absence of middle-ear pathology. They included bone-conduction MRLs for both groups but did not statistically analyze these data. The infants with normal middle-ear status did not appear to show any difference between air- and bone-conduction MRLs across frequency, which is different from the air- and bone-conduction frequency-dependent trends described earlier (Parry et al., 2003; Small & Stapells, 2008a).

Bone-conducted stimuli are directly measured in force levels (dB re: 1 μN) and air-conducted stimuli are measured in sound pressure levels (dB SPL). Because both air- and bone-conduction thresholds measured in these units show frequency-dependent differences in hearing sensitivity, they are converted into comparable units (i.e., "hearing level" or dB HL). At each frequency, mean adult air- and bone-conduction thresholds are converted to 0 dB HL using reference equivalent sound pressure level (RETSPL) and reference equivalent force level

(RETFL) conversion factors, respectively (ANSI S3.6-1996). If there is a difference between air- and bone-conduction thresholds at a given frequency, this is referred to as an air-bone gap which normally indicates the presence of a conductive component to the hearing loss. However, the physiological data obtained for normal-hearing infants suggests that, in the absence of middle-ear pathology, infants present with better bone- compared to air-conduction thresholds (in dB HL), particularly in the low frequencies (Small & Stapells, 2008a; Vander Werff et al., 2009). This reflects differences in hearing sensitivities for air- and bone-conducted stimuli in infants compared to adults (Vander Werff et al., 2009). Therefore, if there is a difference between infant air- and bone-conduction thresholds, this "maturational" air-bone gap may not reflect a conductive hearing loss.

2.1.1 Summary and Rationale for the Study

Because most infants 6-30 months of age are assessed behaviourally, it is important to understand the frequency- and age-dependent developmental trends in normal-hearing infant behavioural bone-conduction MRLs. It is necessary to understand these differences so that conductive and sensorineural hearing impairments can be accurately diagnosed for appropriate and timely management to be provided (Jahrsdoerfer et al., 1985; Stapells & Ruben, 1989).

Because infant-adult differences in behavioural and physiological air-conduction MRLs have already been thoroughly investigated, there is no need to replicate these well-established findings. The goal of the present study is to obtain behavioural bone-conduction MRLs for infants 6-30 months of age with normal cochlear function using a clinical VRA procedure. This study proposes to determine whether the frequency-dependent bone-conduction trends that have been found physiologically are also present when measured behaviourally. By studying frequency-dependent MRLs in infants 7-15 and 18-30 months of age with normal cochlear function, we can improve our understanding of the maturation of the infant auditory system and provide preliminary "normal levels" for infant bone-conduction MRLs obtained by VRA.

2.2 Methods and Materials

2.2.1 Participants

A total of 48 children who were 7-30 months of age were recruited from the community and tested. Eleven children were excluded from the study because either the reliability of their responses was poor or they did not condition to the task. The remaining 37 infants were divided into two groups, (i) 17 "young" infants [age range of 7-15 months; mean age of 10.6 months] and (ii) 20 "older" infants [age range of 18-30 months; mean age of 23.0 months].

Hearing was screened using transient-evoked otoacoustic emissions (*Madsen AccuScreen Pro* TEOAEs). The screening test calculates the statistical probability that an emission was recorded from 1400-4000 Hz. Tympanometry was used for infants on whom the TEOAE results were inconclusive. Tympanograms, when measured, were obtained using a 226-Hz probe tone in screening mode. Abnormal tympanograms were defined as those for which static immitance and tympanometric width could not be calculated (flat tympanograms). Because flat tympanograms are an indication of potential middle-ear pathology, any infant presenting with flat tympanograms was referred for medical follow-up, although they were not excluded from the study.

Table 2.1 describes the hearing status for each of the participants in each age group based on TEOAE and immittance screening findings. Infants who passed the TEOAE and/or tympanometry screening in both ears were considered to be at low risk for significant hearing-loss and were included in the study. There were seven infants on whom the TEOAE and tympanometry screening could not be completed bilaterally, including three infants with a unilaterally flat tympanogram. The reason for being unable to obtain a complete hearing screening did not reflect the infant's hearing abilities, but rather resulted from fussiness and/or the parent's wish to cease testing. These infants were still included[2] in the study because previous research has suggested that a mild conductive component will have minimal-to-no effect on bone-conduction hearing sensitivity (Fria et al., 1985; Gravel, 1989; Stapells & Ruben, 1989).

Table 2.1 Hearing screening results for infant participants in each age group using TEOAEs and immitance (tympanometry) assessment methods (n=37).

TEOAE and Immittance Screening Results				**8-15 mo (n=17)**	**18-30mo (n=20)**
OAE (Ear 1)	**OAE** (Ear 2)	**Tymp** (Ear 1)	**Tymp** (Ear 2)		
PASS	PASS	____	____	8	10
PASS	CNT/Refer	____	Normal	4	2
PASS	CNT/Refer	____	Flat	1	1
CNT/Refer	CNT/Refer	Normal	Normal	2	4
CNT/Refer	CNT/Refer	Normal	CNT	1	0
CNT/Refer	CNT/Refer	Normal	Flat	0	1
CNT/Refer	CNT/Refer	CNT/Refer	CNT/Refer	1	2

[2] Note: the bone-conduction MRLs for these infants were similar to those of infants who passed the hearing screening, being no worse than 20 dB HL across frequencies, which is the current standard in clinical practice that indicates normal bone-conduction hearing sensitivity (B.C. EHP, 2008).

2.2.2 Stimuli

The stimuli were bone-conducted warbled-tones at 500, 1000, 2000 and 4000 Hz. Each stimulus was modulated to +5% of the centre-frequency at a rate of 5 Hz. Each tone was presented for two seconds with no less than five seconds between each stimulus presentation. All stimuli were generated using a GSI-61 audiometer and presented through a Radioear B-71 bone-oscillator.

The bone-oscillator was held in position against the temporal bone or mastoid within two centimetres of the pinna, by either a steel headband, an elastic headband fastened with Velcro™ or by hand. Table 2.2 shows the number of times each coupling method was used. All techniques provided approximately 450-550 g of force coupling the bone-oscillator to the child's head. For some infants it was necessary to switch the coupling method part way through the study. The steel headband was preferentially used over other coupling methods. A small foam sponge was placed under the steel headband, on the end opposite the bone-oscillator, to add comfort. In the instances where an infant would not tolerate the metal headband, the elastic headband was used, wrapping it entirely around the infants' head and positioned bone-oscillator. If an infant would not tolerate the use of either headband, the assistant, who remained in the sound booth to keep the infant's attention centred, was instructed to hold the bone-oscillator with appropriate force against the infant's head. Small et al. (2007) found that a trained assistant makes the elastic and hand-held bone-conduction coupling methods equally effective for sleeping infants. However, this coupling method was avoided, if possible, as it was challenging to hold the bone-oscillator with constant force on an awake and moving child, especially during a head-turn.

Table 2.2 Number of infants using each coupling method.

Bone-Oscillator Coupling Method	Younger	Older
Metal Headband	10	13
Elastic Headband	5	4
Metal Switched to Elastic Part-way through Testing	0	2
Hand-Held	2	1

2.2.3 Calibration

Using a Larsen Davis System 824 sound level meter and an AMC 493 artificial mastoid, bone-conducted stimuli were calibrated in RETFLs in dB re:1μN. The bone-oscillator was coupled to the artificial mastoid with 550 g of force. Stimuli were calibrated to 0 dB HL for the mastoid, complying with ANSI standards (ANSI S3.6-1996). Stimuli were presented at the dial setting in dB HL. However, calibration correction factors were needed and were applied across frequency to express MRLs in actual dB HL.

