

Frequency-Specific ABR and ASSR Threshold Assessment in Young Infants*

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Introduction

The importance of early identification and habilitation of hearing loss for improved access to auditory stimuli and for positive prognosis of speech and language is well established in the literature (American Speech-Language-Hearing Association [ASHA] 2004; Hyde 2005; Joint Commission on Infant Hearing [JCIH] 2007; Kennedy, McCann, Campbell, Kimm and Thornton 2005; Yoshinaga-Itano and Gravel 2001; Yoshinaga-Itano, Sedey, Coulter and Mehl 1998). As a result of the importance of early identification of hearing loss, many countries have established newborn hearing screening programs. Diagnostic audiologic assessment is required for follow-up for infants who do not pass newborn hearing screening, with the goal for most newborn hearing screening, follow-up and intervention programs, including the British Columbia Early Hearing Program (BCEHP), of confirmation and characterization of hearing loss (of a mild degree or worse) by age 3 months, and amplification by the age of 6 months (JCIH 2007). An auditory evoked potential (AEP) with high correlation to behavioral threshold is essential for the young infant

population and for those older infants and children where accurate behavioral thresholds cannot be obtained. This chapter describes the two frequency-specific AEP methods currently considered appropriate for infant threshold measures: the tone-evoked auditory brainstem response (ABR), the current gold-standard measure, and the relatively new brainstem auditory steady-state response (ASSR).

Transient versus Steady-State Responses

Auditory evoked potentials such as wave V of the ABR or N1 of the slow cortical potential are considered “transient” responses, where the response to one stimulus ends before the next stimulus occurs. An ASSR is a repetitive evoked potential, which is best considered in terms of its constituent frequency components rather than in terms of its waveform (Regan 1989, p. 35). If stimulus rates are high enough, the resulting response often resembles a sinusoidal waveform whose fundamental frequency is the same as the stimulation rate, although it may be more complex (Regan 1989, p. 35). In evoking an auditory steady-state response, stimulus rates are sufficiently rapid such that the transient response to one stimulus overlaps with responses to succeeding stimuli (Picton, John, Dimitrijevic and Purcell 2003).

With transient responses, longer latency responses tend to originate from sources higher in the auditory system; for example, wave V, which occurs approximately 6 to 15 ms following a brief stimulus, originates in the brainstem, whereas N1 occurs 80 to 150 ms following a stimulus and has its main sources within the auditory cortex. Latencies and intracranial origins of ASSRs are more complicated. Whereas with transient responses it is relatively straightforward to relate stimulus timing with evoked potential measures (i.e., amplitude

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and latency), with the overlapped nature of ASSRs, this relationship is quite complex (Picton et al. 2003). Different stimulus rates result in ASSRs with different neural origins; ASSRs to faster rates tend to reflect earlier/lower processing. For example, the ASSR to a stimulus with an 80-Hz modulation rate has its main sources in the brainstem (and has thus been termed the “brainstem ASSR”), whereas the 40-Hz ASSR has its main source in the auditory cortex, but also has brainstem contributions (Herdman, Lins et al. 2002).

There also exist, in practice, differences between transient and steady-state responses in how they are detected (presence versus absence) and measured (timing and amplitude). As the ASSR typically resembles a sinusoidal waveform whose fundamental frequency is same as the stimulation rate, it is best (and easily) measured using frequency-domain analyses, such as fast Fourier transforms (FFT). Well-tested procedures exist to provide objective (computer-determined) measures of ASSR presence/absence as well as the amplitude and phase (timing) of the ASSR. In contrast, transient responses such as the ABR typically involve more subjective visual detection (e.g., is a peak replicable?) and measurement of peak latencies/amplitudes. The use of objective measures for the ASSR has been touted as an “advantage” of the ASSR over the transient ABR; however, this advantage may be less than commonly believed, as expert clinicians well-trained in ABR measures can be very accurate; also, objective statistical measures of the ABR are increasingly becoming available (see below).

What Information is Required?

Many of the goals of AEP audiometry in infants are (or should be) the same as those of behavioral threshold estimation in older children and adults. Thus, as is routinely done in behavioral audiometry, AEP thresholds must be obtained for *frequency-specific* (i.e., tonal) stimuli, and to distinguish between sensorineural, conductive and mixed hearing losses, AEP techniques must provide results for both air- and bone-conduction stimuli (Gravel 2002; JCIH 2007). Frequency-specific thresholds and identification of the type of hearing loss are necessary to make decisions regarding medical intervention and planning aural (re)habilitation. Uncertainty with regards to hearing loss type leads to large delays in medical treatment and audiologic intervention (Gravel 2002).

This chapter therefore assumes, as indicated by the 2007 Joint Committee on Infant Hearing Position Statement (JCIH 2007), that clinicians will use frequency-spe-

cific stimuli and, when thresholds are elevated, bone-conduction stimuli. Although frequency-specific (e.g., tone-evoked ABR) testing has been proven reliable for many years, surprisingly many clinicians today persist in using broadband click stimuli for ABR thresholds, even though the inadequacy of click-ABR threshold has been known and documented for many years (e.g., Eggermont 1982; Picton 1978; Picton and Stapells 1985; Stapells 1989; Stapells and Oates 1997). As a single “point” estimate, it is impossible for the click threshold to provide estimates for thresholds at each octave frequency of the audiogram. More importantly, as a broadband stimulus, the click stimulates most of the cochlea, and one cannot say with certainty which frequency the click-ABR threshold represents—at best it represents the “best” hearing in the 500 to 8000 Hz range. Thus, click-ABR should not be routinely used for *threshold* determinations. Interestingly, the use of broadband stimuli has never been an issue with the brainstem ASSR; ASSR threshold testing has always utilized frequency-specific stimuli.¹ However, ASSR and ABR share another problem in their use by many clinicians: although bone-conduction testing is known to be essential, many clinicians still continue to use only air-conduction stimuli when estimating thresholds in infants using the ABR (or ASSR).

A key difference between behavioral assessments in older children and adults and electrophysiologic threshold assessments in infants concerns practical limits on the level of precision one seeks to attain. In behavioral testing of adults, one normally continues a threshold search until actual threshold is obtained, even when well within normal limits (e.g., 0 or -10 dB HL). Furthermore, one normally ends the search using a 5 dB step-size. Electrophysiologic testing of infants does not have the luxury of time for such precision: infants must be tested while sleeping and thus test time is limited. Modern, efficient protocols therefore limit the lowest level tested to those which will indicate the threshold is within normal limits. Most programs consider behavioral thresholds of 25 dB HL or better to be normal, thus minimum ABR intensities are chosen to test no lower than required to indicate if thresholds are 25 dB HL or better. Thus, ABR minimum normal levels for air conducted (AC) stimuli are currently 25 to 35 dB nHL. Similarly, threshold searches normally end with a minimum step-size of 10

¹ That ASSRs from the beginning have utilized tonal stimuli is interesting in itself, as it demonstrates how a new measure avoids the pitfalls of long-held beliefs and practice, even though the brainstem ASSR is quite likely equivalent to ABR wave V.

dB, with the exception of hearing loss greater than 70 dB, where 5 dB may be important given the much reduced dynamic range of hearing (BCEHP 2008; OIHP 2008).

“Response Present,” “No Response,” and “Could Not Assess”

As the above paragraph suggests, problems persist with the current practice of AEP audiometry. In addition to the above, one also sees misinterpretation of results, especially that of indicating a response is “present” or “absent” when the data are not of sufficient quality to make such a statement. Thus, one may get an inaccurate threshold because an ABR wave V was identified as “present” even though it was not significantly greater than the background noise (typically determined through replicability and/or flatness of tracings). As interpretation of the ABR usually relies on visual observation, ASSR thresholds based on statistical measures are thought by some to be more objective and thus better. However, even the ASSR is not immune to misinterpretation, as current clinical use of ASSR measures routinely violates statistical assumptions, and thus even “significant” ASSRs may sometimes be random noise (John and Purcell 2008; Luts, Van Dun, Alaerts and Wouters 2008). Moreover, both ABR and ASSR current clinical practices are plagued by the common mistake of indicating a “no response” when the data are too noisy to say so (i.e., the amplitude of the residual EEG noise is larger than the amplitude of a typical threshold response, and thus a response might have been missed). Fortunately, for both ABR and ASSR, solutions to the above problems are relatively straightforward, and are covered in the sections below.

Clinical Implementation of New Techniques

Widescale clinical implementation of a procedure requires evidence of reasonable quality in a sizeable subject group that is similar to the population requiring the clinical testing. A history of successful clinical use over many patients and over a long enough time to indicate any problems also provides evidence of a procedure’s usefulness. Preferably, these data have been published in peer-reviewed journals and by different research groups. In addition to numerous publications by many different investigators, the ABR to air- and bone-conducted brief tones has had a long history of successful clinical use (BCEHP 2008; OIHP 2008). In compari-

son, the brainstem ASSR has had a more limited history of clinical use. More importantly, there is much diversity in ASSR stimulus and analysis procedures/parameters, thus reducing both the clinical history and the clinical data. As we shall see, this limits the current clinical use of the ASSR.

Estimating Behavioral Thresholds Using AEPs

The primary goal of frequency-specific ABR or ASSR audiometry is to estimate behavioral thresholds. Brief-tone ABR thresholds (typically in dB nHL) and ASSR thresholds (typically in dB HL) are not directly equivalent to perceptual thresholds in dB HL, and there is no reason one should expect them to be. Therefore, offset adjustments for bias of ABR or ASSR thresholds are required. There are several methods of obtaining this estimated behavioral hearing level (EHL; Bagatto 2008; BCEHP 2008; OIHP 2008), with the most common methods being: (i) application of a regression formula (e.g., Rance et al. 2005; Stapells, Gravel and Martin 1995) or (ii) subtraction of a correction factor (BCEHP 2008; OIHP 2008). Recording variables, such as averaging time and residual EEG noise (Picton, Dimitrijevic, Perez-Abalo and van Roon 2005) and subject factors, such as maturation, affect the accuracy of these methods. For example, because of the effects of ear-canal maturation, the observed relationships between ABR/ASSR and behavioral thresholds will incorporate the effects of maturational SPL changes in the developing ear. Due to the effects of changing size/properties of the ear canal with age, less intensity is required to generate a given dB SPL at the eardrum in a neonate as would be required in an older child. The actual SPLs in early infancy will be greater than those for the same stimulus at the time of later behavioral threshold measurement, especially at higher frequencies, so the results may give an impression of progressive impairment (Bagatto 2008). Cognitive maturation also affects thresholds, such that behavioral VRA thresholds in a 7-month-old are typically higher than a behavioral threshold obtained when the child is 3 years of age. ABR/ASSR threshold accuracy (and thus the estimated behavioral hearing level accuracy) is affected by procedural factors, including recording time (longer recording times per intensity typically equal less noisy recordings and thus more accurate thresholds) and final intensity step-size (a 10 dB final step-size could easily miss true threshold by 5-10 dB).² Finally, differences between

AEP and behavioral thresholds typically show standard deviations of about 10 dB; thus, in about one in 20 subjects, behavioral thresholds are under- or over-estimated by 20 dB (Picton et al. 2005). When using any thresholds obtained in infancy, and especially AEP thresholds, one must keep in mind that the estimated behavioral threshold is an estimate, and is often off by 10 dB and occasionally by 15 to 20 dB. Thus, EHL correction factors must take this possibility into account, as must any subsequent fitting of amplification.

