The audiological journey and early outcomes of twelve infants with auditory neuropathy spectrum disorder from birth to two years of age

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To cite this article: Kirsty Gardner-Berry, Suzanne Carolyn Purdy, Teresa Y.C. Ching & Harvey Dillon (2015) The audiological journey and early outcomes of twelve infants with auditory neuropathy spectrum disorder from birth to two years of age, International Journal of Audiology, 54:8, 524-535, DOI: 10.3109/14992027.2015.1007214

To link to this article: http://dx.doi.org/10.3109/14992027.2015.1007214
Auditory neuropathy spectrum disorder (ANSD) is a hearing loss characterized by elevated or abnormal auditory brainstem (ABR) waveforms with evidence of normal cochlear outer hair-cell function. The latter is demonstrated by the presence of otoacoustic emissions (OAEs) and/or a cochlear microphonic (CM) potential (Starr et al, 1996; Berlin et al, 2003; Rance, 2005).

The procedure for determining auditory thresholds in infants using ABR involves identifying the presence of wave V at supra-threshold levels and decreasing the intensity of the stimulus until wave V can no longer be identified. In cases of sensorineural hearing loss (SNHL) the absence of wave V at high-intensities is indicative of auditory thresholds in the severe-profound range. However, in cases of ANSD the absence or abnormal morphology of the ABR at higher stimulus levels does not correlate reliably with behavioural auditory thresholds, which can range anywhere from normal to profound (Sinning & Oba, 2001; Berlin et al, 2010).

There is still considerable controversy surrounding the recommended management of infants with ANSD, which stems primarily from the inability to estimate auditory thresholds using ABR, and the variable outcomes reported with hearing aids and cochlear implants (Berlin et al, 2010). Previously researchers have expressed concerns about providing amplification for three reasons: first, fears of over-amplification and concerns that this might damage surviving cochlear structures such as the outer hair cells (Hood, 1998; Berlin, 1999); second, the assumption that amplification will produce a distorted signal in an ear with ANSD (Berlin, 1999); and third, reports in the literature of variable outcomes reported with hearing aids and cochlear implants (Madden et al, 2002) and ABR morphology (Psarommatis et al, 2006; Attias & Raveh, 2007) improving over time. As a result of these concerns some of the current management recommendations include avoiding or postponing hearing-aid fitting, fitting low-gain hearing aids, or fitting a hearing aid to one ear only and monitoring otoacoustic emissions (OAEs) (Hood, 1998; Berlin, 1999; Rose et al, 2002).

In addition to the concerns outlined above, a pessimistic view has been conveyed in some publications regarding the outcomes of patients with ANSD who have trialled hearing aids (Berlin et al, 2010) and monitoring otoacoustic emissions (OAEs) (Hood, 1998; Berlin, 1999; Rose et al, 2002).
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Those infants who could benefit from hearing aids from accessing the sounds of speech necessary to help develop spoken language.

In cases where speech discrimination is poor, withholding amplification reduces the infant's general awareness of sounds in their environment which may also be detrimental to their auditory development. The key goal therefore is to identify those infants who will only achieve 'detection' from amplification with no improvement in speech 'discrimination' so that additional measures can be put in place to help them to develop speech and language.

In 2008 a panel of experts on ANSD met at the Auditory Neuropathy Guidelines Development Conference in Lake Como, Italy, charged with developing guidelines for the diagnosis and management of infants with ANSD (Hayes, 2008). With regard to amplification, the recommendation was to trial hearing aids once ear-specific, elevated pure-tone and speech detection thresholds were recorded using conditioned responses such as visual reinforcement audiometry (VRA) or conditioned orientation reflex audiometry (Hayes & Sininger, 2008). In cases where the infant is developmentally delayed, and conditioned responses are not possible to obtain, the guidelines suggest that trialling amplification based on behavioural observation audiometry (BOA) could proceed if responses were clearly and consistently outside developmental norms, although this would generally not occur before six months of age.

Infants are not typically able to perform reliable behavioural threshold testing, such as visual reinforcement audiometry (VRA), until they reach approximately eight months developmental age (Moore et al, 1992; Widen et al, 2000). This means that if an infant is born three months prematurely they may not be able to perform VRA reliably until they are approximately 11 months chronological age. This delay can be greater still in infants with additional disabilities who are unable to perform the test due to physical and/or cognitive delays. Ching et al (2013) reported that 30% of the ANSD population in their study were found to have at least one other disability in addition to hearing loss, which included developmental delay, physical disabilities, and autism. The time delay before VRA results can be obtained, in addition to our inability to predict the audiogram using ABR, makes the audiological management of infants with ANSD challenging, particularly over the first twelve months of life.

Cortical auditory evoked potentials (CAEPs) can be used as an objective measure of auditory function during infancy (Golding et al, 2007; Carter et al, 2010; Cone & Whitaker, 2013), and therefore have the potential to assist with the management of infants with ANSD. CAEPs are a series of waves recorded on the scalp that represent the summed neural activity in the auditory cortex to sound. Whilst the ABR represents neural activity from the auditory nerve and brainstem, CAEPs are generated more centrally and can therefore provide us with some information about what is successfully reaching the areas of the brain closer to speech and language processing areas. CAEPs can be recorded from infants within the first few months of life (Kurtzberg et al, 1984; Pasmam et al, 1999; Kushnerenko et al, 2002; Wunderlich et al, 2006), making them a potentially useful tool for clinicians managing infants with ANSD soon after diagnosis.

The infant CAEP at 3–12 months of age is dominated by a positive-polarity peak (P1) with a latency of around 200 ms, followed by broad negative trough (Pasmam et al, 1999). Delays in the latency of P1 have been observed in children who have experienced long periods of auditory deprivation prior to cochlear implantation, and these delays are subsequently improved over the first three months of implant activation for children implanted less than 3.5 years of age (Sharma et al, 2005). It has therefore been suggested
that CAEPs have the potential to provide an index of auditory corti-
cal maturation (Sharma et al, 2009).