2.2.4 Procedure

Testing was performed in a double-walled sound-attenuating booth, at the University of British Columbia in the School of Audiology and Speech Sciences. On average, the ambient noise levels measured in the sound-attenuated booth for one octave bands centred at 500, 1000, 2000 and 4000 Hz were 0, 2, 4 and 6 dB SPL. Each infant participant sat in the centre of the booth on their parent's lap, facing forward. Visual reinforcers were placed approximately 90^0 to the infant's right and left at their eye-level, similar to studies done by Schmida et al. (2003) and

Widen et al. (2000). An assistant was also present in the booth, sitting at a 45^0 angle in front of the infant such that both examiners had a good view of the infant's reactions. The assistant used colourful quiet toys of only moderate interest to focus the child's attention away from the reinforcers between stimulus presentations. The assistant was also responsible for hand-holding the bone-oscillator, if necessary.

The parent wore HDA-200 circumaural earphones (unplugged), Peltor Optime 101 ear-muffs or foam earplugs (E-A-R Classic earplugs). All of these produce enough attenuation to render the bone-conducted test stimuli inaudible to the parent, minimizing the potential for the parent to cue the child's responses. The amount of attenuation provided was not a significant concern as the test stimuli were presented primarily at or near the infants' thresholds/MRLs, making it unlikely that the parent would hear the majority of the stimuli, even without earphones or earplugs.

The examiner communicated with the assistant either through supra-aural earphones or an FM system. The assistant was kept appraised of stimulus presentations so that the infant could be effectively conditioned and sometimes re-conditioned to the task upon request. However, the assistant was not responsible for interpreting infant responses.

An adaptive VRA protocol was followed to obtain infant MRLs to the warbled-tone bone-conducted stimuli (see Appendix B). The order of test conditions was partially randomized and partially prioritized for each subject. Specifically, all initial conditioning occurred to a high-frequency warbled-tone stimulus, randomized between 1000, 2000 or 4000 Hz. A 500-Hz warbled-tone was always tested second, in order to prioritize obtaining MRLs to a high- and low-frequency stimulus for each child. The remaining two high-frequency stimuli were randomized for presentation after 500 Hz. To recondition, the examiner adapted the test protocol, including the order of test conditions, the order of frequency presentation and the type of stimulus (e.g., pure tone, pulsed tone, warbled tone and speech) for infants who proved to be difficult to condition, or to regain the child's attention.

The goal of this test protocol (adapted from Widen et al., 2000) was to obtain accurate MRLs in one visit without considerably deviating from clinical testing protocols. The examiner began each trial with a four-second observation interval, after which a probe tone was presented at 30 dB HL. If the child responded with a head turn during or within four seconds of stimulus presentation, reinforcement was provided by lighting up a mechanical toy or video for two seconds. If the probe tone did not elicit a spontaneous head turn, the stimulus level was increased to 40 or 50 dB HL and the child was conditioned by the assistant to turn to the reinforcer. After two paired conditioning trails, a probe trial was presented where reinforcement was only provided after a correct head turn. In difficult situations, conditioning trials were repeated, changing the stimulus level, type of stimulus, or mode of stimulus presentation (Parry et al., 2003; Widen et al., 2000). Sometimes, when switching the test frequency it was necessary to re-condition the child, which was completed in a similar manner to the first conditioning trial. Once two correct head-turn responses followed two consecutive probe-trials at the same intensity, the examiner proceeded to search for the MRL.

A 10-dB step size was used to estimate the infant's MRL at each frequency (Small & Stapells, 2008a; Widen et al., 2000). To obtain these MRLs, a bracketing system of 20 dB down, 10 dB up was followed. A silent period of at least five seconds was inserted between each stimulus presentation to minimize false responses. During these interstimulus intervals, control trials three seconds in duration were interspersed on a random basis. If the infant falsely responded during more than 30% of the control trials, the test was considered unreliable and was either repeated after a break or the infant was asked to return on another day.

The MRLs were identified as the lowest level at which the child responded correctly to two out of three stimuli at each frequency (Parry et al., 2003; Widen et al., 2000). Testing continued until MRLs at all four frequencies were reliably obtained or until further testing was not possible. The latter occurred for a variety of reasons: failure to condition, habituation to the task or stimulus, crying or fidgeting, refusal to wear the bone oscillator, or because of inconsistent and/or unreliable responses. The examiner ranked each child's responses as having either "good" or "poor" reliability. All infant's results ranked with "poor" reliability (n = 11 infants) were excluded from the study. For the young infant group, MRLS were obtained for 17 subjects at 500, 1000 and 2000 Hz and 16 subjects at 4000 Hz. For the older infant group, MRLs were obtained for 20, 18, 19 and 19 subjects at 500, 1000, 2000 and 4000 Hz, respectively.

The average testing time was one hour, and up to two return visits were possible for infants whose testing could not be completed in one assessment. However, more than one return visit was never required.

2.3.2 Data and Statistical Analyses

MRLs were averaged across all subjects at each frequency within each age group. The 90^{th} percentile represents the number of responses present at each intensity expressed in cumulative percent, calculated for each frequency. A mixed Analysis of Variance (ANOVA) was used to compare infant MRLs across frequencies (500, 1000, 2000 and 4000 Hz) within each age group and across age groups. Huynh-Feldt epsilon corrections for repeated measures were used as appropriate for the mixed ANOVA. In this study, the factors were the age of the participant and the stimulus frequency. Missing data were dealt with using case-wise deletion. Neumann-Keuls *post hoc* comparisons were performed for significant frequency effects and interactions, where present. To analyze the relationship between infant age and MRL, Pearson product-moment correlation coefficients were calculated for each frequency. Statistical significance for the linear regression analysis was determined using a one-way ANOVA. Results of the mixed-ANOVA, *post hoc* tests, and the linear regression were considered significant if $p < .05$.

2.4 Results

2.4.1 90th Percentile Results

Conventionally, "normal hearing levels" refer to the lowest level at which present responses were elicited from greater than 90% of the participants. Figure 2.1 shows the cumulative percent of present behavioural responses for all infants at each frequency (500, 1000, 2000 and 4000 Hz). Specifically, 90% or more of the infants had MRLs at or better than 15, 12, 19 and 21 dB HL at 500, 1000, 2000 and 4000 Hz, respectively. Because no significant age-dependent differences were observed at any frequency in the present behavioural study, it was not necessary to determine the 90^{th} percentile for each age group separately. Therefore, the data used to calculate these 90^{th} percentile results include MRLs from both the younger and older infant age groups.