Auditory neuropathy spectrum disorder (ANSO) or any significant neurologic dysfunction within the VIIIth nerve and/or brainstem will reduce or eliminate both the transient and steady-state brainstem responses. Thus, whenever no clear response is present at highest intensities (and for transient ABR, no clear wave V), one must investigate the possibility that the elevated ASSR/ABR threshold is due to ANSO (e.g., no neural components) or neurologic (e.g., present early waves but absent wave V) disorder. This is accomplished by recording the transient ABR to high-intensity mono-polarity clicks as well as evoked otoacoustic emissions (EOAEs; Rance and Starr 2011). When ANSO or neurologic disorder is present that significantly degrades (or eliminates) ABR wave V, neither the transient ABR nor the brainstem ASSR may provide accurate measures of hearing thresholds.

The Transient Tone-Evoked ABR

The ABR to brief tones has been used successfully for threshold assessment for more than 30 years, since the first publications in the 1970s. Nevertheless, despite early and subsequent success, there existed much misinformation about the tone-evoked ABR. Many clinicians erroneously believed that tone-ABR thresholds lacked frequency specificity especially at low frequencies (i.e., they did not reflect the nominal frequency of the tone), that they did not provide accurate estimates of the behavioral audiogram, and finally, that they were too difficult and too time-consuming to obtain. In fact, there were relatively few research articles noting problems with tone-ABR, and most of these articles had significant technical problems and/or presented results from only a few cases. In contrast, our meta-analysis of the tone-ABR literature in 2000 (Stapells 2000b) demon-

strated that the great majority of research papers considering the tone-ABR for threshold estimation showed reasonably accurate results. More recent studies have confirmed the utility and accuracy of the tone ABR and have expanded the results to even younger infants (Lee, Hsieh, Pan and Hsu 2007; Lee, Jaw, Pan, Hsieh and Hsu 2008; Rance, Tomlin and Rickards 2006; Ribeiro and Carvalho 2008; Vander Werff, Prieve and Georgantas 2009). Importantly, clinical programs have effectively used the ABR to air- (and bone-) conducted tones for many years. Experience with province-wide universal early hearing programs in Ontario and British Columbia indicates that with appropriate training and use of efficient parameters and test sequences, a substantial amount of information is typically obtained within one test session, thus the tone-ABR is neither too difficult nor too time consuming (Janssen, Usher and Stapells 2010). Figure 1 shows typical tone-ABR recordings from a young infant in response to brief tones presented at “normal” levels (25-35 dB nHL, see below).

How well the air-conduction tone-ABR threshold estimates threshold in infants with normal hearing or hearing loss is presented in tables 1 and 2, which show results from the previous meta-analysis, as well as results from several more recent studies, and compares these to adults. As shown in table 1, normal infants show mean thresholds of about 15 to 20 dB nHL for 500 through 4000 Hz, similar to adult thresholds. However, not all normal-hearing infants show responses at 20 dB nHL, and for clinical purposes programs are rarely interested in determining normal thresholds better than 25 to 30 dB EHL, thus criteria for “normal” are higher than

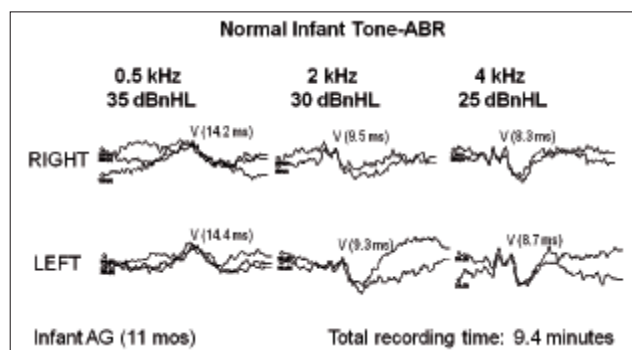


Figure 1. Tone-evoked ABR waveforms obtained from an infant (aged 11 months) with normal hearing. Brief-tone stimuli were presented at the “normal” intensity levels for each frequency. Replicable responses are clearly present for each waveform set, with wave V location and latency indicated. Total time required to obtain these results was 9.4 minutes. Timebase for waveforms is 25.6 ms. Results obtained in collaboration with Renée Janssen.

² However, due to test-time constraints imposed by the requirement that infants must sleep during ABR/ASSR testing, normally one uses a final step-size of 10 dB for ABR/ASSR testing.

Table 1. Air-conduction tone-ABR thresholds (in dB nHL) in infants and young children with normal hearing. Adult results from Stapells (2000b) meta-analysis are shown for comparison.

AC TONE-ABR STUDY	500 Hz	1000 Hz	2000 Hz	4000 Hz
<i>Meta-analysis of adult data</i> (1977-1999; 22 studies); Stapells, 2000b	20±13 (271)	16±10 (271)	13±8 (216)	12±8 (258)
Meta-analysis of infant data (1977-1999; 9 studies) Stapells, 2000b	20±9 (369)	17±6 (78)	14±7 (65)	15±10 (209)
Rance et al., 2006 (age 6 weeks data; thresholds converted using nHL calibrations in Table 5)	30±7 (17)			15±6 (17)
Lee et al., 2007	18±8 (88)	17±7 (75)	13±7 (69)	11±6 (56)
Vander Werff et al., 2009	27±8 (40)		14±6 (40)	12±6 (30)

Mean (dB nHL) ± standard deviation; Results rounded off to closest decibels; Number of subjects in parentheses.

the mean thresholds. Typically, these normal levels are in the range of 30 to 40 dB nHL for 500 Hz, 25 to 35 dB nHL for 1000 Hz, 20 to 30 dB nHL for 2000 Hz, and 20 to 25 dB nHL for 4000 Hz. Currently, the BCEHP specifies normal levels of 35 dB nHL for 500 Hz, 30-35 dB nHL for 1000 Hz, 30 dB nHL for 2000 Hz, and 25 dB nHL for 4000 Hz (BCEHP 2008). If a response is present at the normal level, the EHLs at that frequency are within the normal range.

The scatterplots presented in Figure 2 plot tone-ABR (in dB nHL) and follow-up behavioral thresholds (in dB HL) for a relatively large group of infants with normal hearing and hearing loss (Stapells et al. 1995). Typical of the literature, correlations between infant tone-ABR and behavioral thresholds in this study were high: $r = .94$, $r = .95$ and $r = .97$ for 500, 2000, and 4000 Hz, respectively. Table 2 presents difference scores (i.e., tone-ABR threshold in dB nHL minus pure-tone behavioral threshold in dB HL) from many studies for infants and young children with hearing loss, and compares these to those from adults. Typically, tone-ABR thresholds are within 5 to 10 dB of the behavioral thresholds. Across most studies, standard deviations

are typically on the order of 9 to 12 dB (Stapells 2000b), and differences of 20 dB are occasionally found, although most ($\geq 65\%$) thresholds are within 10 dB. Figure 3 shows ABR-predicted and behavioral audiograms for several infants. Table 2 also suggests there may be somewhat greater variability in tone-ABR minus-behavioral threshold differences scores for infants with otitis media, highlighting the importance of obtaining bone-conduction results for these infants (Gravel 2002; Stapells 1989).

Although it is widely held that difference scores decrease (i.e., tone-ABR threshold is closer to behavioral threshold) as hearing loss increases, the existing data do not clearly support this (Singer and Hyde 2009). Slope of ABR versus behavioral threshold regression lines are typically close to unity, indicating thresholds are not closer with severe loss. However, the issue is complicated by the fact that: (i) most ABR measures in the normal range do not seek true thresholds and (ii) the presence of no-response results for ABR occur at a lower intensity (in dB nHL) than for pure-tone behavioral (in dB HL), due in part to transducer limitations.

Table 2. Air-conduction tone-ABR minus behavioral threshold difference scores in infants and young children with hearing loss. Adult results from Stapells (2000b) meta-analysis are shown for comparison.

AC TONE-ABR STUDY	HL type	500	1000	2000	4000
<i>Meta-analysis of adult data</i> (1977-1999; 8 studies); Stapells, 2000b	ADULT SNHL	+13±11 (85)	+10±12 (167)	+8±10 (100)	+5±13 (84)
Meta-analysis of infant data (1977-1999; 6 studies); Stapells, 2000b	SNHL	+6±14 (125)	+5±14 (118)	+1±11 (110)	-8±12 (35)
Lee et al., 2008 † (Group with behavioral thresholds >40dBHL)	SNHL	+5±5 (135)	0±5 (119)	-5±8 (112)	-5±8 (91)
Vander Werff et al., 2009	SNHL	+13±12 (3)		0±9 (7)	-3±14 (6)
Stapells & Gravel, unpublished (ABR and behavioral obtained on same day)	Otitis Media	+10±19 (30)		+1±18 (26)	-11±15 (11)

Difference score (dB) – tone_ABR threshold (in dB nHL) minus pure_tone behavioral threshold (in dB HL); Mean (dB) ± standard deviation († Lee et al. results are median difference scores ±1 quartile); Results rounded off to closest decibels; Number of subjects in parentheses.

It does appear that it is difficult to get close to true normal threshold (e.g., -5 to 10 dB nHL) in individuals with normal hearing, but this is complicated by acoustic noise (ambient noise in room) and electrical noise (room and subject) issues. Given near-unity slopes, estimation of behavioral thresholds (EHL) using either regression functions or correction factors should yield equivalent results. Importantly, as table 2 shows, difference scores for infants and young children are clearly different from those of adults; it is therefore important that we use infant data to determine appropriate correction factors. The British Columbia and Ontario provincial programs currently use conservative correction factors of -15, -10, -5, and 0 dB for estimating 500-, 1000-, 2000-, and 4000- Hz pure-tone behavioral thresholds (in dB HL) from tone-ABR thresholds (in dB nHL; BCEHP 2008; OIHP 2008; Sininger and Hyde 2009).