Robust CAEPs have been measured to speech stimuli presented
at normal conversational levels in infants with normal hearing
(Kurtzberg, 1989; Steinschneider et al, 1992; Cone-Wesson & Wunderlich, 2003), and have been used to evaluate amplification
settings in infants with SNHL (Cone-Wesson & Wunderlich, 2003;
Dillon, 2005; Purdy et al, 2005; Pearce et al, 2007; Carter et al, 2010;
Chang et al, 2012; Van Dun et al, 2012). Using the speech stimuli
/mi/, /gi/, and /ti/ a monotonous pattern has been observed in infants
with normal hearing (Carter et al, 2010) and SNHL (Van Dun et al, 2012)
whereby an increase in stimulus sensation level is associated with an
increase in the detection rate of CAEPs. CAEPs can therefore provide
audiologists with information about auditory function in infants who
are not yet able to provide reliable behavioural responses to sound.

The parent’s evaluation of aural/oral performance of children
(PEACH) questionnaire was developed by Ching and Hill (2007) to
evaluate the effectiveness of amplification in infants and children,
and is another tool that may assist in the management of infants
with ANSD. The PEACH is comprised of a series of thirteen items
designed to document the amount of daily hearing aid/cochlear
implant use, loudness discomfort, and to evaluate the infant/child’s
responses to a variety of speech and environmental sounds in quiet
and noisy environments. Details about the responses observed are
collated using both a structured diary and interview with a habilita-
tionist, and each item is scored on a rating scale ranging from zero
to four based on the frequency with which the parent observed a
response pertaining to that item.

Golding et al (2007) investigated the relationship between aided
CAEPs and PEACH results in 28 infants fitted with hearing aids
using the NAL-NL1 prescription (Golding et al, 2007). The three
speech stimuli /mi/, /gi/, and /ti/ were presented at 65 dB SPL to evalu-
ate CAEPs to sounds with low, mid, and high-frequency emphasis
respectively. Each subject was assigned a score between 0–3; a score
of 0 indicated no CAEP responses were present, and a score of 3 indicated responses were present to all three stimuli. A positive
correlation was identified; subjects with higher CAEP scores also
demonstrated higher PEACH scores. Fifteen subjects in this study
had sensorineural hearing loss, six had a mixed loss, and seven had
ANSD, however the relationship between CAEPs and the PEACH
score was not described for each group separately.

Sharma et al (2011) reported CAEP results from a group of chil-
dren with ANSD aged 9.5 months to 11 years. Children demon-
strating abnormal or absent CAEP responses also had significantly
lower infant toddler meaningful auditory integration scale (IT-
MAIS) scores. A significant correlation between the latency of P1
of the CAEP response and scores on the IT-MAIS was also reported.
Delayed P1 latencies were associated with lower IT-MAIS scores.

A number of studies have looked at CAEP responses in subjects
with ANSD and have compared them to speech perception ability
(Starr et al, 1991; Kraus et al, 2000; Rance et al, 2002; Starr et al,
2003; Kumar & Jayaram, 2005; Narne & Vanaja, 2008; Michalewski
ANSD and have compared them to speech perception ability
with ANSD and the different methodologies used. Variations in method-
ologies include the use of different stimuli such as tone bursts (Starr
et al, 1991; Rance et al, 2002; Starr et al, 2003; Michalewski et al,
2009), clicks (Starr et al, 1991; Narne & Vanaja, 2008), and speech
tokens (Kraus et al, 2000; Rance et al, 2002; Kumar & Jayaram,
2005; Sharma et al, 2011). Waveform analysis techniques also differ
and include peak latency and amplitude measures (Starr et al, 2003;
Kumar & Jayaram, 2005; Narne & Vanaja, 2008; Michalewski et al,
2009; Sharma et al, 2011), response morphology characteristics
(Kraus et al, 2000), and response presence vs. absence (Starr et al,
1991; Rose et al, 2002; Starr et al, 2003; Narne & Vanaja, 2008;
Michalewski et al, 2009).

There are currently no empirical studies published that report
on the early audiological management of infants with ANSD. The
current paper will describe the audiological journey of a group of
infants with ANSD from the first fitting of amplification to the time
when reliable behavioural results and measures of functional audi-
tory behaviour became available. Specifically, this study investigates
the potential benefits of including CAEP testing, and the PEACH
questionnaire during infancy to assist with audiological management
and recommendations for infants with ANSD.

**Methodology**

1. **Participants**

The participants were twelve infants (nine male and three female)
diagnosed with ANSD following newborn hearing screening. The
infants all had absent ABR or abnormal ABR waveforms present
only at very high presentation levels, and all had preserved pre-
neural responses demonstrated by the presence of a cochlear micro-
phonic. Of the 24 ears tested OAEs were present in eight, partially
present in five, and absent in eight. There was middle-ear pathology
present in the remaining three ears so the presence or absence of
OAEs could not be determined.

Parents of the infants were informed of the study by the audiolo-
gists overseeing their management at Australian Hearing. Written
consent was obtained from the parents by the researcher to perform
CAEP testing and to access the audiological records of their child if
they agreed to participate.

The medical details for each participant are listed in Table 1. All
participants had hypoxia during the neonatal period and 11 were born
prematurely at ≤ 32 weeks gestation (mean 29 weeks, SD 4). Imaging
results were available for only five subjects and showed an essentially
normal auditory nerve, cochlea, and vestibular apparatus bilaterally.

2. **Age at assessments**

Table 2 shows the chronological age and age corrected for gestation
at hearing-aid fitting and assessments.

3. **Chart review of audiological information**

Information obtained from the audiological file included the mini-
imum response levels (MRL) to noisemakers of known frequency
content for unaided and aided behavioural observation audiometry
(BOA); the estimated audiometric thresholds used at the time of
the first fitting; the re-estimated audiometric thresholds used fol-
lowing aided BOA testing (follow-up); amplification characteristics;
parent observations of their infant’s unaided and aided behavioural
responses to sound outside the clinic; ABR, OAE, and tymanom-
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3.1. ESTIMATED AUDIOGRAMS USING BOA AND PARENT OBSERVATIONS

Estimated audiograms had already been determined by the clinical audiologist managing the infant in accordance with national Australian Hearing infant hearing-aid fitting guidelines (King, 2010). Testing typically involves performing BOA using speech sounds and noisemakers of known frequency content and intensity. This is to identify infants who only responded to sounds presented above age-appropriate levels, and to establish whether responses to some frequencies were elevated in relation to others. For infants under five months of age with normal hearing the minimum response level (MRL) to broadband noisemakers is expected to be approximately 55 dBA (Northern & Downs, 1991). If responses from the infant are elevated above 55 dBA, amplification is considered. In order to minimize the risk of over amplification, when estimating an audiogram based on MRLs, the audiologist assumes the best-possible thresholds in the first instance and adjusts the hearing-aid gain if aided BOA testing suggests the aid has provided less functional gain than expected. Clinician discretion with regard to the estimated audiogram may also be used in instances where there may be discrepancies between BOA results and parental observations.