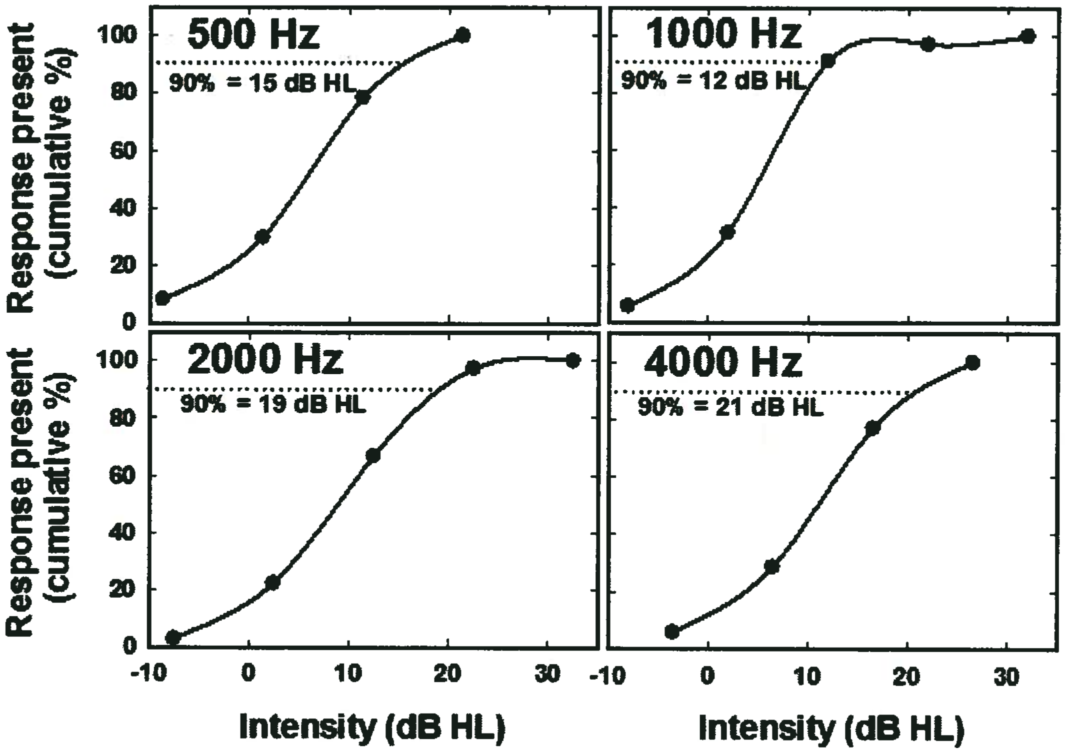

Figure 2.1 Cumulative percentage of present behavioural responses at 500, 1000, 2000 and 4000 Hz for all infants (n=37).

2.4.2 Behavioural Bone-Conduction MRLs

Overall, both infant groups show better mean MRLs in the low (500 and 1000 Hz) compared to high frequencies (2000 and 4000 Hz). As shown in Figure 2.2, the same frequency-dependent trends were observed for both age groups: the mean MRLs were 4-5 and 3-8 dB better for low compared to high frequencies for younger and older groups, respectively. The distribution of all MRLs (500-4000 Hz) for each infant are represented in Figure 2.3 with a linear regression showing no significant age-effects ($r = 0.07$, $p = .415$). Similarly, no age-effects were observed at individual frequencies (500 Hz: $r = 0.14$, $p = 0.339$; 1000 Hz: $r = 0.12$, $p = .511$; 2000 Hz: $r = 0.04$, $p = .812$; 4000 Hz: $r = 0.25$, $p = .150$).

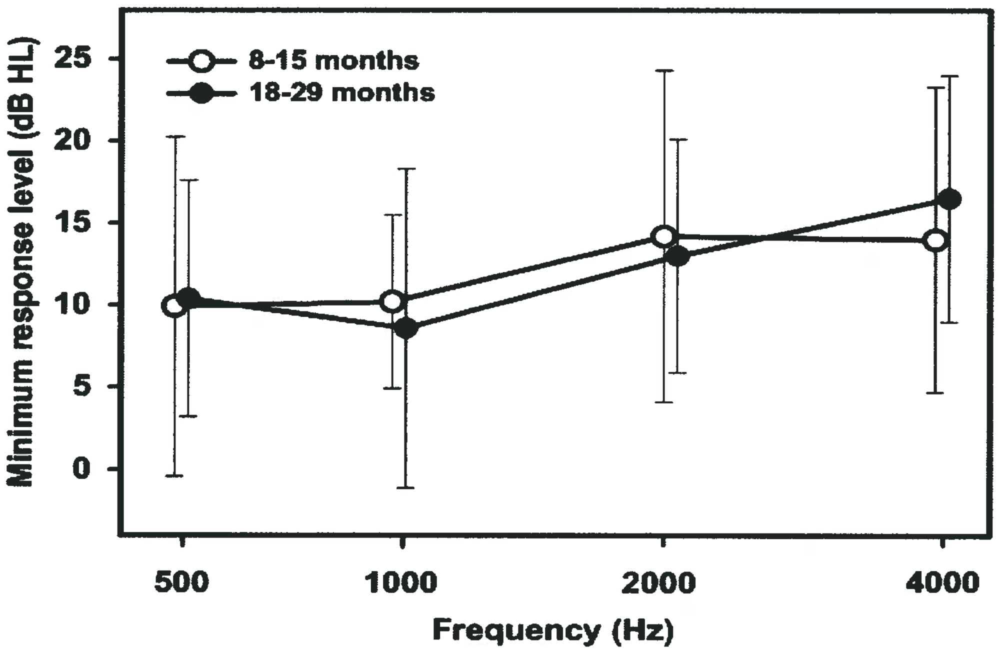

Figure 2.2 The effect of frequency on mean behavioural MRLs (+/-1 SD) for young infants (n = 16-17) and older infants (n = 18-20) with normal cochlear functioning.

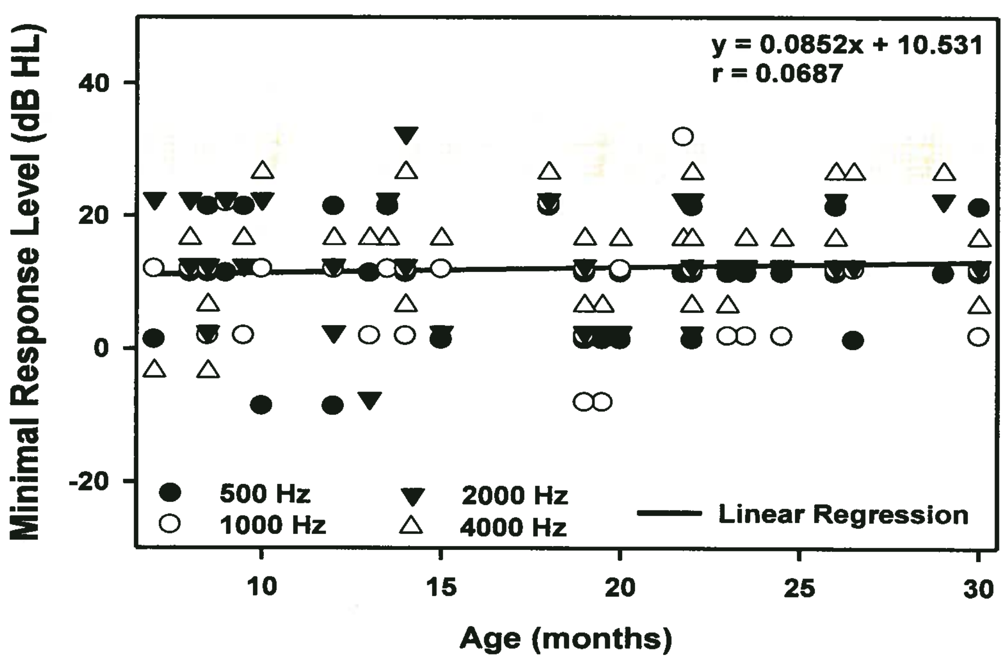

Figure 2.3 Graphical representation of a linear regression analysis comparing age in months to MRLs (n=143) obtained from all 37 infants. The regression equation (y = mx + b; where y is the MRL (dB HL), m is the slope of the regression, x is age (months), and b is the y-intercept) and correlation coefficient (r) are shown in the upper right corner of the graph.