ABR Assessment of Conductive Loss

The most common cause of elevated ABR (or ASSR) thresholds in young infants is conductive loss

(Canadian Working Group on Childhood Hearing 2005; Gravel 2002). This is especially so for young infants referred for diagnostic ABR/ASSR testing after failing one or more newborn hearing screenings. Protocols, therefore, must be able to determine whether a significant conductive component is present. When testing older children and adults, this assessment is primarily achieved through comparison of air- versus bone-conduction thresholds. Additional information may be gained from immittance and EOAE measures; however, these latter measures are unable to quantify the degree of conductive loss. In the presence of conductive pathology, they are typically abnormal whether the conductive component is relatively minor (e.g., only 5 dB) or substantial (e.g., 30 dB). Others have suggested that analysis of ABR wave V or wave I latencies in response to air-conducted clicks can differentiate conductive from sensorineural losses, and perhaps can even quantify the conductive component (e.g., Fria and Sabo 1979; McGee and Clemis 1982; Yamada, Yagi, Yamane and Suzuki 1975). Our research, using click-ABR wave I latencies, has indicated that although air-conducted latencies are indeed prolonged on average in infants with

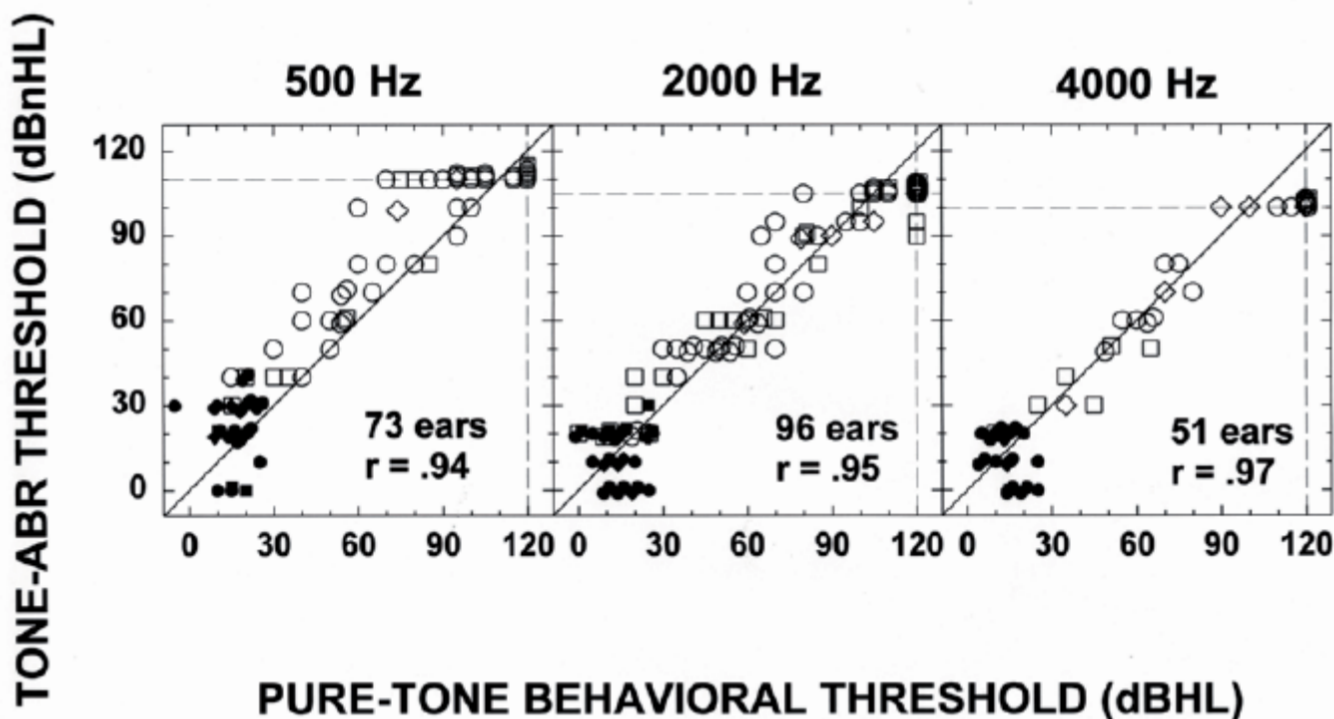


Figure 2. Threshold estimation using the ABR to 500 Hz (*left*), 2000 Hz (*middle*), and 4000 Hz (*right*) tones presented in notched noise. Results for normal hearing (*filled symbols*) and sensorineural impaired (*open symbols*) ears are plotted with three age ranges (at time of ABR) identified: 0 to 6 months (*diamonds*); 7 to 48 months (*circles*); 49 months or greater (*squares*). Shown also are the correlation coefficients for each frequency across all subjects and the number of ears involved. Dashed lines (---) indicate the no response range for each frequency and test, equivalent to the equipment maximum output plus 10 dB. Points plotted \geq the dashed line indicate no response for the measure. Points with multiple subjects have symbols offset (± 1 dB per subject) to show clearly the overlapping data. Diagonals (*solid lines*) represent perfect ABR-behavioral threshold correspondence and are not regression lines. Reproduced with permission from Stapells, D. R., Gravel, J. S., and Martin, B. A. (1995). Thresholds for auditory brain stem responses to tones in notched noise from infants and young children with normal hearing or sensorineural hearing loss. *Ear and Hearing* 16 (4): 361–371. Copyright 1995 Lippincott Williams and Wilkins.

conductive hearing loss, latency-based measures of the conductive component are not reliable. Some infants with conductive loss showed normal latencies (Figure 4), whereas some infants with either sensorineural hearing loss or normal thresholds showed prolonged latencies (Mackersie and Stapells 1994). The overlap between groups is even greater for wave V latencies (Vander Werff et al. 2009). Given these overlaps, it should not be surprising that attempts to quantify the amount of conductive component using AC click-ABR wave V or wave I latency shifts have not proven reliable, with large errors in many infants (Eggermont 1982; Mackersie and Stapells 1994) and relatively low correlations between latency and the size of the air-bone gap (Vander Werff et al. 2009). Furthermore latency-based measures typically require responses to air-conducted clicks (especially for wave I measures); as discussed above, no frequency-specific information can be reli-

ably obtained using clicks; given the large amount of information required from sleeping infants, modern ABR protocols thus rarely use clicks, except when assessing infants suspected of ANSD or other neurologic problem that may disrupt the ABR.

The problems with latency-based measures are demonstrated in Figure 4, which presents results from an infant whose air-conducted click-ABR wave V thresholds were normal (20 dB nHL or better) for the left ear but mildly elevated (40 dB nHL) for the right ear; wave V latencies for both ears were both well within normal limits; indeed, latencies for the right ear with elevated thresholds were shorter in latency. Relying on latency shifts, one might interpret no conductive component was present in either ear and the right-ear threshold elevation was a sensorineural loss. This infant, however, had normal thresholds for bone-conduction stimuli and otoscopic examination revealed bilateral otitis media;

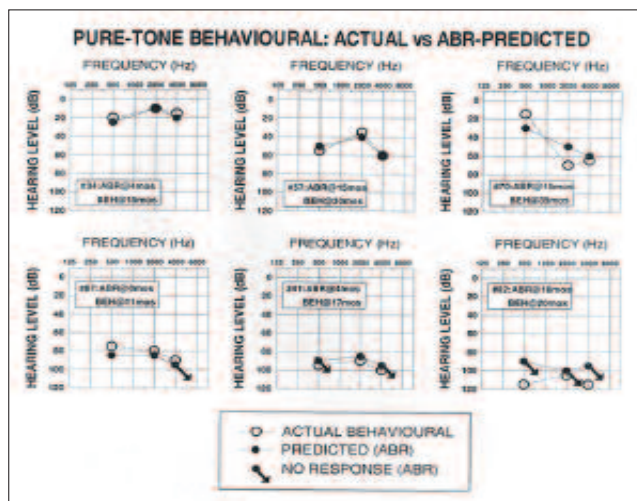


Figure 3. Comparison of ABR predicted audiograms with actual behavioral audiograms obtained on follow up testing for six infants. Results for individuals with normal hearing (*upper left corner*) to profound sensorineural hearing loss (*lower right corner*) are shown. ABR predicted thresholds were determined using the linear regression equations presented in Stapells, Gravel, and Martin (1995). Predicted thresholds with arrows were ABR “no response” results—note the ABR’s inability to differentiate between 90 and 110 dB HL. Otherwise, most ABR predicted thresholds are quite close to actual behavioral thresholds. BEH = behavioral. Reproduced with permission from Stapells, D. R. (2000a). Frequency specific evoked potential audiometry in infants. In R. C. Seewald (ed.), *A sound foundation through early amplification: Proceedings of an international conference* (pp. 13–31). Stäfa, Switzerland: Phonak AG. Copyright 2000 Phonak.

air-conduction thresholds returned to normal at a subsequent visit.

It is therefore not possible to reliably determine the presence or degree of a conductive component using air-conduction ABR latency information. With the exception of ABR assessment of ANSD and/or neurologic involvement, we do not use any ABR latency results when determining *threshold*.³ Rather, we rely on the combination of air- (AC) and bone- (BC) conduction tone-ABR results. An elevated tone-ABR (or ASSR) threshold to air-conduction stimuli with tone-ABR responses to bone-conduction stimuli at normal levels clearly indicates the presence and degree of a conductive loss; if ABR thresholds to bone-conduction stimuli are elevated, a sensorineural component is present. Current comprehensive diagnostic protocols for infants emphasize the importance of obtaining bone-conduction information early in the process (i.e., as soon as an elevation in air-conduction thresholds is indicated)—this information is needed to determine the next test step and is important both for appropriate follow-up and for parent counseling. Indeed, when bone-conduction thresholds turn out to be within normal lim-

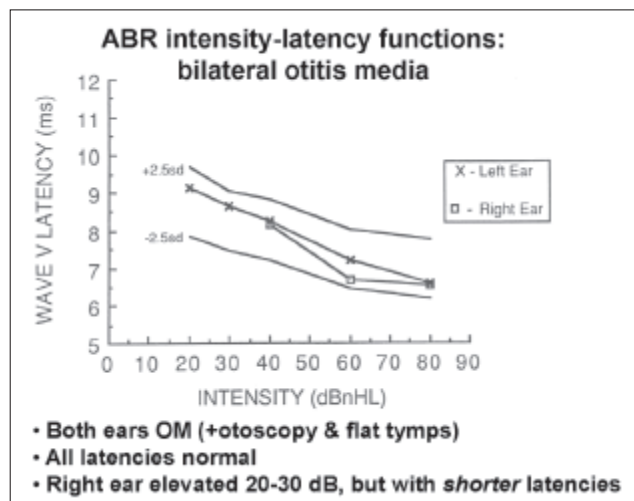


Figure 4. Click-evoked air-conduction ABR wave V intensity-latency functions in an infant with bilateral otitis media (and normal bone-conduction hearing). Otitis media indicated by pneumatic otoscopy (i.e., presence of fluid) and flat tympanograms bilaterally. Despite bilateral otitis media and a 20 to 30 dB elevation for the right-ear ABR, all latencies are well within normal limits, with latencies for right-ear stimulation slightly shorter than for the left ear. Follow-up testing indicated normal ABR and behavioral thresholds, and normal middle-ear function, indicating sensorineural loss was not present and the elevation was conductive in nature. Thus, reliance on air-conduction ABR intensity-latency functions could have erroneously suggested no conductive loss, with the right-ear elevation being sensorineural in nature. Results obtained in collaboration with Judy Gravel.

its, indicating a conductive loss, the thresholds for air-conduction stimuli in many cases are of less importance because, when resulting from fluctuating conditions such as otitis media, they may be quite different in days following the assessment. Unfortunately, currently many clinicians routinely fail to obtain ABR results for bone-conduction stimuli after finding elevated air-conduction threshold(s), relying instead on immittance results. Tone-ABR (and to a much lesser extent, ASSR) protocols, test parameters, and results are currently available for the assessment of conductive loss.