Table 1. Participant medical details.

<table>
<thead>
<tr>
<th>Subject</th>
<th>Gender</th>
<th>Gestation</th>
<th>Risk factor</th>
<th>Additional disabilities</th>
<th>Imaging - auditory nerve</th>
<th>Imaging - cochlea and vestibular system</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>M</td>
<td>26</td>
<td>Prematurity with hypoxia</td>
<td>Cerebral palsy and vision impairment</td>
<td>Unknown</td>
<td>Unknown</td>
</tr>
<tr>
<td>2</td>
<td>F</td>
<td>25</td>
<td>Prematurity with hypoxia</td>
<td>Nil</td>
<td>Unknown</td>
<td>Unknown</td>
</tr>
<tr>
<td>3</td>
<td>F</td>
<td>32</td>
<td>Prematurity with hypoxia</td>
<td>Nil</td>
<td>Unknown</td>
<td>Unknown</td>
</tr>
<tr>
<td>4</td>
<td>M</td>
<td>28</td>
<td>Prematurity with hypoxia</td>
<td>Nil</td>
<td>Unknown</td>
<td>Unknown</td>
</tr>
<tr>
<td>5</td>
<td>F</td>
<td>32</td>
<td>Prematurity with hypoxia</td>
<td>Developmental delay</td>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>6</td>
<td>M</td>
<td>25</td>
<td>Prematurity with hypoxia</td>
<td>Cerebral palsy and vision impairment</td>
<td>Slightly smaller on left side</td>
<td>Normal</td>
</tr>
<tr>
<td>7</td>
<td>M</td>
<td>27</td>
<td>Prematurity with hypoxia</td>
<td>Cerebral palsy and vision impairment</td>
<td>Unknown</td>
<td>Unknown</td>
</tr>
<tr>
<td>8</td>
<td>M</td>
<td>28</td>
<td>Prematurity with hypoxia</td>
<td>Nil</td>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>9</td>
<td>M</td>
<td>27</td>
<td>Prematurity with hypoxia</td>
<td>Nil</td>
<td>Unknown</td>
<td>Unknown</td>
</tr>
<tr>
<td>10</td>
<td>M</td>
<td>28</td>
<td>Prematurity with hypoxia</td>
<td>Nil</td>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>11</td>
<td>M</td>
<td>37</td>
<td>Hypoxia</td>
<td>Cerebral palsy and vision impairment</td>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>12</td>
<td>M</td>
<td>25</td>
<td>Prematurity with hypoxia</td>
<td>Cerebral palsy and vision impairment</td>
<td>Unknown</td>
<td>Unknown</td>
</tr>
<tr>
<td>Mean</td>
<td>29</td>
<td>SD 4</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

4. Evaluations

4.1. CORTICAL AUDITORY EVOKED POTENTIALS (CAEPs)

4.1.1. Test environment. Unaided and aided CAEPs were recorded with the subject in a sound-proof booth sitting either on a parent’s lap or in a high-chair. The stimuli were presented via a loudspeaker positioned at 0° azimuth, approximately 1.8 m from the infant’s head. To maintain the infant in a relatively settled state a distracter engaged with the baby using quiet toys and/or a children’s DVD was played on a screen with the sound off.

4.1.2. Stimuli. The stimuli were the same as those used by Golding et al (2009). Natural speech stimuli were extracted from a digitized recording of continuous discourse spoken by a female speaker with an Australian accent.

The test stimuli /m/, /g/, and /t/ were chosen as they have spectral emphasis in the low- (0.250 kHz), mid- (2 kHz), and high-frequencies (4 kHz) respectively. The duration of the stimuli was 30 ms for /m/ and /t/, and 20 ms for /g/. Stimuli were presented with alternating onset polarity, an inter-stimulus interval of 1125 ms, at a level of 65 dB SPL, measured using the impulse setting, with a time constant of 35 ms, on a Brüel and Kjær measuring amplifier at the position of the baby’s head.

4.1.3. Recordings. CAEPs were recorded using the Neuroscan™ system with disposable Ambu® Blue Sensor ECG recording electrodes positioned at Cz referenced to the right mastoid with forehead as ground.

Table 2. Chronological age and corrected for gestation age in months for first fitting and assessments. Standard deviations are shown in parentheses.

<table>
<thead>
<tr>
<th>Subject</th>
<th>Age at first fitting</th>
<th>Age at unaided CAEPs</th>
<th>Age at aided CAEPs</th>
<th>Age at first binaural VRA</th>
<th>Age at PEACH</th>
<th>Age at first separate ear VRA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean chronological age (SD)</td>
<td>7 (4)</td>
<td>9 (5)</td>
<td>11 (5)</td>
<td>13 (2)</td>
<td>18 (3)</td>
<td>26 (18)</td>
</tr>
<tr>
<td>Mean corrected age (SD)</td>
<td>4 (5)</td>
<td>6 (6)</td>
<td>8 (6)</td>
<td>10 (3)</td>
<td>16 (4)</td>
<td>23 (18)</td>
</tr>
</tbody>
</table>
Recordings were made using an online low-pass filter of 100 Hz and high-pass filter of 0.1 Hz (24 dB/octave slope). The recording window was 700 ms, including a 100 ms pre-stimulus baseline, and artifact rejection was set at 150 μV. The sampling rate was 1 kHz. A 30-Hz low-pass filter was applied before offline analyses were performed. Where possible, each stimulus was presented in a block until 100 artifact-free electroencephalography (EEG) samples were acquired and the same block of stimuli was presented on two occasions, with order of stimulus presentation randomized.