A mixed-ANOVA comparing bone-conduction mean MRLs across age and frequency revealed no significant effect of age on mean MRLs [$F(1,31)=0.001$, $p=.972$], nor any interaction between age and frequency [$F(3,93)=0.541$, $\varepsilon = 0.981$, $p=.652$]. However, there was a significant effect of frequency on mean infant MRLs [$F(9,93)=4.411$, $\varepsilon = 0.981$, $p=.006$]. *Post-hoc* comparisons of this frequency effect indicated no significant difference between MRLs at 500 and 1000 Hz ($p=0.998$) or between MRLs at 2000 and 4000 Hz ($p=.506$). However, the MRL at 500 Hz was significantly better than MRLs at both 2000 Hz ($p=.031$) and 4000 Hz ($p=.014$). The MRL at 1000 Hz was also significantly better than MRLs at 4000 Hz ($p=.026$) and approaching significance when compared to 2000 Hz ($p=.077$).

To ensure our inclusion criteria were valid, a sub-analysis of the data was performed comparing the mean infant MRLs obtained from all infant data (n=37) with the mean infant MRLs obtained only from infants who passed the TEOAE and/or tympanometry screening bilaterally (n=30) (i.e., subgroup), as shown in Table 2.3. The differences between the mean MRLs of these groups varied from zero to 1.8 dB. For the subgroup, a mixed-ANOVA comparing bone-conduction mean MRLs across age and frequency also revealed no significant effect of age on mean MRLs [$F(1,26)=0.334$, $p=.567$], nor any interactions between age and frequency [$F(3,78)=0.966$, $\varepsilon = 0.972$, $p=.959$]. However, there was a significant effect of frequency on mean infant MRLs [$F(3,78)=2.89$, $\varepsilon = 0.972$, $p=.042$]. Because the results of both mixed-ANOVAs (i.e., for all infant data and for the subgroup) revealed the same trends, and because the mean MRLs are no more than 1.8 dB different between groups at any frequency, we included all 37 infants in this study[3].

[3] For (i) the 3 young and (ii) the 4 older infants with inconclusive screening results and/or a unilaterally flat tympanogram, mean MRLs in dB HL (+/- 1SD) are (i) 4.7 (11.5), 11.9 (0), 22.5 (10) and 16.5 (17) and (ii) 6.4 (5.8), 5.3 (5.8), 15.8 (5.8) and 16.5 (10) at 500, 1000, 2000 and 4000 Hz, respectively.

Table 2.3 Sub-analysis: the mean infant MRLs in dB HL (+/-1 SD) calculated from all infant data compared to those calculated only from those infants who passed the hearing screening bilaterally.

		n	500 Hz	1000 Hz	2000 Hz	4000 Hz
			Frequency			
7-15 months	Subgroup*	14	9.92 (10.2)	9.80 (5.8)	12.5 (10.1)	13.4 (9.3)
	All †	**17**	**9.0** (10.3)	**9.81** (5.3)	**14.3** (10.1)	**14.0** (9.3)
18-30 months	Subgroup*	16	11.35 (7.3)	9.28 (10.3)	12.5 (7.3)	16.5 (7.3)
	All †	**20**	**10.4** (7.2)	**8.6** (9.7)	**13.0** (7.1)	**16.5** (7.5)

* Only infants who passed the TEOAE and/or tympanometry screening bilaterally.
† Includes all infants who were reliably tested, including those with inconclusive screening results and/or unilaterally flat tympanograms.

CHAPTER 3: Discussion and Conclusion

3.1 Discussion

This is the first study to examine age- and frequency-dependent maturational changes in bone-conduction MRLs for younger and older infants using a behavioural VRA technique. The results show that frequency-dependent differences exist in bone-conduction MRLs of infants to warbled-tones. Similar to previously reported physiological bone-conduction thresholds, low frequencies are better than high frequencies (in dB HL) (Foxe & Stapells, 1993; Small & Stapells, 2008a).

The present study found that the mean low-frequency MRLs at 500 and 1000 Hz are 3-8 dB better across both infant groups compared to the mean high-frequency MRLs at 2000 and 4000 Hz. No significant differences were observed in the mean MRLs at 500 versus 1000 Hz or at 2000 versus 4000 Hz. Small and Stapells (2008a) found trends that were consistent with the these findings where low-frequency thresholds were significantly better than the high frequency thresholds. However, they observed slight differences in statistical significance across frequencies. In particular, Small and Stapells (2008a) found that the differences between 500 and 1000 Hz ASSR thresholds were not significant, although their *p*-value closely approached significance. They also found that 2000 and 4000 Hz ASSR thresholds were significantly different from each other for infants younger than 24 months of age.

No significant interactions were observed between age and MRL at any frequency in the present study. From 500-4000 Hz, the mean behavioural bone-conduction MRLs ranged from 9-14 dB HL in young infants and 8-16 dB HL in older infants. There were no significant interactions between frequency and age, nor were there any significant differences in MRLs across age. This differs from ASSR studies which found a significant difference in bone-conduction thresholds across age obtained from infants 0-11 months of age (mean age of 4 months) and 12-24 months of age (mean age of 18 months) at 500 and 1000 Hz (Small & Stapells, 2008a).

Small and Stapells (2008a) compared infant-adult differences in ASSR thresholds across frequencies. In order to achieve a similar behavioural comparison, adult behavioural thresholds must be compared to the present study's infant MRLs, preferably using thresholds obtained with the same warbled-tone stimuli. However, no studies have directly assessed adult behavioural bone-conduction thresholds in response to warbled-tone stimuli. Although this limits our ability to make an accurate comparison, it can be assumed that because normal-hearing adults show a 0 dB air-bone gap in dB HL, their air-conduction thresholds should accurately reflect their bone-conduction thresholds when reported in these units. Infant-adult differences in the present study are identified by comparing Franklin et al.'s (2009) adult behavioural air-conduction thresholds in response to warbled-tone stimuli with the infant behavioural bone-conduction MRLs in response to warbled-tone stimuli obtained from the present study, as shown in Table 3.1. Comparatively, infant bone-conduction MRLs are better in the low frequencies and worse in the high frequencies compared to adults, similar to infant-adult ASSR differences (Small & Stapells, 2008a). However, the extent of the infant-adult differences at each frequency differs between physiological and behavioural studies. Specifically, (i) at 500 Hz, infant bone-conduction ASSR thresholds were 8-19 dB better than adult ASSR thresholds, whereas infant behavioural bone-conduction MRLs were only 3-5 dB better than adult behavioural thresholds; similarly, (ii) at 1000 Hz, infant bone-conduction ASSR thresholds were 8-19 dB better than adult bone-conduction ASSR thresholds, while no more than a 1 dB difference was observed between infant and adult behavioural bone-conduction thresholds/MRLs; (iii) at 2000 Hz, infant bone-conduction ASSR thresholds were 6 dB worse than adult bone-conduction ASSR thresholds, whereas infant behavioural bone-conduction MRLs were 3-4 dB worse than adult behavioural thresholds; and finally (iv) at 4000 Hz, infant bone-conduction ASSR thresholds were no more than 3 dB worse than adult bone-conduction ASSR thresholds, whereas infant behavioural bone-conduction MRLs were 6-8 dB worse than adult behavioural thresholds. All behavioural infant-adult differences in bone-conduction hearing, except at 4000 Hz, were smaller compared to the physiological bone-conduction ASSR infant-adult differences obtained by Small and Stapells (2008a).