³ We do not evaluate whether a tone-ABR wave V latency is “normal” or “prolonged,” as this typically provides no extra (or reliable) information over AC versus BC tone-ABR results. We do use latency differences when considering differences between wave V recorded in ipsilateral and contralateral EEG channels (see below). Also, if a “wave V” latency appears to be too early to be wave V, we will be concerned the thresholds are unreliable (e.g., neurologic or ANSD concerns). Of course, for neurologic/ANSD assessment, we do consider normality of click-ABR latency measures.

Bone-Conduction Tone-ABR

Bone-conduction tone-ABR has a history of over two decades of regular use in the clinic (Gravel, Kurtzberg, Stapells, Vaughan and Wallace 1989; Stapells 1989; Stapells and Ruben 1989), and protocols using bone-conduction tonal stimuli are currently routinely employed in large programs such as BCEHP (2008) and OIHP (2008).⁴ Despite their history of clinical use and importance for clinical assessment, it is somewhat surprising that relatively few bone-conduction tone-ABR data in infants have been published in the peer-reviewed literature (Cone-Wesson 1995; Cone-Wesson and Ramirez 1997; Foxe and Stapells 1993; Nousak and Stapells 1992; Stapells and Ruben 1989; Vander Werff et al. 2009), with most published for data in infants having normal hearing or conductive hearing loss.

Young infants' thresholds for bone-conduction stimuli differ significantly from adults (Foxe and Stapells 1993; Small and Stapells 2006, 2008c; Stapells and Ruben 1989; Stuart, Yang and Green 1994; Stuart et al. 1993; Vander Werff et al. 2009; Yang et al. 1987), likely due primarily to the immaturity of the infant skull (Anson and Donaldson 1981; Small and Stapells 2008c; Yang et al. 1987). Table 3 shows normal infant BC tone-ABR thresholds obtained by several studies. There is some variability in the literature, but all show mean thresholds that are: (i) better for low versus high frequencies, and (ii) better than expected compared to those for adults. Thus adult "normal" levels for bone-conduction stimuli

do not apply to infants; criteria for infants must be determined directly from infant BC ABR results. We have found that to be considered "normal" (for bone-conduction hearing), infants should show ABRs to bone-conducted tones presented at 20 dB nHL for 500 Hz and at 30 dB nHL for 2000 Hz (Stapells 1989; Stapells and Ruben 1989). Currently, there are too few infant ABR data for 1000- and 4000-Hz bone-conduction tones (see table 3), so these frequencies are not routinely tested using bone-conducted stimuli. Because the upper limits (before distortion) of the most commonly used bone oscillator (B71) for brief tones is 51 dB nHL at 500 Hz and 63 dB nHL at 2000 Hz (Small and Stapells 2003), a range of only 30 dB above these normal levels can be tested. Due to several reasons (limited dynamic range; 10 dB step-size; lack of published data for AC-BC differences in infants), the "air-bone gap" is usually not calculated. Rather, the BC results are primarily used to indicate whether bone thresholds are "normal" or "elevated" and thus whether or not there is a sensorineural component (i.e., BC elevated) to an elevated AC threshold. The approximately 30 dB dynamic range essentially only allows one to classify bone thresholds as "normal," "mild/moderate elevated" or "moderate or greater" (Hatton, Janssen and Stapells in preparation). Figure 5 shows bone-conduction tone-ABR results from young children with conductive and sensorineural hearing loss.

Bone-Conduction ABR: Isolating the Responding Cochlea

Masking of the contralateral ear, typically required with bone-conduction testing in adults, is currently not feasible and likely not necessary for ABR audiometry in young infants. Masking is not feasible because: (i) effective masking levels for bone-conduction brief-tone stimuli in infants are not known and (ii) time is too limited to record using several masking levels, such as one might when attempting plateau masking (Stapells 2000a).

Table 3. Bone-conduction tone-ABR thresholds (in dB nHL) in infants and young children with normal bone-conduction hearing.

BC TONE-ABR STUDY	500	1000	2000	4000
Stapells & Ruben, 1989 (normal group)	2* (24)		6* (24)	
Stapells & Ruben, 1989 (all infants)	-2* (66)		4* (66)	
Foxe & Stapells, 1993	3±10 (9)		14±7 (8)	
Cone-Wesson & Ramirez, 1997 (age: 1-2 days)	-15±10† (24)			7±7† (20)
Vander Werff et al., 2009	7±8† (40)		8±7† (40)	

Mean (dB nHL) ± standard deviation (where available); Results rounded off to closest decibels; Number of subjects in parentheses; * Threshold = 50% point on cumulative response-presence distribution for "normal" and "all" infants; † Thresholds in nHL adjusted using Table 5 zero dB nHL calibrations; Standard deviations estimated from graph in original study.

⁴ The ABR to bone-conduction clicks has also been used clinically, preceding the use of bone-conducted tones (e.g., Cone-Wesson 1995; Cornacchia, Martini and Morra 1983; Hooks and Weber 1984; Kavanagh and Beardsley 1979; Mauldin and Jerger 1979; Muchnik, Neeman and Hildesheimer 1995; Stuart, Yang, Stenstrom and Reindorp 1993; Yang, Rupert and Moushegian 1987; Yang and Stuart 1990). However, as with air-conducted clicks, bone-conducted clicks lack frequency specificity (Kramer 1992); also, due to maturational issues, the "effective" spectra for air- and bone-conducted clicks differ (Small and Stapells 2008c), making comparison between the two difficult in infants.

However, because of their immature skulls, young infants show substantial interaural attenuation of bone-conducted stimuli, as much as 25 dB (Small and Stapells 2008b; Yang et al. 1987). Thus stimuli presented to the temporal bone at the low stimulus levels (20-30 dB nHL) required to demonstrate normal versus impaired cochlear function will stimulate primarily the cochlea ipsilateral to the oscillator placement, and masking may not be required. Furthermore, the laterality of ABR origin (i.e., which cochlea is resulting in the recorded ABR) can be determined using 2-channel EEG recordings, and observing the large ipsilateral/contralateral wave V latency and amplitude asymmetries present in infants and young children (but not in older children or adults). As shown in Figure 5, in the infant with a normal ABR to BC tones, wave V is larger and earlier in the EEG channel ipsilateral to the stimulated cochlea (Edwards, Durieux-Smith and Picton 1985; Foxe and Stapells 1993; Stapells 1989; Stapells and Mosseri 1991); thus, if one sees this pattern in the channel on the same side as the bone oscillator, one can infer that stimulation of the cochlea on the same side has resulted in the ABR. However, if one sees the opposite pattern, as shown in the

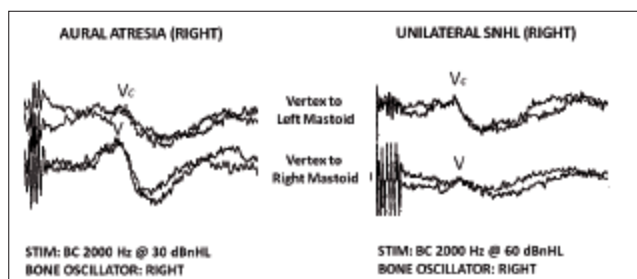


Figure 5. ABR to 2000-Hz bone-conducted tones in two children, one with conductive hearing loss (*right panel*) and one with unilateral sensorineural hearing loss (*left panel*). Shown are the results for the left (“Vertex to Left Mastoid”) and right (“Vertex to Right Mastoid”) EEG channels, obtained simultaneously, with the bone oscillator placed on the right temporal bone. In the infant with conductive loss due to right-ear atresia, wave V in the right EEG channel (i.e., ipsilateral to bone oscillator placement) is both earlier and larger than the wave V in the left (contralateral) EEG channel. This is a *normal asymmetry* and indicates the right cochlea is the primary contributor to the response to these bone-conduction tones at the normal (30 dB nHL) intensity. This indicates a normal 2000-Hz bone-conduction response for this ear. In the child with a unilateral (right-ear) sensorineural loss, 60 dB nHL 2000-Hz bone-conduction tones presented to the right temporal bone resulted a wave V in the right EEG channel (i.e., ipsilateral to bone oscillator placement) that is much smaller and later than the wave V seen in left (contralateral) EEG channel. This is an *abnormal asymmetry*, indicating the left ear is the primary contributor to the response, and thus indicating the presence of a sensorineural hearing loss. Further ABR and behavioral testing indicated a severe unilateral sensorineural hearing loss in the right ear. Vc: wave V in contralateral EEG channel. Waveform timebase: 25 ms.

child with sensorineural hearing loss (SNHL) in Figure 5, then the opposite cochlea has produced the response, and a sensorineural impairment is present (Singer and Hyde 2009; Stapells 1989). Although reasonably well-tested in infants with conductive loss (Stapells 1989; Stapells and Ruben 1989), the ipsi/contra technique requires further assessment in infants with sensorineural or mixed loss; the author’s clinical experience as well as that of larger programs (e.g., BCEHP, OIHP) indicates reasonable results in these latter groups (Hatton et al. in preparation).⁵

Tone-ABR Technical Details

Tables 4 and 5 present specific recording and stimulus parameters we recommend for tone-ABR, based on more than 30 years of research and 20 years of clinical application. The data supporting each choice are discussed in detail elsewhere (BCEHP 2008; Stapells 2000a; Stapells and Oates 1997) and thus are not elaborated on here. Test sequences for tone-ABR are provided below in a later section concerning clinical ABR/ASSR protocols.