4.2. Hearing aid measures
The gain of the hearing aids was measured in a 2cc coupler at the time of CAEP testing using a Fonix 6500 test box from Frye Electronics Inc. The stimulus used was a speech weighted noise with an input level of 65 dB SPL. Maximum output was measured using a swept pure tone with an input level of 90 dB SPL.

5. Analysis methods
5.1. BOA and the estimated audiogram
BOA minimum response levels were categorized so they could be compared to parental observations and discussed in relation to the estimated audiograms. Given age-appropriate responses to broadband sounds for infants < 5 months with normal hearing are expected to be approximately 55 dBA (Northern & Downs, 1991), responses of 65–75 dB were classified as mildly elevated, 75–85 dB moderately elevated, and 85–95 dB severely elevated.

5.2. Relating BOA results to parent observations in the unaided and aided condition
Unaided and aided BOA results were compared for consistency to parent observations of their infant’s behavioural responses in the unaided and aided condition. Unaided parental observations were classified broadly in relation to the regularity of the infant’s responses (if any) to everyday sounds in their home environment without access to visual cues. Observations were classified as ‘multiple responses seen’ if the infant was reported to have responded to sounds which were likely to be below or around normal conversational levels. Observations were classified as ‘inconsistent’ if the infant appeared to respond to everyday sounds at conversational levels on some days but not others. Observations were classified as ‘occasional’ if they only responded to loud sounds and these responses were not necessarily consistent from one day to the next.

In addition to the above classifications, aided parental observations took into account whether parents noticed a difference when the hearing aids were worn compared to when their infant was unaided. ‘No improvement re unaided’ was documented if the parents did not notice any difference in the infant’s responses compared to when they were unaided.

5.3. Relating estimated thresholds at fitting & follow-up to VRA
Estimated audiometric thresholds used at the first fitting and re-estimated audiometric thresholds following aided BOA were compared to binaural VRA thresholds at 0.5, 1, 2, and 4 kHz.

5.4. CAEP waveform analysis
The epoched Neuroscan files were exported to MATLAB where the presence/absence of CAEP responses were determined using a Hotelling’s T² statistic as described by Golding et al (2009). The analysis period consisted of 450 points covering the 450 ms period between 50 ms and 500 ms post-stimulus onset. The number of sampling points was then reduced by averaging each group of 50 adjoining points such that the 450 ms analysis period was reduced to form a ‘response’ vector that contained nine variables. The Hotelling’s T² statistic, which calculates the probability that the mean value of any linear combination of the nine variables is significantly different from zero, was then applied to objectively determine CAEP response presence (Golding et al, 2009).

5.5. CAEP stimulus audibility calculations
The audibility of the CAEP stimulus could not be determined at the time of CAEP testing as reliable VRA thresholds were not yet available. Audibility of the CAEP stimuli was therefore calculated retrospectively once VRA thresholds were obtained. This assumes that the auditory thresholds at the time of CAEP testing (6–8 months corrected age) were the same as when VRA was performed (approximately 10 months corrected age).

CAEP stimulus sensation levels were predicted using an audibility calculator. The predicted audibility of the speech stimuli was calculated using the 2 cc coupler measures obtained from the hearing aids at the time of CAEP testing. A real-ear to coupler correction factor was used to account for the size of the infant’s ear canal, based on the age of the infant. This was included to more accurately predict the expected sound pressure level at the infant’s ear drum (Dillon, 2012). Correction factors ranged from 6–22 dB SPL dependent on the infant’s age and stimulus frequency.

The sequence of calculations to determine aided ‘audibility’ for each infant was as follows:

1. The spectral content of each of the three stimuli (m, g, t) was measured in 1/3 octave band widths for an overall level of 65 dB SPL in the free field.
2. Unaided VRA thresholds were subtracted from the measured 1/3 octave band levels of each speech stimulus to estimate the unaided dB sensation level for each frequency band of the stimulus.
3. The insertion gain of the hearing aid was estimated based on the measured coupler gain, by adding the age-appropriate average real-ear to coupler difference and subtracting the average age-appropriate real-ear unaided (ear canal) gain (Dillon, 2012).
4. These estimated insertion gains were added to the unaided sensation levels for each frequency band.
5. The sensation levels across the different frequencies were compared to determine which 1/3-octave bandwidth was the highest, and this maximum figure was used as the final aided ‘audibility’. This audibility value was used as an estimation of stimulus sensation level.

5.6. CAEP response presence/absence and stimulus audibility
The presence or absence of a CAEP response was compared to what might be expected given the calculated audibility of the stimulus and previously published research on response detection at different sensation levels for infants with normal hearing (Carter et al, 2010) and SNHL (Van Dun et al, 2012).

5.7. CAEP score
In the binaural, unaided condition each subject was given a score out of three to denote how many responses were present to each of the three stimuli /m/, /g/, and /t/. In the aided CAEP condition each ear was tested separately by switching the hearing aid in the contralateral
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ear off and leaving it in place to occlude the ear canal and minimize the contribution of the non-test ear. In the aided condition each subject was given a score out of six to denote how many responses were present to each of the three stimuli in each ear separately.

5.8. STATISTICAL ANALYSIS

Binomial probability statistics were used to compare the CAEP detection rate at different sensation levels in infants with ANSD compared to those with normal hearing and SNHL. Spearman rank order correlations were used to investigate the relationship between aided CAEP scores and PEACH results.

Results

Audiogram configurations

Figure 1 shows the estimated audiogram used at the first fitting (left), re-estimated audiogram after aided BOA (centre), and binaural VRA thresholds (right) for individual infants at 0.5, 1, 2, & 4 kHz. At the time of the first fitting, and following aided BOA the estimated audiograms were primarily flat in configuration. The majority of audiograms at VRA showed a flat or gently sloping configuration with the exception of three subjects who demonstrated a more steeply sloping high-frequency loss.

Amplification characteristics

The mean corrected age of infants at the first fitting was four months (SD 5). All infants had been fitted with digital hearing aids with wide dynamic range compression/input compression and output compression limiting. Hearing aids were fitted according to the National Acoustic Laboratories’ prescription for non-linear hearing aids, version 1 (NAL-NL1) or the Desired Sensation Level, version 4.1 (DSL) prescription (Seewald et al, 1997). Only one infant was fitted with the DSL prescription, as part of this child’s involvement in another study.