Table 3.1 Infant and adult air- and bone-conduction behavioural thresholds/MRLs in dB HL (+/- 1 SD) obtained using warbled-tone stimuli.

STUDY	MODE	AGE	500 Hz	1000 Hz	2000 Hz	4000 Hz
PRESENT STUDY*	BONE*	7-15 mo	9.0 (10.3)	9.81 (5.3)	14.3 (10.1)	14.0 (9.3)
	BONE**	18-30 mo	10.4 (7.2)	8.6 (9.7)	13.0 (7.1)	16.5 (7.5)
Parry et al. (2003)	AIR†	8-12.5 mo	16.4 (5.9)	13.3 (6.1)	7.1 (5.5)	6.4 (6.2)
Franklin et al. (2009)	AIR◊	Adult	13.8 (5.5)	9.8 (5.3)	10.2 (4.9)	8.2 (5.2)

Warbled tones, mastoid placement , unoccluded , 10 dB step size, n=17, n=20**
†Warbled tones, insert phones, 5 dB step size, n=46
◊Warbled tones, insert phones, 5 dB step size, n= 25

Overall, opposite frequency-dependent trends are observed for air- and bone-conduction thresholds/MRLs during infancy. Although mean infant air-conduction thresholds/MRLs vary across studies, most appear to be poorer in the low compared to high frequencies (Cone-Wesson et al., 2002b; Lins et al., 1996; Luts & Wouters, 2004; Moore & Wilson, 1978; Nozza, 1995; Nozza & Hensen, 1999; Nozza & Wilson, 1984; Parry et al., 2003; Picton et al., 1998, 2003, 2005; Rance et al., 2006; Trehub et al., 1980). In contrast, physiological studies together with the present behavioural study have all indicated that infant bone-conduction thresholds are poorer in the high compared to low frequencies (Foxe & Stapells, 1993; Rance et al., 2006; Small &

Stapells, 2006, 2008a). As displayed in Table 3.1, comparisons of normal-hearing infant air- and bone-conduction MRLs (Parry et al., 2003; present study) show a difference between air- and bone-conduction thresholds across all frequencies. In the low frequencies, infant bone-conduction MRLs are better than air-conduction MRLs by approximately 6.0-7.5 dB at 500 Hz and 3.5-5.0 dB at 1000 Hz. This difference between air- and bone-conduction MRLs is unlikely to be the result of a conductive hearing loss (i.e., instead it suggests "maturational" air-bone gap). At 2000 and 4000 Hz, however, the mean infant bone-conduction MRLs are at least 6 dB poorer compared to the mean air-conduction MRLs.

Although both physiological and behavioural studies have identified the same overall frequency-dependent trend where infant thresholds/MRLs are better in the low- compared to high-frequencies, slight differences are observed at individual frequencies across studies. Specifically, Small and Stapells' (2008a) ASSR study shows larger frequency- and age-effects along with larger infant-adult differences (except at 4000 Hz) compared to the present behavioural study. However, comparisons between behavioural and physiological results are complicated because of the differences between studies; including differences in participants' ages and the nature of MRL versus physiological threshold measurements. As a result, it becomes difficult to make direct comparisons across studies.

Because physiological methods of threshold assessment are used clinically for infants from birth through two years of age, physiological studies tend to assess infants across this entire age range. Therefore, the mean ages of participants in the younger and older groups for Small and Stapells' (2008a) were 4.0 and 18.2 months, respectively. Unfortunately, VRA assessment techniques are only effective once infants reach approximately six months of age, and cannot be used to elicit reliable responses from younger infants. Because of this, the mean ages of participants in the present study's younger and older age groups were 10.6- and 23.0-months, respectively. Because many of the physiological changes which contribute to infant maturation occur within the first six months of life (i.e., middle-ear changes, skull growth, suture fusion, etc.), even slight differences in the age of infants tested have the potential to introduce variability when comparing data across studies. In particular, age-effects and infant-adult differences are likely to be larger in physiological studies including younger infants, as they were in Small and Stapells (2006, 2008a), because the data include thresholds of younger infants who are likely to have more immature responses compared to infants six months of age or older (Klein, 1984; Picton et al., 1997).

Although behavioural methods of assessment are designed to elicit threshold responses close to an individual's true hearing sensitivities, infant MRLs are potentially more affected by individual preferences and responsiveness than adult thresholds would be. Although any behavioural thresholds (infant or adult) may be elevated in comparison to an individual's true hearing sensitivity, this is particularly the case for infants. Infant MRLs can be affected by the child's interest in the stimulus, reinforcer and task. Because infant's are expected to respond more preferentially to high-frequency speech sounds (i.e., infant-directed speech) (Fernald, 1985; Fernald & Kuhl, 1987; Panneton-Cooper et al., 1997; Pegg et al., 1992), they may also be expected to respond preferentially, with MRLs closer to their true hearing sensitivity, to high-frequency tonal stimuli, while their low-frequency MRLs may be more elevated, appearing worse than their true low-frequency hearing sensitivity. Unlike behavioural methods of assessment, physiological threshold assessment techniques are not affected by infant preferences in this manner, and therefore may more closely estimate an infant's true hearing sensitivity in both the high- and low-frequencies. This could account for the smaller behavioural compared to physiological differences observed between low- and high-frequency infant MRLs. For example, assume an infant has true bone-conduction hearing sensitivity of 0 dB HL at 500 Hz and 20 dB HL at 2000 Hz. Their MRL at 2000 Hz may be close to 20 dB HL because the infant preferentially responds at threshold levels to high-frequency sounds. However, their MRL at 500 Hz may be close to 10 dB HL, slightly suprathreshold compared to their true hearing sensitivity. Assuming that physiological measures do not elicit preferential responses, and estimate infant hearing thresholds similar to their true hearing sensitivity, 0 dB HL at 500 Hz and 20 dB HL at 2000 Hz, we would expect to see larger physiological compared to behavioural differences in low- compared to high-frequencies. For instance, in this example a 20 dB difference would be observed physiologically, whereas a 10 dB difference would be observed behaviourally. This reflects the same trend observed in the present study where the differences observed between high- and low-frequency MRLs are smaller when measured behaviourally compared to physiologically.

Infant-adult differences have also been attributed to the maturational changes in the size and structure of an infant's skull during the first two years of life, including (i) skull growth, (ii) the fusion of membranous sutures particularly around the temporal bone (Anson & Donaldson, 1981), as well as (iii) the rapid increase in width, length and thickness of the mastoid bone (Eby & Nadol, 1986). Yang and colleagues (1987) suggested that the smaller, more isolated temporal bone of infants allows for more efficient transmission of bone-conducted stimuli to the auditory system (Yang et al., 1987), contributing to infants' improved bone-conduction hearing sensitivities. Other studies have suggested that membranous sutures in the infant skull have the effect of isolating the temporal bone, allowing it to oscillate without transferring energy across other cranial bones (Small & Stapells, 2008a; Sohmer et al., 2000; Stuart et al., 1990; Yang et al., 1987). These findings suggest that during infancy, bone-conduction stimulation is more effective across all frequencies, but especially in the conduction of low-frequency sounds.