Most clinical AEP equipment is reasonably capable of basic tone-evoked ABR measures. However, not all systems are optimal and some are not up to the task. Optimally, a very wide and flexible range of stimulus and recording settings should be available. Currently, we consider the following to be minimum requirements for tone-ABR systems (additional capabilities are required for other AEPs such as slow-cortical responses):

Recording requirements: Two EEG channels allowing for simultaneous ipsilateral/contralateral recordings (with artifact reject locked/chained across channels); EEG filters allowing for 30- to 3000-Hz and 30- to 1500-Hz settings; flexible stimulus artifact setting (allowing for $\pm 10 \mu V$ to $\pm 25 \mu V$), which can be set to exclude rejection due to voltages within the region of stimulus artifact; flexible recording sweep time, with at least a 24 to 25 ms sweep time allowed; an online calculation and display of residual noise (RN) in the waveform (e.g., “RN” from “ \pm ” average: Özdamar and Delgado 1996; Picton, Linden, Hamel and Maru 1983; or “single-point variance”: Don and Elberling 1996), to indicate whether the

⁵ The normal infant ABR wave V ipsi/contra asymmetries are also useful when recording responses to high-intensity for air-conduction stimuli when one suspects a significant interaural difference in the degree of hearing loss.

waveform is quiet enough to conclude “no-response,” with flexible parameters such the duration and location of the window over which the noise is calculated; a signal-to-noise measure (preferably calculated automatically while recording data) to assist clinicians in concluding a response is present (e.g., standard deviation ratio [SDR; Picton et al. 1983]; or signal-to-noise ratio [SNR; Özdamar and Delgado 1996]; F-test using single-point variance [Fsp; Don, Elberling and Waring 1984]; or correlation between waveforms [CCR; Hyde, Sininger and Don 1998; Picton et al. 1983]), again, all with flexible parameters; ability to add or subtract waveforms offline (e.g., to increase the number of trials; to calculate “alternating” from rarefaction and condensation click results, etc.); and standard measures of latency and amplitude.

Stimuli requirements: Possibility of air- (insert and supra-aural earphones) and bone-conduction transducers; acoustic calibrations specific to each stimulus and transducer (with the possibility of the user adjusting the calibrations); octave frequencies from 500 through 8000 Hz; linear and/or Blackman (or exact-Blackman) windowing functions, with flexible rise/fall times, and plateau times (or total durations) allowing for stimuli with total durations of 5 cycles (e.g., linear windows with 2 cycles rise, 1 cycle plateau, and 2 cycles fall times, or Blackman-windowed tones with 5-cycle total duration and no plateau); stimulus rates of at least 37 per second when using a 24- to 25-ms sweep time (i.e., without skipping stimuli); ability to use rarefaction, condensation and alternating onset polarity.

Preferably, the above recording and stimulus criteria are only a minimum, and tone-ABR systems will provide the above *plus* wider ranges of settings and additional features; better systems are those with maximum flexibility and allow for speedy changing of stimulus parameters, addition of waves, marking/measuring of waveforms and subsequent printouts. Because some infants will have neurologic dysfunction or ANSD, all systems must also allow for switching to click-ABR or slow-cortical potential parameters.

Interpretation of Tone-ABR Waveforms

Although the tone-ABR has the capability to provide reasonably accurate estimates of threshold, a continuing major problem with the clinical use of the ABR today lies largely with the clinicians who carry out the testing and/or interpret the waveforms, rather than with the ABR itself. Currently, clinicians typically determine response presence/absence and waveform noisiness “sub-

jectively” by visually assessing the repeatability and noisiness of multiple “replicate” waveforms. Most clinicians become reasonably proficient in this; some become so good as to be considered “experts”; however, some clinicians seem never to gain the skill. The differences are likely due to training, experience (e.g., number and diversity of cases) and inherent abilities. Fortunately, with modern systems, clinicians need not base their interpretation solely on their visualization of the responses (although for very experienced and proficient observers, this may currently be the best method). Objective measures of response replicability/signal-to-noise ratio and, importantly, response noisiness, are available and should be used.

Too often, clinicians indicate a response is “present” or “absent” when they do not have the data of sufficient quality to make such a statement. As noted above, to conclude a response is present, the clinician must have evidence of a significant signal-to-noise ratio. When assessed visually, a “present” response must contain a replicable waveform, one which is repeatable over its total duration, usually at least 3 to 4 ms for wave V. To be sure it has a significant signal-to-noise ratio, the waveform’s peak-to-peak amplitude (the average of all replications) must be at least three times the average difference between the replications (Don and Elberling 1996; Picton et al. 1983; Picton and Maru 1984). On the other hand, a decision that a wave is “absent” can only be made if replications are essentially flat and show little or no difference between them (i.e., repeatably flat over at least the 3- to 4-ms duration in the region of wave V). If the waveform peak in question is not repeatable or if the overall average of the replications is not flat (i.e., noisy), the clinician must obtain more replications. Otherwise, the result should be interpreted only as “could not evaluate” or “data incomplete” (Sininger and Hyde 2009; Stapells 2000a). Figure 6 shows examples of waveforms in each of these three categories. Much of the variability of ABR thresholds and the inconsistency with subsequent behavioral thresholds are the result of basing waveform interpretation on insufficiently replicable responses and waveform tracings too noisy to be called “no response.” Fortunately, the solutions to this problem are quite simple: obtain additional replications when needed (this assumes one has made every attempt to ensure the infant is quietly asleep), average together replications to increase the number of trials in an average and thus reduce residual noise in waveform, and do not interpret conditions with insufficient replications and/or noisy data.

Table 4. Recommended recording parameters for tone-ABR.

	Air Conduction	Bone Conduction
EEG channels	Minimum: 1 channel Cz- Mastoid-ipsi Preferred: 2 channels † Cz- Mastoid-ipsi Cz- Mastoid-contra	Minimum: 2 channels † Cz- Mastoid-ipsi Cz- Mastoid-contra
EEG filters (12 dB/octave slope)	30 Hz (high pass) to 1500-3000 Hz (low pass)	
Gain	50,000 - 100,000	
Artifact rejection	Trials exceeding $\pm 25 \mu\text{V}$ ($\pm 15 \mu\text{V}$ is acceptable if there are <10% rejections). Set artifact region to start <i>after</i> end of stimulus so that stimulus artifact does not trigger artifact rejection (if available)	
Number of accepted trials per replication	Typically 2000 per replication; additional trials may be required to reduce noise (achieved either by increasing the number of trials per replication or by averaging together replications) * Minimum 1000 per replication *After 1000 trials, if online residual noise measure available, may stop when waveform noise reduced to \leq criterion (e.g., IHS RN $\leq 0.08 \mu\text{V}$ or Bio-Logic sp-variance $\leq 20\text{-}30 \text{ nV}$)	
Number of replications	At least two (very often three, sometimes four)	
Recording (time) window and stimulus rate	Typically 25 ms which usually allows a rate up to about 39.1/s ‡ Some systems are slower, thus either a slightly shorter window (e.g., 23-24 ms) or a slightly slower rate (e.g., 37.1/s) must be used. Clinicians must check that their system <i>averages</i> at 39.1/s and does not skip stimuli. 2000 trials should take about 51 seconds; if it requires substantially longer, it is skipping stimuli and either a slower rate or a shorter recording window is required.	
Visual Display Scale	Waveforms must be displayed with a sufficient display gain such that very small responses would not be missed. A rule of thumb is to “blow-up” waves such that peak-to-peak height of largest wave is <i>at least</i> 1/4 the length of the recording window (i.e., if ABR waveform displayed is 10 cm in length then the display should be increased such that the peak-to-peak amplitude of wave V-V’ is <i>at least</i> 2.5 cm in height; e.g., IHS Smart-EP amplitude scale of $0.5 \mu\text{V}$ & 20% plot size, split page display)	

† Laterality (cochlear origin) of BC-ABR determined from wave V ipsi/contra asymmetries (infants/young children only). Consider this also for air conduction if a large difference in thresholds between ears exists.

‡ Although a 25-ms window works for all frequencies, infant responses to 2000- and 4000-Hz stimuli are shorter in latency and thus a shorter time window (18–20 ms) *and* a faster rate (49.1/s) would be acceptable and faster.

Table 5. Stimuli for tone-ABR: rise/fall times, durations, acoustic calibrations for 0 dB nHL, and signal-to-noise (SNR) regions.

Frequency (Hz)	Linear window	Blackman window	Acoustic calibration for 0 dB nHL			SNR region †† (begin to end, in ms)	
			Rise/Fall (r/f) & Plateau (2-1-2 cycles)	Total Duration (5 cycles total)	Insert (AC) ER-3A dB ppe SPL†	Supra (AC) TDH-49 dB ppe SPL	Bone (BC) B-71 dB ppe re: 1 µN RMS
500	4-ms r/f 2-ms plateau	10-ms total	22	25	67	10.5-20.5	20dB: 10.5-20.5 ≥30dB: 14-24‡
1000	2-ms r/f 1-ms plateau	5-ms total	25	23	54	7.5-17.5	
2000	1-ms r/f 0.5-ms plateau	2.5-ms total	20	26	49	6.5-16.5	6.5-16.5
4000*	AC: 0.5-ms r/f 0.25-ms plateau	AC: 1.25-ms total	26	29	46	5-15	
	BC: 1-ms r/f 0.25-ms plateau	BC: 2.25-ms total					

Rate: 37.1 to 39.1/s (assuming 23-25 ms averaging window) – faster rate/shorter time window for 2000 and 4000 Hz (49.1/s; 18-20 ms) may be considered; Polarity: alternating; ppe: peak-to-peak equivalent dB (“peak” = ppe + 3 dB for brief tones); † Insert earphones calibrated using a DB0138 2-cc coupler; †† SNR region (for waveform noise and response presence measures) must not include stimulus artifact. May be a problem for high-intensity 500-Hz stimuli. ‡ Window later to exclude stimulus artifact but also excludes much of response. Valid for residual noise measures only (i.e., not CCR, SNR or Fsp) . * BC stimuli at 4000 Hz must be extended in total duration to reduce ringing by bone oscillator.