Estimating the audiogram using BOA and parental observations

Table 3 documents unaided BOA and parental observations, and the estimated binaural 4FA used at the time of the first fitting. Seven infants had both unaided BOA and parent observations available for review. Parent observations were consistent with BOA results for all but one infant (infant 3). In this case BOA results suggested a severe-profound loss but the parents reported repeatable unaided responses to soft-moderate level sound outside the clinic.

Table 3 also documents aided BOA and/or parent observations, and the re-estimated 4FA used prior to CAEP testing. Four infants had both aided BOA and aided parental observations available for review. Parent observations were consistent with BOA results for all but one infant (infant 3). The same discrepancy was noted as for the unaided condition whereby BOA results suggested a more significant degree of hearing loss than what the parents had observed.

Comparison between the estimated and measured audiogram

Table 3 shows that at the time of the first fitting 67% of infants were estimated to have a moderate hearing loss (40–65 dB HL) and the remaining 33% were estimated to have a severe hearing loss (70–95 dB HL).

Figure 2 shows the relationship between the thresholds estimated at the time of the first fitting and binaural VRA (filled diamonds). The estimated thresholds were within ± 10 dB in 58%, 67%, 17%, and 17% of the infants for 0.5, 1, 2, and 4 kHz results respectively. The earlier thresholds were under-estimated for high-frequencies (2 and 4 kHz) more than low and mid-frequencies (0.5 and 1 kHz).

Figure 2 also shows the relationship between the re-estimated thresholds and binaural VRA results (open squares) determined following aided BOA and aided parental observations. The re-estimated thresholds were within ± 10 dB of the VRA results in 50%, 58%, 58%, and 33% for 0.5, 1, 2 and 4 kHz respectively. Figure 2 shows that, once again, the audiograms were predominantly under-estimated for high-frequencies (4 kHz) more than they were for low- and mid-frequency sounds.

CAEP response presence/absence and stimulus audibility

Unaided CAEP results were available for ten infants and aided results for twelve (see Table 4). Six out of ten infants showed an increase in their CAEP score when they went from unaided to aided (1, 3, 4, 7, 8, and 10), one showed a decrease in their score (5), and the remaining three showed no change (2, 11, 12).

The results for /m, g and t/ in the aided condition were collapsed into one group so that comparisons could be made between CAEP presence/absence at different sensation levels. Table 5 shows the percentage of CAEP responses present at predicted audibility levels of 1–10, 11–20, and >20 dB SL were 36%, 44%, and 38% respectively.

Figure 1. Estimated audiogram used at the first fitting (left), re-estimated audiogram after aided BOA (centre), and binaural VRA thresholds (right) for individual infants at 0.5, 1, 2, and 4 kHz.
Table 5 also shows the equivalent results from previous studies for infants with normal hearing (Carter et al, 2010), and infants with sensorineural hearing loss (Van Dun et al, 2012) using the same speech stimuli and assessment methods. For infants in the studies by Carter et al (2010) and Van Dun et al (2012) sensation levels were calculated based on behavioural thresholds to the speech stimuli. For infants in the current study sensation level was estimated based on calculated stimulus audibility and VRA results to frequency-specific warble tones.

The number of CAEP responses present in infants with normal hearing and SNHL increases with stimulus audibility levels, however as a group the infants with ANSD in the present study do not show an increase in the percentage of CAEP responses present as stimulus level increases. Using binomial probability statistics the detection rate for CAEPs at 11 – 20 dB SL and 20 dB SL in infants with ANSD was significantly lower than infants with SNHL (p < 0.005 and 0.002 respectively). The CAEP detection rate was also significantly lower in infants with ANSD compared to those with normal hearing at sensation levels > 20 dB SL (p < 0.003).

Aided CAEPs and PEACH

Figure 3 shows the summed left and right ear aided CAEP score for each of the 12 subjects plotted against the age-corrected PEACH score. These results show a significant relationship between the two measures whereby infants with higher CAEP scores also had higher PEACH scores (r = 0.71; p < 0.01). There was no significant relationship between estimated audibility and PEACH scores (r = 0.16; p = 0.71), or estimated audibility and CAEP scores (r = 0.12; p = 0.71).

Case study (infant 3)

Figure 4 shows the audiogram obtained using VRA for infant 3. In this case, unaided BOA results were significantly elevated (reliable responses could not be seen at > 90 dBA) which was not consistent with parental observations of multiple responses to moderate level sounds (e.g. stops crying when she hears mother’s voice). As a result of the parental observations, amplification was fitted using a conservatively estimated audiogram in the moderate range (4FA = 45 dB HL).

Table 3. Unaided and aided behavioural audimetry (BOA and VRA), parent observations of auditory behaviour, estimated 4FA at the first fitting, and re-estimated 4FA prior to CAEP testing.