Researchers have also attempted to explain the improvements in infant low-frequency bone-conduction hearing based on the infant-adult differences in SPL at the ear canal (Cone-Wesson & Ramirez, 1997). Cone-Wesson and Ramirez (1997) found that the SPL of a 500 Hz bone-conducted stimulus measured in an unoccluded ear at the tympanic membrane is 4-22 dB greater in an infant ear canal compared to an adult. They suggested that this increase in SPL in the ear canal gets transmitted through the middle ear and results in an improvement in infant low-frequency bone-conduction thresholds (Cone-Wesson & Ramirez, 1997). If this theory were correct, infants with middle-ear fluid should not show the same improvement in low-frequency bone-conduction thresholds because the middle-ear fluid would prohibit most of the acoustic energy in the ear canal from reaching the cochlea. However, Stapells and Ruben (1989) have shown that this is not the case: they reported that both infants with normal hearing as well as those with conductive hearing loss showed improved thresholds at 500 Hz compared to adults. Also, occlusion of the ear canal, which is known to enhance the SPL at the tympanic membrane in adult ears and improve adult low-frequency bone-conduction thresholds (i.e., the "occlusion effect") (Tonndorf, 1966), does not show the same effect in infants (Small & Hu, submitted; Small et al., 2007). Occlusion of infant ear canals has been found to enhance the SPL of bone-conducted stimuli in the ear canal, particularly in the low-frequencies; however, it does not translate into improved low-frequency bone-conduction thresholds (Small & Hu, submitted). Consequently, this absence of an "occlusion effect" in infant ears also refutes Cone-Wesson and Ramirez's (1997) claim that improved bone-conduction thresholds in infants compared to adults are a result of the greater SPL in an infant ear canal. Therefore, it is likely that ear canal and middle ear structures are not main contributors to the infant-adult differences in bone-conduction thresholds. In order to better understand the bone-conduction mechanism in infant hearing, it is necessary to further investigate these differences: a potential goal for future research in this field.

Neural maturation, particularly at the level of the brainstem, has also been proposed to explain infant-adult differences (Rance & Tomlin, 2006; Sininger et al., 1997). The improved efficiency of synaptic transmission throughout the first 36 months-of-life supports this hypothesis (Moore et al., 1996; Ponton et al., 1992, 1993, 1994, 1996). Small and Stapells (2008a) suggested that infants who have less efficient neural transmission (i.e., newborn infants) may require greater stimulus intensities to elicit threshold responses. This could account for the improvement in thresholds with age as well as the frequency-dependent maturational changes observed. However, further research is also required to prove or disprove this hypothesis. Because the present study does not investigate infant skull and middle-ear characteristics and their contributions to bone-conduction hearing, no new conclusions can be drawn regarding the cause of these infant-adult differences. Further investigation of behavioural as well as physiological bone-conduction mechanisms in larger groups of infants at more discrete ages would be needed to explain how and when the maturational changes observed in bone-conduction hearing occur.

Many studies have identified infant-adult differences in bone-conduction hearing (e.g., Cone-Wesson & Ramirez, 1997; Stapells & Ruben, 1989; Small & Stapells, 2008a). A particular limitation of the present study is that it does not rule out the presence of a mild conductive hearing loss. Shahnaz et al. (2008) as well as Keefe et al. (1993) have shown that the middle-ear structure matures, changing the efficiency of the middle-ear mechanism in young infants. However, studies, including Fria et al. (1985) and Gravel (1989) suggest that even the presence of a significant conductive pathology due to otitis media shows minimal-to-no effect on behavioural bone-conduction responses in infants. Similarly, in a bone-conduction ABR study by Stapells and Ruben (1989), no difference was observed in bone-conduction thresholds at 500 and 2000 Hz for infants presenting with various external and middle ear states (i.e., normal, auditory meatal atresia and otitis media). Other physiological studies have also suggested that no occlusion effect exists for infants younger than two years of age (Small et al., 2007). It would be of interest to the infant bone-conduction mechanism whether the same lack of an occlusion effect exists when measured behaviourally, and because limited data has been collected in reference to the impact of ear canal occlusion and middle-ear status on bone-conduction hearing sensitivity in infancy, it is a clear avenue for further research.

One step further, research should also be performed analyzing the bone-conduction MRLs of infants with all types of hearing impairments (i.e., atresia, otitis media, sensorineural hearing loss, etc.). This is necessary in order for bone-conduction auditory assessment to be accurate in its identification the differences between the normal and abnormal responses for infants of different ages.

3.1.1 Clinical Implications

The findings of the present study indicate that infants up to 30 months of age have normal bone-conduction hearing if they have responses present at 15, 12, 19 and 21 dB HL at 500, 1000, 2000 and 4000 Hz, respectively. These preliminary normative values can be used to establish whether and infant has normal bone-conduction hearing sensitivity.

Due to the opposite trends observed for air- and bone-conduction MRLs in infancy, infants younger than 30 months of age with normal cochlear sensitivity and who are at minimal-to-no risk for conductive pathology are likely to show a "maturational" air-bone-gap in the low frequencies. Although the present study did not assess both air- and bone-conduction MRLs, comparisons between the present bone-conduction study and a similar behavioural air-conduction study (Parry et al., 2003) predicts a 6.0-7.5 dB "maturational" air-bone gap at 500 Hz and a 3.5-5.0 dB "maturational" air-bone gap at 1000 Hz. It is important to realize that this "maturational" air-bone gap must not be considered indicative of a conductive hearing loss, as would be the case if the same air-bone gap were observed in an adult. The possible presence of a "maturational" air-bone gap raises concerns about (i) whether conductive hearing losses are being misdiagnosed (e.g., over-diagnosed) in infants 7-30 months of age, and (ii) whether adjustments should be made in amplification when fitting hearing aids for infants with a conductive hearing loss.

Because current behavioural and physiological studies suggest that comparisons of infant air- and bone-conduction MRLs result in a "maturational" air-bone gap, even in the absence of conductive pathology, there is potential risk for over-diagnosing conductive hearing losses in infancy. According to the present study, it is considered normal for an infant 7-30 months of age to have a "maturational" air-bone gap of approximately 6.0-7.5 dB at 500 Hz. Taking into account the potential for 5 dB error (Studebaker, 1967) on both air- and bone-conduction scores may cause the presence of a 12 or 17 dB air-bone gap in the low-frequencies to be diagnostically irrelevant and not indicative of conductive pathology. As a result, clinicians who diagnose a conductive pathology based on a 15 dB air-bone gap in infant hearing assessments may, in fact, be over-diagnosing conductive impairments assuming this 15 dB is actually due to maturation, rather than to conductive pathology.

It should also be noted that differences in infant air- and bone-conduction MRLs at 2000 and 4000 Hz (i.e., a reversed air-bone gap) may also affect the diagnosis of sensorineural and conductive hearing loss in infants. Conventionally, sensorineural hearing loss is diagnosed by the presence of elevated air- and bone-conduction MRLs with no difference between air- and bone-conduction. However, given that infants in the present study show bone-conduction MRLs that are worse than air-conduction MRLs at 2000 and 4000 Hz, caution must be taken when attempting to differentiate conductive versus sensorineural hearing loss. For example, if air- and bone-conduction MRLs in infants are the same at 2000 and 4000 Hz, there appears to be no air-bone gap and therefore suggests a sensorineural hearing loss. However, in this case, air-conduction thresholds are elevated and bone-conduction thresholds are normal which is actually consistent with a conductive hearing loss.