As noted above, statistical measures of ABR signal-to-noise ratio and waveform noisiness are available. Currently, of the two, an online measure of waveform noisiness is the most important and must be considered a requirement when considering any new clinical ABR system.⁶ It is important that any system implementing these statistical measures must allow for flexibility in their parameters, as they differ depending upon stimulus and response characteristics (e.g., settings are different for 500 versus 2000 Hz tones; as well as wave V versus later responses). Table 5 includes recommendations for latency windows (“SNR Regions,” each 10 ms in duration) over which these measures are calculated. Exact parameters and especially criteria are not easily available; some information is provided below (further details are provided in BCEHP 2008; HAPLAB 2009). Statistical measures of waveform noisiness or response presence/absence (signal-to-noise) are discussed below.

Waveform Noisiness (Residual Noise)

Single-point (sp) variance (waveform noise; Don and Elberling 1996; Don et al. 1984): This measure, available on only a couple of systems, measures the trial (stimulus) by trial variance in amplitude of a single time point in the evoked potential waveform, usually in the region of the expected response and always beyond any stimulus artifact. As the number of trials averaged increases, the variance goes down. The location of the single point is typically placed in the middle of the signal to noise ratio (SNR) region. For threshold measures, in order to conclude “no response,” one usually must have the final sp variance down to 10 to 20 nV, a level smaller

⁶ At the time of writing this chapter, appropriate statistical measures, especially waveform noise, were available on only a few clinical systems. However, several other manufacturers were in the process of implementing these measures.

than a typical threshold wave V response. *Residual noise* (RN; i.e., waveform noise; Özdamar and Delgado 1996; Picton et al. 1983) as with sp variance, is available on only one or two systems. The standard deviation of the plus-minus average is similar to that used on transient EOAE systems (“A-B” in dB). RN (from average of all replications) must be lower than a set value to conclude a “no response.” Currently, BCEHP ABR protocols require the RN for the average waveform of all replications to be $0.08 \times V$ or less before a “no response” is concluded (plus the waveforms must appear visually flat).⁷ Details are available in the BCEHP protocols (BCEHP 2008), as well as on the HAPLAB Web site (HAPLAB 2009). Figure 6 shows RN values (calculated for the average of all replications) for results showing “response present,” “no response,” and “could not interpret” (i.e., too noisy to conclude no response).

Response Presence/Absence (Waveform Signal-to-Noise Ratio)

Correlation coefficient between replications (CCR; Hyde et al. 1998; Picton et al. 1983): Most current clinical ABR machines have the capability to calculate the correlation coefficient between two replications (Picton, Durieux-Smith and Moran 1994; Picton et al. 1983), a measure similar to the “reproducibility” measure used in transient EOAEs (Kemp 1988; Picton et al. 1994). However, few systems calculate and update the correlation online as trials are averaged. Normally calculated using a 10-ms window centered on the typical response (see table 5), a correlation of 0.5 and higher provides clinicians with an indication that a response is present—the higher the correlation, the more likely a response is present. Although it is not a perfect measure, individual clinicians can determine their own criterion correlation (over many sets of waves) and use this objective measure to aid in their response determination. *F-test using single-point variance* (Fsp; Don et al. 1984; Elberling and Don 1984; Hyde et al. 1998): A somewhat better measure than correlation, the “Fsp,” also provides an on-line/ongoing indication of response presence/absence. Unfortunately, Fsp is implemented on only a few clinical machines and few data are available. Typically calculated over a 10-ms window, “significant” Fsp values are typically in the range of 2.9 to 3.1 (Sininger and Hyde 2009). *Signal-to-noise ratio (SNR) or standard deviation ratio (SDR)*; Özdamar and Delgado 1996; Picton et al. 1994; Picton et al. 1983).⁸ Also, calculated over a 10-ms window (see table 5), the SNR (or SDR) provides an on-

line/on-going calculation but is implemented on only a few clinical machines. SNR is nearly identical to the transient EOAE signal-to-noise measures. After a study of SNRs of tone-ABRs in nearly 100 infants with normal or impaired hearing (Haboosheh 2007), the BCEHP has recently implemented the use of SNR for determination of response presence in tone-ABR waves (BCEHP 2008). Typically, SNR values of 1.0 or greater (or SDR ≥ 2) suggest a likely response (occasionally, “present” responses show SNR values < 1.0). Figure 6 shows SNR values (calculated for the average of all replications) for results showing “response present,” “no response,” and “could not interpret” (i.e., too noisy to conclude no response).

None of the measures above are perfect, and occasionally suggest “no response” when visual examination by experts conclude otherwise. Moreover, these measures are quite sensitive to the presence of stimulus artifact or 60-Hz (50-Hz in Europe) line noise, thus care must be taken to ensure these are excluded from the SNR region. As noted above, measures of waveform noise (RN or sp-variance) are currently most important and essential. Statistical measures described above may be particularly helpful in training new clinicians and in ensuring consistency among clinicians within a facility or across multiple facilities within a larger program (such as the BCEHP).

Current Issues and Questions Concerning the Tone-ABR

Frequency Specificity of the Tone-ABR

In order to evoke ABRs of reasonable amplitude, brief tones with relatively short rise/fall times and durations must be used (Beattie and Torre 1997; Brinkmann and Scherg 1979; Kodera, Yamane, Yamada and Suzuki

⁷ The Intelligent Hearing Systems (IHS) SmartEP calculation of “RN” does not divide the A-B difference wave by 2 (required to calculate the plus-minus average), thus this measure over-estimates the residual noise in the waveforms by a factor of 2. The BCEHP RN criterion of 0.08 μ V is thus equivalent to 0.04 μ V (i.e., 40 nanovolts). Others have recommended lower noise levels (e.g., Don and Elberling 1996).

⁸ Due to overestimation of the residual noise by RN (see preceding footnote), the IHS SmartEP system’s SNR measure is equivalent to SDR/2. Both SNR and SDR measures use a measure of the “signal” that contains both response and noise. One can estimate the true signal-to-noise ratio by $[(\text{SNR} * 2)^2 - 1]$ or $[\text{SDR}^2 - 1]$ (Picton et al. 1983).

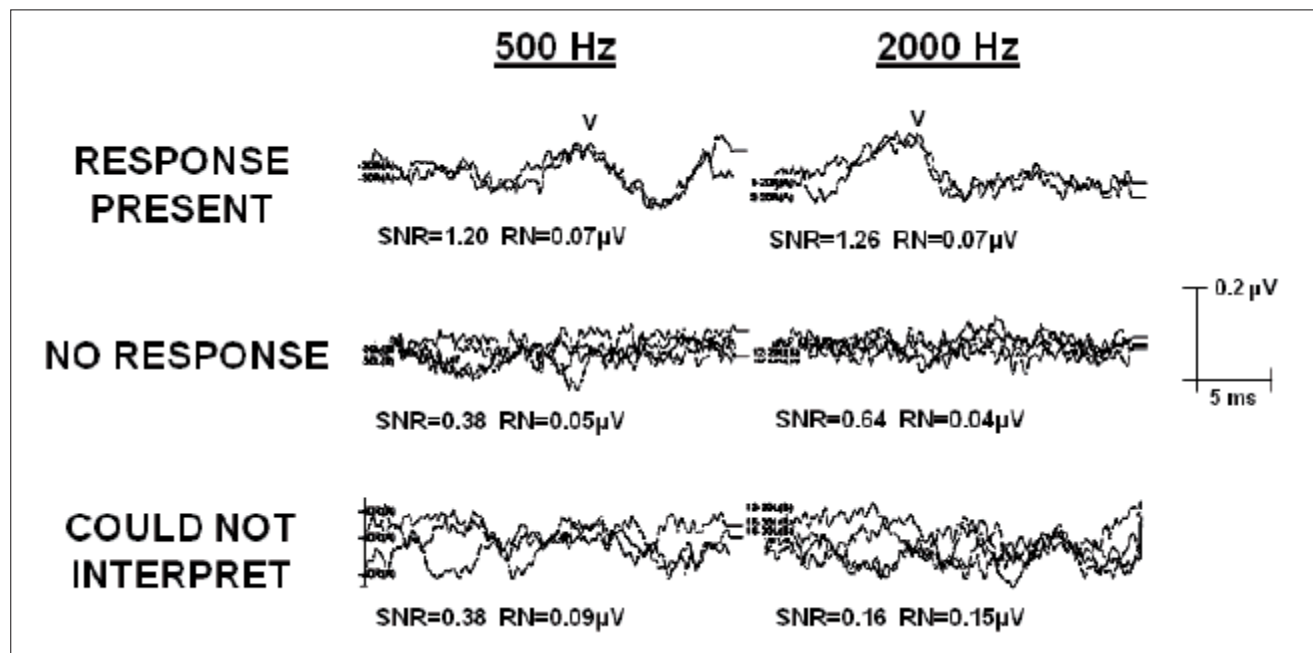


Figure 6. Interpretation of ABR waveforms. Infant ABR waveforms in response to 500- and 2000-Hz brief tones typical of “response present” (top row), “no response” (middle row), and “could not interpret” (bottom row) results. Shown also are the IHS Smart-EP “SNR” and “RN” measures calculated over a 10-ms window (see Table 5) on the average of all replications for a given set. The “response present” waveforms show a clear repeatable wave V, the peak-to-peak amplitude of which is at least three times the average difference between the replications in the 3- to 4-ms region surrounding wave V. The SNR measures are above 1.0, also consistent with response presence. Although not required for a present response, the RN values of 0.07 μV indicate reasonably quiet results. The “no response” waveforms do not show a repeatable waveform that is larger than the background noise (i.e., difference between replications is at least as large as any peak), and the waveforms are essentially flat. SNR values are well below 1.0 and thus consistent with no response. Most importantly, the waves are acceptably quiet (indicated both visually and by the low RN values which are less than the 0.08- μV criterion). The “could not interpret” waveforms do not show any repeatable peak and SNR values are well below 1.0; hence, they do not show any response. However, one cannot be sure a small, threshold-level response was not missed as these recordings are noisy. Thus, because the waves are too noisy (indicated by large differences between replications and nonflat waveforms and RN values that are above the 0.08- μV criterion) one must interpret these waves as “could not interpret.” SNR: IHS Smart-EP “signal-to-noise ratio”; RN: IHS Smart-EP “residual noise level.” Waveform timebase: 25.6 ms.