<table>
<thead>
<tr>
<th>Infant</th>
<th>Unaided BOA</th>
<th>Unaided parental observation</th>
<th>Estimated 4FA at 1st fitting</th>
<th>Aided BOA</th>
<th>Aided parental observation</th>
<th>Re-estimated 4FA prior to aided CAEPs</th>
<th>Measured 4FA using binaural VRA</th>
<th>Measured 4FA for Left ear VRA</th>
<th>Measured 4FA for right ear VRA</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>NR &gt; 90 dBA</td>
<td>Occasional responses seen</td>
<td>40</td>
<td>NR &gt; 90 dBA</td>
<td>No improvement re unaided</td>
<td>61</td>
<td>60</td>
<td>20</td>
<td>20</td>
</tr>
<tr>
<td>2</td>
<td>Moderately elevated</td>
<td>NA</td>
<td>61</td>
<td>NA</td>
<td>Multiple responses seen</td>
<td>61</td>
<td>69</td>
<td>51</td>
<td>41</td>
</tr>
<tr>
<td>3</td>
<td>NR &gt; 90 dBA</td>
<td>Multiple responses seen</td>
<td>45</td>
<td>NR &gt; 90 dBA</td>
<td>Multiple responses seen</td>
<td>55</td>
<td>57</td>
<td>56</td>
<td>50</td>
</tr>
<tr>
<td>4</td>
<td>Mildly elevated</td>
<td>Multiple responses seen</td>
<td>50</td>
<td>Moderately elevated</td>
<td>NA</td>
<td>65</td>
<td>55</td>
<td>47</td>
<td>57</td>
</tr>
<tr>
<td>5</td>
<td>Inconsistent</td>
<td>Inconsistent</td>
<td>70</td>
<td>Inconsistent</td>
<td>Inconsistent</td>
<td>80</td>
<td>60</td>
<td>60</td>
<td>59</td>
</tr>
<tr>
<td>6</td>
<td>Moderately elevated</td>
<td>NA</td>
<td>59</td>
<td>Mildly elevated</td>
<td>NA</td>
<td>75</td>
<td>78</td>
<td>65</td>
<td>66</td>
</tr>
<tr>
<td>7</td>
<td>Mildly elevated</td>
<td>Multiple responses seen</td>
<td>45</td>
<td>NA</td>
<td>NA</td>
<td>65</td>
<td>69</td>
<td>63</td>
<td>67</td>
</tr>
<tr>
<td>8</td>
<td>NR &gt; 90 dBA</td>
<td>Occasional responses seen</td>
<td>94</td>
<td>NA</td>
<td>Multiple responses seen</td>
<td>63</td>
<td>66</td>
<td>67</td>
<td>64</td>
</tr>
<tr>
<td>9</td>
<td>NA</td>
<td>Multiple responses seen</td>
<td>81</td>
<td>Mildly elevated</td>
<td>NA</td>
<td>81</td>
<td>72</td>
<td>69</td>
<td>66</td>
</tr>
<tr>
<td>10</td>
<td>Severely elevated</td>
<td>NA</td>
<td>56</td>
<td>Severely elevated</td>
<td>No improvement re unaided</td>
<td>56</td>
<td>75</td>
<td>80</td>
<td>75</td>
</tr>
<tr>
<td>11</td>
<td>NA</td>
<td>NA</td>
<td>70</td>
<td>NA</td>
<td>No improvement re unaided</td>
<td>83</td>
<td>75</td>
<td>85</td>
<td>85</td>
</tr>
<tr>
<td>12</td>
<td>Inconsistent</td>
<td>Not repeatable</td>
<td>55</td>
<td>NA</td>
<td>Small improvement re unaided</td>
<td>64</td>
<td>74</td>
<td>89</td>
<td>101</td>
</tr>
</tbody>
</table>

Table 4. Binaural unaided and summed left- and right-ear aided CAEP scores.

<table>
<thead>
<tr>
<th>Infant</th>
<th>Binaural unaided CAEP score</th>
<th>Left &amp; right aided CAEP score</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>NT</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>3</td>
<td>12</td>
<td>17</td>
</tr>
<tr>
<td>4</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>5</td>
<td>11</td>
<td>11</td>
</tr>
<tr>
<td>6</td>
<td>9</td>
<td>9</td>
</tr>
<tr>
<td>7</td>
<td>12</td>
<td>12</td>
</tr>
<tr>
<td>8</td>
<td>12</td>
<td>12</td>
</tr>
<tr>
<td>9</td>
<td>11</td>
<td>11</td>
</tr>
<tr>
<td>10</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>11</td>
<td>11</td>
<td>11</td>
</tr>
<tr>
<td>12</td>
<td>12</td>
<td>12</td>
</tr>
</tbody>
</table>

Age-appropriate normal at < 5 months = 55 dBA to broadband sounds. Mildly elevated = 65–75 dBA; Moderately elevated = 75–85 dBA; Severely elevated = 85–95 dBA. No response = > 90 dBA; NA = Not available.
The unaided CAEP score was 0 out of 3, and the aided CAEP score increased to 5 out of 6. The PEACH score for this infant was within 2 standard deviations of the normative mean for age.

Discussion

The purpose of this paper was to follow the audiological journey of a group of infants with ANSD over the first two years of life in order to gain a greater understanding of what clinicians are faced with when managing infants with this type of hearing loss. Of specific interest was the information clinicians used to estimate the audiogram when threshold information from ABR testing was not available (i.e. could not be relied upon in cases with ANSD), and to see how closely initial hearing estimates agreed with subsequent VRA results. Improving our understanding in this area is of particular importance given the conflict that currently exists between the recommendations made at the Auditory Neuropathy Guidelines Development Conference (Hayes, 2008) and the goals of newborn hearing screening which specify that intervention should occur by six months of age (JCIH, 2007). We also wanted to investigate whether CAEP testing together with the PEACH questionnaire could assist with audiological management in the first two years of life.

1. Age at first fitting and VRA

One of the recommendations made following the Auditory Neuropathy Guidelines Development Conference in 2008 was to wait until ear-specific, elevated pure-tone thresholds were available using

![Figure 2](image-url). Comparison between the later-measured binaural VRA thresholds and estimated pure-tone thresholds used for the first fitting (filled diamonds,) and re-estimated thresholds used to program the hearing aids following aided BOA and parental observations (open squares).

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1–10 dB SL*</td>
<td>27% (n = 22) 64% (n = 22)</td>
<td>36% (n = 14)</td>
<td>0.57</td>
<td>0.09</td>
</tr>
<tr>
<td>11–20 dB SL*</td>
<td>55% (n = 22) 72% (n = 32)</td>
<td>44% (n = 25)</td>
<td>0.45</td>
<td>0.03</td>
</tr>
<tr>
<td>&gt; 20 dB SL</td>
<td>77% (n = 22) 77% (n = 26)</td>
<td>38% (n = 34)</td>
<td>0.003</td>
<td>0.002</td>
</tr>
</tbody>
</table>

N = number of infants in study; n = number of data points recorded at each sensation level for /m/, /g/ and /t/ collectively; NT = Not tested; *N.B. For infants with normal hearing from Carter et al (2010) behavioural sensation levels of +10, +20, and +30 exactly were used.
VRA before considering amplification. The mean chronological age at which infants were first able to provide reliable binaural VRA results in this study was 13 months (SD 2). One of the key goals of newborn hearing screening is to commence intervention before six months of age in order to prevent delays in language development. All the infants in this study had bilateral moderate or greater hearing losses, and were fitted with hearing aids at a mean corrected for gestational age of four months (SD 5). Delaying amplification until VRA results were available would have led to a significant period of auditory deprivation.