The frequency-dependent differences observed in both air- and bone-conduction may also affect the amount of amplification that should be provided to an infant when aiding a conductive hearing loss. For example, if a 9-month-old infant presents with a low-frequency air-bone gap of 30 dB (i.e., estimated 500 Hz air- and bone-conduction thresholds at 60 and 30 dB HL, respectively), the present study suggests that, on average, 7 dB of this air-bone gap is likely due to normal differences in air- and bone-conduction hearing sensitivities. It should be concluded that any amplification provided should account for only the conductive impairment (i.e., a 23 dB air-bone gap), and should not amplify for the maturational component (i.e., 7 dB) of the air-bone gap. Therefore, in order to conservatively amplify for an infant's conductive hearing loss, less gain should be provided than would be suggested by the diagnosed air-bone gap. It should also be noted it is necessary to consider adjusting the amount of amplification across different frequencies, to accommodate only for the conductive impairment, and not the "maturational" air-bone gap to avoid over-amplification.

3.2 Conclusion

To conclude, infants 7-30 months of age show frequency-dependent differences in the bone-conduction MRLs when assessed behaviourally using a clinical VRA protocol. Infant MRLs are significantly better in the low compared to high frequencies, reflecting the same frequency-dependent trends that have been observed physiologically. However, unlike physiological findings, the present behavioural study shows smaller frequency-dependent differences between the low and high frequencies and did not find any differences in the MRLs obtained from younger and older infants at any individual frequency or across frequencies.

In normal hearing infants when compared to previously documented air-conduction MRLs (Parry et al., 2003), the present study suggests the existence of a "maturational" air-bone gap that is not indicative of a conductive pathology, when measured in adult dB HL. This raises concern about the accuracy of current clinical diagnostic criteria, which may misdiagnose conductive hearing losses in infants as a result of the identified frequency-dependent differences. Further research must be conducted to estimate behavioural air- and bone-conduction MRLs in the same infant to directly determine the size of the "maturational" air-bone gap. It is also essential to determine whether different pathologies affect infant behavioural bone-conduction MRLs. Finally, based on all of the infant thresholds obtained through ABR, ASSR and behavioural studies, I would also propose to establish an "infant" dB HL value that will reflect infant hearing sensitivities, rather than adults.

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Appendix A: Certificate of Ethics Approval

The University of British Columbia
Office of Research Services
Clinical Research Ethics Board – Room 210, 828 West 10th Avenue
Vancouver, BC V5Z 1L8

ETHICS CERTIFICATE OF FULL BOARD APPROVAL

PRINCIPAL INVESTIGATOR:	INSTITUTION / DEPARTMENT:	UBC CREB NUMBER:
Susan A. Small	UBC/Medicine, Faculty of/Audiology & Speech Sciences	H09-00493

INSTITUTION(S) WHERE RESEARCH WILL BE CARRIED OUT:

Institution	Site
UBC	Vancouver (excludes UBC Hospital)

Other locations where the research will be conducted:
N/A

CO-INVESTIGATOR(S):
N/A

SPONSORING AGENCIES:
- Natural Sciences and Engineering Research Council of Canada (NSERC) - "Maturation of hearing"

PROJECT TITLE:
Behavioral bone-conduction responses of infants 8 months and 18 months of age to pulsed pure-tone stimuli.

THE CURRENT UBC CREB APPROVAL FOR THIS STUDY EXPIRES: March 24, 2010

The full UBC Clinical Research Ethics Board has reviewed the above described research project, including associated documentation noted below, and finds the research project acceptable on ethical grounds for research involving human subjects and hereby grants approval.

REB FULL BOARD MEETING REVIEW DATE:
March 24, 2009

DOCUMENTS INCLUDED IN THIS APPROVAL:

Document Name	Version	Date	DATE DOCUMENTS APPROVED:
Protocol:			
Behavioural BC Proposal	1	March 2, 2009	
Consent Forms:			
Behavioural BC Consent Form	3 (tracked changes)	April 6, 2009	**April 16, 2009**
Advertisements:			
Behavioural BC Recruitment Poster	3	April 5, 2009	
Behavioural BC Recruitment Poster	3 (tracked changes)	April 6, 2009	

CERTIFICATION:

In respect of clinical trials:

1. The membership of this Research Ethics Board complies with the membership requirements for Research Ethics Boards defined in Division 5 of the Food and Drug Regulations.

2. The Research Ethics Board carries out its functions in a manner consistent with Good Clinical Practices.

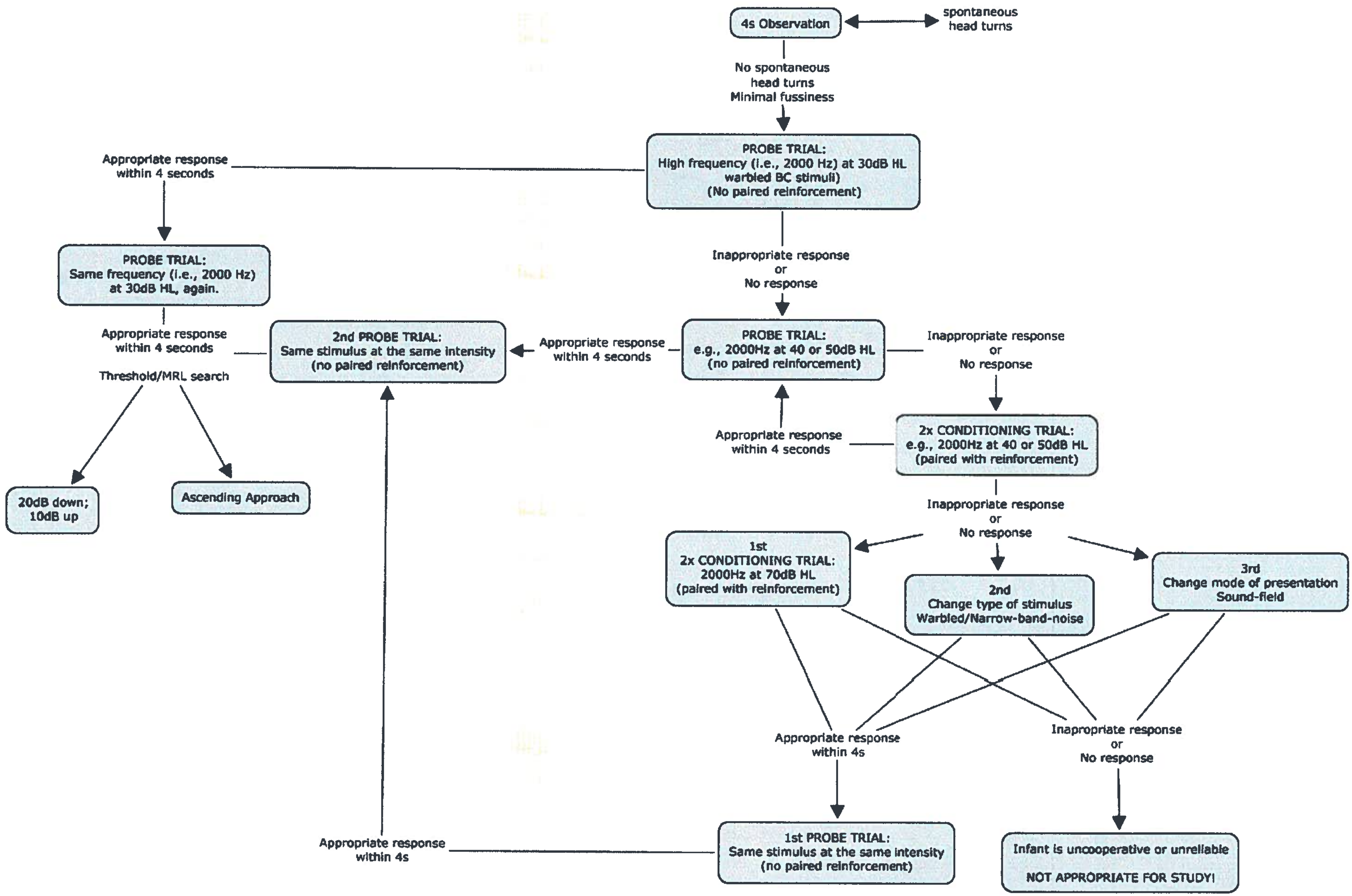
3. This Research Ethics Board has reviewed and approved the clinical trial protocol and informed consent form for the trial which is to be conducted by the qualified investigator named above at the specified clinical trial site. This approval and the views of this Research Ethics Board have been documented in writing.