1977; Stapells and Picton 1981; Suzuki and Horiuchi 1981). As shown in table 5, we (as well as others) recommend brief tones with total durations of 5 cycles and rise/fall times of 2 to 2.5 cycles. Such brief tones demonstrate reasonable frequency specificity (Klein 1983; Nousak and Stapells 1992; Oates and Stapells 1997a, 1997b; Purdy and Abbas 2002; Stapells and Oates 1997; Stapells, Picton and Durieux-Smith 1994), and many studies have shown these brief stimuli provide adequate estimates of the audiogram for all but very steep (≥ 50 dB/octave slope) hearing losses. When hearing losses are very steep, the tone-ABR threshold will indicate an elevated threshold, but may underestimate the amount of hearing loss; this occurs as a result of the acoustic splatter to the better hearing at adjacent frequencies (Purdy and Abbas 2002). Fortunately hearing losses with such steep slopes (≥ 50 dB/octave) are relatively uncommon, especially in infants, thus the ABR thresh-

old to brief (5-cycle) tones provides a good estimate of the audiogram for the large majority of infants.

It has been claimed that the frequency-specificity of the tone-ABR threshold estimate can be improved by using more complex nonlinear stimulus windowing functions, such as Blackman or exact-Blackman windows (Gorga 2002; Gorga and Thornton 1989). Although the acoustics based on the total duration of the stimuli might lead one to conclude these nonlinear windows would be better, such a claim assumes the ABR reflects the whole stimulus, whereas the “effective” portion of the stimulus is almost certainly less than the whole stimulus. The ABR appears not to be sensitive to the small differences in the temporal waveforms of the linear versus Blackman stimuli. Results published to date do not support the claim for superiority of these nonlinear windows, with at least five studies showing equivalent ABR results between linear and nonlinear (Blackman or ex-

act-Blackman) windows (Beattie, Kenworthy and Vanides 2005; Johnson and Brown 2005; Oates and Stapells 1997a, 1997b; Purdy and Abbas 2002). Thus, either linear- or Blackman-windowed stimuli may be used with equal accuracy.

Another technique proposed to improve the frequency specificity of the ABR to brief tones, especially in the presence of very steep losses, is that of band-reject (“notched”) noise masking (Picton, Ouellette, Hamel and Smith 1979; Stapells and Picton 1981; Stapells et al. 1994). The notched noise restricts the region of the basilar membrane that is capable of contributing to the response to the frequencies within the notch. The noise has a 1-octave-wide notch centered on the tone’s nominal frequency; slopes of the noise filters must be quite steep (at least 48 dB/octave slope) and the intensity of the noise (before filtering) set 20 dB below the peak-to-peak equivalent SPL of the brief-tone stimulus. In recent years, we have de-emphasized the need for notched noise, as it adds complexity to equipment setup and test protocol, few clinical machines provide the capability for notched noise, and more importantly, results have shown the need for notched noise is limited to only very steep losses. Thus, ABR threshold results with and without notched noise masking are similar for more typical groups of individuals with hearing loss (Johnson and Brown 2005; Stapells 2000b).

It is important to remind readers that without special noise masking procedures, *no measure* is cochlear place-specific when using moderate-to-high stimulus levels; not even a behavioral response to long-duration pure-tone stimuli. That is, when presented at 60 to 80 dB HL (and higher), even pure-tone stimuli result in fairly wide cochlear excitation (Moore 2004). Thus, elevated thresholds obtained using behavioral pure-tone audiometry are affected by this broad cochlear excitation, and it is unreasonable to expect the ABR (or ASSR) at these intensities to exhibit any better frequency specificity (Picton et al. 2003).

Stimulus Onset Polarity: Alternating or Single Polarity?

Concern has often been expressed about the use of alternating onset polarity. Specifically, it has been suggested that response amplitudes with alternating polarity will be reduced due to phase cancellation, and thus thresholds elevated (e.g., Gorga et al. 2006; Gorga, Kaminski and Beauchaine 1991). However, there is no evidence for this concern, especially concerning thresh-

olds in infants. Indeed, in an unpublished study in our lab, in nine normal infants, we found no difference between single polarity (rarefaction or condensation onset polarity) and alternating polarity for wave V amplitudes and thresholds for clicks, 500-Hz brief tones, or 2000-Hz brief tones (Wu and Stapells unpublished). This is consistent with the fact that the majority of tone-ABR threshold studies have utilized alternating onset polarity and, as noted above, threshold estimates have been quite accurate (see Tables 1 through 3). In fact, there are good reasons for employing alternating polarity tones: (i) at high intensities, electromagnetic stimulus artifact can significantly contaminate responses, especially at 500 and 1000 Hz. This artifact can make it difficult to recognize the physiologic response; if objective response detection measures are employed, the artifact can render these measures useless. Alternating polarity largely removes the artifact (though not completely at highest intensities); and (ii) especially for moderate and higher stimulus intensities, there may be steady-state responses to each cycle of the tone’s carrier frequency, such as the cochlear microphonic and/or the frequency following response, which often make it more difficult to recognize or measure the transient (e.g., wave V-V’) response. Alternating the polarity, for the most part, removes these unwanted responses. Although we recommend routine use of alternating polarity for all brief-tone intensities, at lower stimulus intensities there is likely no difference and little concern about polarity, and either single polarity or alternating polarity are fine. It is important to note, however, that due to the very large electromagnetic stimulus artifact occurring with bone-conduction transducers, alternating polarity should always be used for bone-conduction stimuli.

Maximum Stimulus Intensities for ABR

For several reasons, there are limits to the maximum intensities of stimuli for the ABR. First, current transducers have limitations, beyond which significant distortion occurs. Insert earphones (ER-3A) typically are limited to a maximum of about 120 dB SPL. This limits 500- to 4000-Hz pure-tone stimuli to about 110 dB HL. Because behavioral and ABR thresholds for the brief stimuli used to elicit the ABR are in the 20 to 30 dB SPL range (see table 5), maximum intensities are thus limited to about 90 to 100 dB nHL. This is not necessarily the maximum possible output for ABR stimuli, as other air-conduction transducers, including sound-field speakers, do have higher output. The maximum outputs (before distortion) are

even more limited for the B-71 bone oscillator: about 70 dB HL for pure-tone stimuli, and 50 to 60 dB nHL for brief-tone stimuli (Small and Stapells 2003).⁹ A second reason there are maximum output limitations is the contamination of responses by large stimulus artifact at very high intensities. For the most part, the presence of stimulus artifact does not preclude interpretable recordings, as ABR wave V-V' usually occurs later than the artifact. Furthermore, stimulus polarity may be alternated to at least partially cancel stimulus artifact, and in extreme cases special shielding can reduce artifact. High-amplitude stimulus artifact has been shown to result in artifactual ASSRs (Gorga et al. 2004; Jeng, Brown, Johnson and Vander Werff 2004; Small and Stapells 2004), although appropriate processing of the EEG largely removes these nonphysiologic spurious responses (Brooke, Brennan and Stevens 2009; Picton and John 2004; Small and Stapells 2004). A third cause of output limitation is the possibility of high stimulus levels producing non-auditory responses. Vibrotactile responses, especially to bone-conduction stimuli, place well-known limits for behavioral audiometry (Boothroyd and Cawkwell 1970). Although vibrotactile responses are not likely to produce an ABR or brainstem ASSR, there is evidence that stimulation of the vestibular system can produce responses in the ABR and brainstem-ASSR time frame. Vestibular responses are especially problematic for interpretation of ASSRs to high-intensity stimuli in individuals with severe-profound hearing loss. This issue is discussed in the ASSR section below. Finally, a fourth cause of output limits is the real concern that maximum output stimuli may cause cochlear damage. This is of greatest concern for the ASSR where at least 10 minutes of averaging may be required to reduce the residual EEG noise to a level below that of the amplitude of a near-threshold response. As ASSR stimuli are continuous, stimulation at levels such as 90 to 110 dB HL must be regularly interrupted in order to rest the cochlea and protect it from damage. This is less of a concern for the transient ABR, as stimuli are already presented with a less than 50% duty cycle (a 500-Hz brief tone present using a 39 per second rate has at least a 15 ms quiet blank between each 10-ms stimulus). Similarly, damage from high-intensity stimuli is much less of a concern for behavioral testing, as stimuli are presented for only very brief durations.

⁹ As with air conduction, there are other bone-conduction transducers with a higher maximum output (e.g., MAICO KLH96), but for which there are no published ABR (or ASSR) data.

How to Couple the Bone Oscillator to an Infant's Head

In our early research, we had an assistant hand-hold the bone oscillator to the infant's head during bone-conduction ABR testing, and found little difficulty with this procedure (Gravel et al. 1989; Stapells 1989; Stapells and Ruben 1989). However, other researchers expressed concern with this practice, so our subsequent bone-conduction research (Foxe and Stapells 1993; Ishida, Cuthbert and Stapells 2011; Nousak and Stapells 1992; Small and Stapells 2003, 2004, 2005, 2006, 2008b, 2008c) utilized the technique described by Yang and colleagues (Yang, Stuart, Stenstrom and Hollett 1991; Yang, Stuart, Mencher, Mencher and Vincer 1993), which uses a wide elastic band with Velcro. However, we find this technique often awkward clinically, sometimes waking an infant and always requiring a longer time. Subsequently, we carried-out research comparing the elastic-band and hand-held procedures, and found the hand-held procedure was at least as reliable (indeed, it was less variable) and accurate as the elastic band procedure, provided assistants were appropriately trained (Small, Hatton and Stapells 2007). For clinical use, we currently recommend hand-holding the bone oscillator, given the relative ease and, importantly, speed and non-intrusiveness, of hand-holding.¹⁰

Establishing Normative Data

Many popular textbooks instruct clinicians to obtain (i) normal hearing levels (nHL) for their ABR stimuli, and (ii) their own normative latency data. Both of these practices have significant problems. Obtaining nHLs for click and brief-tone stimuli requires appropriate quiet sound booths, careful psychoacoustic procedures, and appropriate subjects (e.g., large number of normal young adults)—error in any of these can make a clinic's results uninterpretable, especially if no acoustic calibration of the obtained 0 dB nHL is made. Unless using a radically different stimulus for which no research exists, clinicians should use the acoustic calibrations of published research—in the same fashion (but with different calibration values) as how they calibrate their equipment for behavioral audiometry. Although official “standards” for ABR stimuli are not yet available, there are

¹⁰ The elastic-band technique is preferable when it is difficult to hand-hold the bone oscillator due to equipment setup or lack of a trained assistant.

several publications providing well-researched acoustic levels of normal thresholds for these stimuli. Table 5 presents our recommended 0 dB nHL values for three transducers.