The age at which infants in this study could perform VRA was older than the eight months reported in the literature (Moore, 1992). One of the reasons for this is because all but one of the infants in this study was born prematurely with a mean gestational age at birth of 29 weeks (SD 4). After correcting for prematurity the mean age at binaural VRA was ten months (SD 3). In addition, four out of the twelve infants had cerebral palsy and vision impairment, and a further infant had developmental delay, all of which can make it difficult for an infant to perform behavioral audiometry. Given significant prematurity is one of the risk factors for ANSD, the infants included in this study are likely to be reflective of those seen in other paediatric audiology clinics around the world.

The mean chronological age at which ear-specific VRA results were obtained for infants in this study was 26 months (SD 18). The time taken to obtain ear-specific VRA results was not necessarily due to the inability of the infant to perform the test. Rather, the priority clinicians placed on this information needed to be weighed up against the need to assist parents in the management of amplification, continuing to update ear moulds as infants grew out of them, and scheduling follow-up appointments around competing appointments with other professionals involved in the care of the infant. In the future it would be desirable to obtain ear-specific information earlier, however for this sample 92% of infants had approximately symmetrical (4FA within 10 dB) hearing thresholds in left and right ears. In the majority of cases studied here ear-specific information was being obtained using CAEPs so early indications of significant ear asymmetries could be identified.

### 2. Estimating the audiogram using BOA and parental observations

#### 2.1. First fitting

The audiogram used for each infant at the first fitting had been estimated by the audiologist based on a combination of BOA and parental observations. For three infants (1, 3, and 10) markedly under-estimated hearing thresholds (relative to later binaural VRA results) were used to fit the hearing aid, despite significantly elevated/absent BOA responses. In two instances (infants 1 and 10) this was because of the diagnosis of ANSD and the clinician’s desire to start with a more conservative fitting. For infant 1 a mild loss (4FA = 40 dB HL) with flat configuration was used, and for infant 10 a moderate loss (4FA = 56 dB HL) with flat configuration was used. In one instance (infant 3) a more conservative audiogram was estimated (4FA = 45 dB HL) because the parents had observed multiple responses to everyday sounds in the home environment.

Thresholds used for the first fitting were underestimated for high-frequencies (2 and 4 kHz) more than for low-frequencies. It was noted that for the majority of infants the audiologist had chosen a flat configuration audiogram as a starting point for the first fitting (see Figure 1), which was then reviewed at the follow-up appointment. Assumption of a flat audiogram does not seem an optimal strategy given the preponderance of downward sloping audiograms evident in Figure 1, a finding that is consistent with the shape of child audiograms based on a much larger sample (Dillon, 2012).

Neither unaided BOA testing alone nor parent observation alone were accurate in estimating the audiogram at the first fitting, however when used together they were complementary and provided a reasonable initial estimate of hearing thresholds for the lower frequencies (see Figure 2).

Discrepancies between BOA results and parental observations can occur for a variety of reasons. The most typical is that the infant may not be in the ideal state for behavioural testing at the time of the clinic appointment. If an infant is unsettled or in a deep sleep they may not respond to sounds that are audible to them and appear to have a more severe hearing loss than they truly have. Early studies of BOA thresholds in infants with normal hearing (Widen, 1993) show wide variability for these reasons. Parents have the opportunity to observe their baby over a longer period of time, including times...
when they are settled or in a light sleep. Furthermore, environmental sounds and familiar voices may be more appealing and relevant to an infant than the noisemakers used for clinical testing, which may lead the infant to be more responsive in the home environment. The disadvantage of parental observation alone is that the exact intensity and frequency content of the stimuli is unknown, and it is not always clear whether the infant had access to visual cues when the sound occurred.

2.2. Re-estimation of the audiogram following aided BOA and parental observation

The re-estimated audiogram was considerably closer to the VRA results when aided BOA together with aided parental observations of the child were incorporated. If no, or limited improvement in the MRLs was seen in behavioural responses after aiding, the audiogram was assumed to be worse than initially estimated. The estimated 4FA was within ±10 dB of the binaural VRA results in 42% of infants at the first fitting and this improved to 75% after re-estimation based on aided testing and parental observation.

The improvement was predominantly at 2 and 4 kHz where the proportion of estimated thresholds that were within ±10 dB of the VRA results improved from 17% to 58%, and 17% to 33% of infants respectively. There is no clear explanation as to why the improvement in accuracy was greatest for high-frequencies. The re-estimated audiograms shown in Figure 1 are still predominantly flat in configuration, although a gentle slope was introduced in some cases. The reason for choosing a gentle slope was not necessarily stated in the file.

It is important to note that the comparison made in this study between the estimated thresholds and VRA results assumes that there was no change in hearing between the time of the first fitting and binaural VRA testing, which is not necessarily the case. Patients with ANSD can show improvements, deterioration, or stable audiograms over time (Sininger & Oba, 2001). In fact, two of the infants (1 and 2) in this study were reported to show a clear and sudden improvement in their responsiveness to sound between the time when binaural and separate ear VRA results became available. For one infant this was associated with ceasing oxygen therapy and the other after commencing a medication used to treat epilepsy. This highlights the critical importance of on-going assessment and considerations of parental observations in this population.

3. Contribution of CAEPs to the infant test battery

Increasing the audibility of the stimulus with hearing aids increased the number of CAEPs elicited in some infants, however there was not a monotonic relationship between stimulus audibility and CAEP detection when evaluating the group data. At stimulus sensation levels of 21–30 dB SL Carter et al. (2010) reported a CAEP detection rate of 77% in infants with normal hearing, and Van Dun et al. (2012) reported a detection rate of 71% in infants with SNHL using the same stimuli and sensation levels. The current study showed a significantly lower detection rate of 42% in children with ANSD using the same sensation level range (see Table 5). This pattern of results suggests that increasing stimulus sensation level does not have the same beneficial effect for at least some babies with ANSD as it does for babies with normal hearing or SNHL.

Increasing stimulus intensity is expected to elicit a larger and broader displacement of the basilar membrane, increased activation of hair cells, and release of neurotransmitters, and activation of a larger number of nerve fibres from the auditory nerve to the cortex and hence larger CAEPs. Improved understanding of the underlying auditory pathology in children with ANSD is needed to understand why the usual pattern of CAEP amplitude growth and improved detectability was not observed.