The documentation included for the above-named project has been reviewed by the UBC CREB, and the research study, as presented in the documentation, was found to be acceptable on ethical grounds for research involving human subjects and was approved by the UBC CREB.

Approval of the Clinical Research Ethics Board by:

Dr. Peter Loewen, Chair

Appendix B: VRA Testing Protocol



VRA protocol

Appendix C: Individual MRLs and Bone-Oscillator Coupling Methods

Individual MRLs and bone-oscillator coupling methods for 7-15 month-old infants.

Infant #	Age (mo)	Thresholds (dB HL)				Bone-Oscillator Coupling Method
		500 Hz	1000 Hz	2000 Hz	4000 Hz	
36	**7**	1.35	11.95	22.5	-3.5	elastic
17	**8**	11.35	11.95	12.5	16.5	metal
42	**8**	11.35	11.95	22.5	16.5	elastic
13	**8.5**	11.35	1.95	2.5	6.5	elastic
47	**8.5**	11.35	11.95	12.5	-3.5	elastic
41	**8.5**	21.35	11.95	12.5	6.5	metal
35	**9**	11.35	21.95	22.5	---	metal
43	**9.5**	21.35	1.95	12.5	16.5	metal
19	**10**	-8.65	11.95	22.5	26.5	metal
45	**10**	-8.65	11.95	22.5	26.5	elastic
10	**12**	21.35	11.95	2.5	16.5	metal/elastic
15	**12**	-8.65	11.95	12.5	16.5	metal
32	**13**	11.35	1.95	-7.5	16.5	metal
8	**13.5**	21.35	11.95	22.5	16.5	metal
9	**14**	11.35	11.95	32.5	26.5	metal
25	**14**	11.35	1.95	12.5	6.5	metal
33	**15**	1.35	11.95	2.5	16.5	metal/elastic

Note: '---' indicates that an individual MRL could not be obtained at this frequency.

Individual MRLs and bone-oscillator coupling methods for 18-29 month-old infants.

Infant #	Age (mo)	Thresholds (dB HL)				Bone-Oscillator Coupling Method
		500 Hz	1000 Hz	2000 Hz	4000 Hz	
7	**18**	21.35	21.95	22.5	26.5	metal
26	**19**	11.35	-8.05	2.5	16.5	metal
27	**19**	1.35	1.95	12.5	6.5	metal
37	**19**	1.35	11.95	12.5	16.5	elastic
22	**19.5**	1.35	-8.05	2.5	6.5	elastic
28	**20**	11.35	11.95	2.5	16.5	metal
16	**20**	1.35	11.95	---	---	hand-held
5	**21.5**	11.35	31.95	22.5	16.5	metal
4	**22**	11.35	11.95	22.5	26.5	metal/elastic
24	**22**	21.35	11.95	2.5	16.5	metal
18	**22**	1.35	11.95	12.5	6.5	metal
39	**23**	11.35	1.95	12.5	6.5	metal
1	**23.5**	11.35	1.95	12.5	16.5	metal
14	**24.5**	11.35	1.95	12.5	16.5	elastic
11	**26**	21.35	---	12.5	26.5	metal
29	**26**	11.35	11.95	22.5	16.5	metal
34	**26.5**	1.35	11.95	12.5	26.5	elastic
2	**29**	11.35	---	22.5	26.5	metal
23	**30**	21.35	11.95	12.5	16.5	hand-held
48	**30**	11.35	1.95	12.5	6.5	metal

Note: '---' indicates that an individual MRL could not be obtained at this frequency.

Appendix D: Individual TEOAE and Tympanometry Screening Results

Individual TEOAE and tympanometry screening results for 7-15 month-old infants.

		TEOAE Ear 1:	Pass	Pass		CNT/Refer		
		TEOAE Ear 2:	Pass	CNT/Refer		CNT/Refer		
Infant	**Age**	Tympanogram Ear 1:	---	---	---	Normal	Normal	CNT
#	(mo)	Tympanogram Ear 2:	---	Normal	Flat	Normal	CNT	CNT
36	7		•					
17	**8**		•					
42	**8**					•		
13	**8.5**		•					
47	**8.5**				•			
41	**8.5**			•				
35	**9**		•					
43	**9.5**		•					
19	**10**						•	
45	**10**			•				
10	**12**		•					
15	**12**					•		
32	**13**			•				
8	**13.5**		•					
9	**14**							•
25	**14**			•				
33	**15**		•					

Note: Dots represent which screening results (i.e., TEOAE and/or tympanograms) were obtained individually. Each column is labeled by the screening results of Ear 1 and Ear 2. Therefore, the screening results of each infant are represented only once (i.e., one dot per row). '---' represents tympanometry tests that were not completed because TEOAE screening was passed. CNT means the TEOAE and/or tympanometry tests could not be completed.

Individual TEOAE and tympanometry screening results for 18-30 month-old infants.

		TEOAE Ear 1:	**Pass**	**Pass**		**CNT/Refer**		
		TEOAE Ear 2:	**Pass**	**CNT/Refer**		**CNT/Refer**		
		Tympanogram Ear 1:	---	---	---	**Normal**	**Normal**	**CNT**
Infant #	**Age (mo)**	Tympanogram Ear 2:	---	**Normal**	**Flat**	**Normal**	**Flat**	**CNT**
7	**18**		•					
26	**19**			•				
27	**19**						•	
37	**19**		•					
22	**19.5**					•		
28	**20**					•		
16	**20**							•
5	**21.5**		•					
4	**22**		•					
24	**22**			•				
18	**22**		•					
39	**23**		•					
1	**23.5**					•		
14	**24.5**				•			
11	**26**		•					
29	**26**		•					
34	**26.5**		•					
2	**29**							•
23	**30**					•		
48	**30**		•					

Note: Dots represent which screening results (i.e., TEOAE and/or tympanograms) were obtained individually. Each column is labeled by the screening results of Ear 1 and Ear 2. Therefore, the screening results of each infant are represented only once (i.e., one dot per row). '---' represents tympanometry tests that were not completed because TEOAE screening was passed. CNT means the TEOAE and/or tympanometry tests could not be completed.