Whatever the mechanism, the observed lack of increase of cortical response detection rate with increasing estimated sensation level (once audible) must be considered when using CAEPs to evaluate hearing-aid fittings. An absent CAEP may mean one of three things. First, the stimulus may be inaudible to the infant, in which case amplification, or more amplification, must be used. Second, the infant is not responding to amplification in the same way as an infant with a typical SNHL and amplification may need to be reduced. Third, in some people it may not be possible to elicit a cortical response with any degree of amplification. For these reasons, in the event that CAEPs are absent BOA results and parental observations should be considered before deciding whether to increase or decrease the gain of the hearing aids. However, given the relationship between cortical response presence and functional hearing ability found in this study and in other studies on children with ANSD (Rance et al., 2002; Golding et al., 2007; Sharma et al., 2011), there is every reason to believe that better functional hearing will be achieved with an amplification setting that produces CAEPs than one that doesn’t.

It is important to keep in mind that the calculations for estimated sensation levels used in this study have considerable uncertainty as they are based on the VRA results, average ear canal correction factors, and assumptions about how signal power is integrated across time and frequency (i.e. 1/3 octave band levels were compared to hearing thresholds). They also assume that the estimated thresholds used for the fitting at the time of CAEP testing were the same as those measured later using VRA, which is not necessarily the case. These uncertainties may have contributed to the lack of correlations between audibility and each of PEACH and CAEP scores whereas there was a significant correlation found between PEACH scores and CAEP scores. The uncertainty of the threshold estimates and the potential for thresholds to have changed over time is likely to have also contributed to some cortical responses occurring for stimuli estimated to be below threshold.

4. Contribution of the PEACH diary to the infant test battery

There was a significant relationship between the binaural aided CAEP and age-corrected PEACH scores whereby infants with higher CAEP scores also showed higher PEACH scores. These results are consistent with those reported by Golding et al. (2007). There was no significant relationship between estimated audibility and PEACH scores. That is, increasing audibility was not associated with higher scores on measures of functional auditory behaviour. These results are in keeping with the observation that the percentage of CAEP responses present did not increase with higher stimulus sensation levels.

The positive relationship between the CAEP and PEACH results suggests that both the CAEPs and the PEACH are useful inclusions in the audiological test battery for infants with ANSD. Of particular interest are infants 5, 11, and 12, all of whom had a summed aided CAEP score of only 0 or 1, PEACH scores that were greater than 2 SD below the mean, and went on to receive a cochlear implant.

5. Benefits of combining BOA, parent observations, CAEPs, and PEACH to the infant test battery

The results for the case study (infant 3) shows an example where initial unaided BOA results were significantly elevated (reliable responses could not be seen at >90 dBA) which was not consis-
tent with parental observations of multiple responses to moderate level sounds in the home environment (e.g. stops crying when she hears mother’s voice). In this case unaided CAEPs were absent for all three stimuli, which suggested there was some degree of hearing loss. Amplification was fitted based on an estimated 4FA of 45 dB HL and aided CAEPs were present for five out of the six stimuli. The PEACH score for this infant was within 2 standard deviations of the normative mean for age. The CAEP results in this case were consistent with the parent’s observations, degree of the hearing loss shown on VRA, and level of amplification provided using the initial estimated audiogram. The information from CAEP testing and parent observations supported the decision to be cautious about the BOA results that showed no responses. This infant continues to wear hearing aids.

6. Limitations

This is a descriptive study on a small group of infants designed to reveal specific questions that need to be addressed in relation to the presentation and management of infants with ANSD. The small sample size and variable results across infants means that further investigations are required before firm clinical recommendations can be provided. In addition, calculations for auditibility were based on VRA results obtained after CAEP testing. This assumes that there was no change in hearing thresholds over the course of the study, which is not necessarily correct.

Conclusions

In keeping with previous studies the audiological profiles of infants with ANSD in this study varied considerably. If the fitting of amplification had been delayed until reliable VRA results were available all infants in this study would have experienced an extensive period of auditory deprivation. However, the process of determining the appropriate level of amplification was not straightforward, and none of the assessment tools used could accurately determine hearing thresholds when used in isolation, highlighting the importance of integrating information from a range of sources when making audiological decisions.

The results of this study demonstrate that the use of BOA together with parent observations in both the unaided and aided condition is of assistance when estimating the degree of the hearing loss prior to VRA results being available. Using this combination of information the infants in this study were able to commence the use of amplification at a mean corrected for gestational age of four months (SD 5), and achieve closer to optimal amplification before a mean corrected age of eight months (SD 6).

The results of unaided and aided CAEP testing were consistent with BOA, VRA, and PEACH results for some infants. However higher stimulus sensation levels did not monotonically increase the CAEP detection rate. For this reason clinicians need to take care when interpreting CAEP results and be aware that an absent CAEP response does not necessarily mean the stimulus is not audible.

It is important to note that aiming for optimal amplification based on VRA thresholds, and a prescriptive approach to hearing-aid fitting should be viewed only as the beginning of the audiological journey for infants with ANSD. Given that Ching et al (2013) reported no significant difference in speech and language outcomes for children with ANSD vs. SNHL, and a prescriptive approach to amplification was applied to all children in the study, the approach described here appears to be warranted, and delaying hearing-aid provision until after VRA thresholds are obtained is not recommended. Close monitoring of speech, language, and auditory behaviour on an ongoing basis is required, as it should be for infants with any type of hearing loss.

In future studies it would be beneficial to test unaided CAEPs at multiple intensity levels in individual infants with normal hearing and different degrees and types of hearing loss to establish the sensation level at which a CAEP can be reliably detected. In addition, if an increase in sensation level does not increasingly evoke CAEPs in infants with ANSD, as occurs for infants with SNHL (Van Dun et al, 2012), alternative amplification strategies may need to be considered.

Acknowledgements

We gratefully thank all the children, their families and their teachers for participation in this study. The authors acknowledge the financial support of the HEARing CRC, established and supported under the Cooperative Research Centres Program - an initiative of the Australian Government.

Declaration of interest: The authors declare no conflicts of interest.

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