Clinicians often ask for tone-ABR latency normative data. As noted above, we do not assess whether latencies are normal or prolonged when evaluating ABR thresholds. Thus, tone-ABR latency “norms” are not that helpful, other than to give an idea of where wave V typically occurs. This information is available from the waveforms in Figures 1 and 5 (as well as other publications) and quickly comes after testing a few infants. On the more-general question of clinicians obtaining their own latency norms (e.g., for click-ABRs), we strongly believe that the literature already contains excellent normative data, obtained for a greater number of subjects than is typically possible for most clinicians (good latency norms require large samples of subjects—sample sizes of 10-20 are too small). The most important click-ABR latency measures—the I-V interpeak interval and wave V interaural latency difference—are quite consistent across most studies and little affected by stimulus and recording factors (except for rates >20 per second), making it quite acceptable to use published norms. Thus, we do not recommend that clinicians determine their own norms; rather, we suggest they use published norms from a larger study for reasonably similar parameters and subject population (for a listing of many normative samples, see textbook by Hall 1992). To ensure their results are similar, clinicians may test a small group (e.g., 10 subjects) and then compare statistically their results with the larger study. If no practically significant differences exist, clinicians can feel comfortable using the larger sample published norms for their clinical testing.

The Brainstem Auditory Steady-State Response

The auditory steady-state responses to stimuli presented using repetition (or modulation) rates in the 70- to 110-Hz range (the “80-Hz” or “brainstem” ASSR) have recently gained considerable attention and some excitement by audiologists, especially by those involved in the assessment and subsequent hearing-aid fitting of very young infants identified as having a hearing loss. Equipment manufacturers are marketing their new ASSR systems for such testing. Readers will find the recent text edited by G. Rance contains many excellent up-to-date chapters describing in detail the brainstem ASSR (Rance 2008b).

What Is the Auditory Steady-State Response?

First recorded in 1960 from the scalp of humans by Geisler (1960), ASSRs were subsequently recorded in response to clicks, to sinusoidally modulated tones, and to square-wave modulated tones by Campbell and colleagues (Campbell, Atkinson, Francis and Green 1977). Major audiologic interest in the ASSRs came with the publication by Galambos et al. in 1981 concerning the “40-Hz ASSR” (Galambos, Makeig and Talmachoff 1981). Subsequent studies indicated frequency-based (Fourier) analyses could be used to accurately measure the ASSRs (e.g., Rickards and Clark 1984; Stapells, Linden, Suffield, Hamel and Picton 1984). From 1981 through to the mid-1990s, the clinical audiology community went through its first phase of excitement concerning this new evoked potential threshold measure, with one manufacturer developing and marketing “the first objective infant audiometer” utilizing the ASSR to stimuli presented with a 40-Hz repetition rate. Unfortunately, subsequent research showed the 40-Hz ASSR was decreased in sleeping subjects (e.g., Cohen, Rickards and Clark 1991; Linden, Campbell, Hamel and Picton 1985) and, more importantly, it is very difficult to record in infants (e.g., Stapells, Galambos, Costello and Makeig 1988; Suzuki and Kobayashi 1984). Interest and use of ASSRs by clinicians thus quickly disappeared. However, some researchers persevered and demonstrated that ASSRs to near-threshold stimuli presented with rates of 70- to 110-Hz—the brainstem ASSR—are easily recordable in sleeping infants (e.g., Lins and Picton 1995; Lins, Picton, Picton, Champagne and Durieux-Smith 1995; Lins et al. 1996; Rance, Rickards, Cohen, De Vidi and Clark 1995), and today there is a growing body of data as well as availability of clinical systems that automatically stimulate and analyze these responses.

Discussion concerning the generators of the ASSR has thus far primarily focused on the ASSRs evoked by stimulus rates in the 30- to 50-Hz range. Studies investigating the neural sources of the 40-Hz response have concluded the response has both brainstem and cortical generators (e.g., Herdman, Lins et al., 2002; Mauer and Döring 1999). Recent studies investigating the neural sources of the 80-Hz ASSRs in humans and animals indicate they originate primarily from brainstem structures (Herdman, Lins et al. 2002; Kuwada et al. 2002; Mauer and Döring 1999). Although not yet confirmed, it is quite likely that the 80-Hz ASSRs are actually ABR waves V to rapidly presented stimuli. The ASSR stimulation and analysis techniques may differ, but the underlying phys-

iology and interpretation of these brainstem ASSRs are likely very similar to those for ABR wave V.

ASSR Analysis Techniques

As noted above, an important feature of the ASSR is that frequency-domain analyses, such as the fast Fourier transform (FFT), provide excellent measures of the response, and there are clear procedures to determine response presence and absence. For example, similar to procedures for distortion-product otoacoustic emissions (DPOAEs), an FFT of the response provides the amplitude at exactly the stimulus modulation rate, which is compared to the amplitudes of “noise” frequencies immediately surrounding the modulation rate (“sidebins”; Figure 7). Thus, the amplitude and phase of the response at the rate of stimulation, as well as measures of response noise, are measured entirely objectively and automatically by a computer. In contrast to DPOAE measures, however, ASSR systems go a step further, and determine the statistical probability of a response being present. A number of statistical tests have been employed, with most studies employing either a measure of phase variability (“phase coherence”) or comparison of the amplitude at the stimulus rate (or modulation frequency) to amplitudes of surrounding noise frequencies (“F-test”; for detailed reviews, see John and Purcell 2008; Picton et al. 2003). Thus, with current ASSR systems, response determination is entirely objective; a human interpreter does not view waveforms or determine the replicability and location of peaks. This objectivity of response determination is a major advantage of the ASSR over the transient ABR, although as noted above, objective techniques are also available for the ABR.

As when interpreting the ABR, the “response noise” estimate is also an essential measure for ASSR interpretation. When concluding a “no-response” result, it is important that a clinician continues recording until the level of response noise is below the typical amplitude of a threshold-level response. That is, ensure that a small-amplitude response was not missed because of a noisy recording. Unfortunately, not all ASSR systems provide this noise measure and, importantly, not all research studies (or clinicians) have employed such noise measures. Furthermore, there remains some uncertainty concerning what are the appropriate noise criteria (e.g., what is an acceptably low level of noise?). Because near-threshold 80-Hz ASSRs have amplitudes of about 20 to 30 nV, mean noise levels (e.g., side-bin noise) of 10 nV

Figure 7a

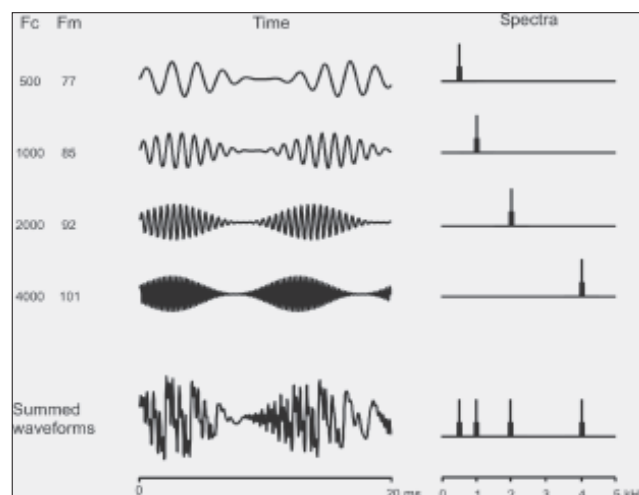


Figure 7b

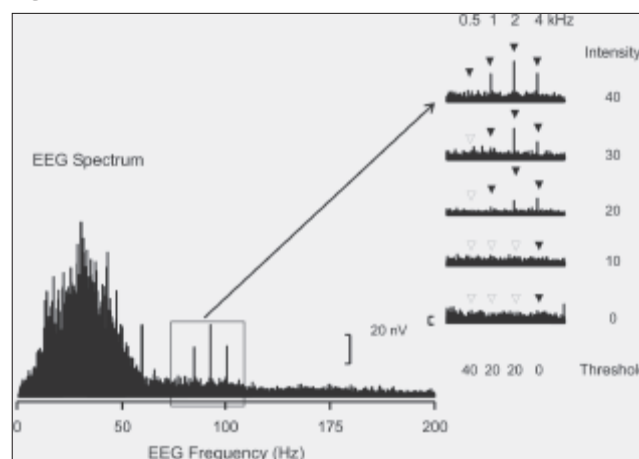


Figure 7. A. ASSR stimuli: Time and frequency spectra of multiple auditory steady state stimuli. Four individual amplitude-modulated stimuli with carrier frequencies (F_c) ranging from 77 to 101 Hz and modulation frequencies (F_m) ranging from 77 to 101 Hz are shown (*left panel*). The corresponding spectra are shown in the right panel. The summed time and frequency spectra are shown at the bottom left and right panels, respectively. **B.** Response analyses: Threshold intensity series of multiple auditory steady state responses recorded from an 11-week-old infant with normal hearing. Intensities are in dB nHL (Herdman and Stapells, 2001, 2003). Responses were elicited using the stimuli shown in figure 7A. Bottom right shows the entire EEG frequency spectra. Right panel shows the spectra over the frequency range near the modulation frequency. Carrier frequencies corresponding to the four signals are shown on the top. Filled triangles indicate responses that reached significance ($p < .05$); open triangles indicate no-response ($p \geq .05$ and EEG noise $< 11\text{nV}$). Thresholds of 40, 20, 20, and 0 dB nHL at 500, 1000, 2000, and 4000 Hz are equivalent to 46, 29, 24, and 2 dB HL. Reproduced with permission from Stapells, D. R., Herdman, A., Small, S. A., Dimitrijevic, A., and Hatton, J. (2005). Current status of the auditory steady state responses for estimating an infant's audiogram. In R. Seewald and J. Bamford (eds.), *A sound foundation through early amplification 2004: Proceedings of the third international conference* (pp. 43–59). Stäfa, Switzerland: Phonak AG. Copyright 2005 Phonak.

or lower are typically required before one can conclude that no response is present, although this level appears to differ somewhat for different analysis methods (van Maanen and Stapells 2009). The above notwithstanding, an appropriate noise criterion must be reached before concluding “no response.”

As indicated above, there is considerable research demonstrating the effectiveness of phase coherence and F-test response statistics, and some ASSR systems employ these well-tested measures (for review: John and Purcell 2008). Some recent ASSR systems, however, use modifications of these measures, or altogether entirely different algorithms. Few studies, however, have assessed these new or modified measures—it may be premature for individuals to consider purchase of these new and relatively untested systems.

ASSR Stimulus Paradigms

Although the earliest studies of the ASSRs tended to use brief tonal stimuli, similar to those used to evoke the ABR, most recent research has focused on continuous sinusoidally amplitude-modulated (AM) tonal stimuli, sometimes with 10 to 25% frequency modulation. Most current ASSR systems use such stimuli, as have most research studies. The acoustics of continuous sinusoidal AM stimuli are very frequency specific: their spectra show energy at the carrier frequency plus two sidelobes at frequencies equal to the carrier frequency plus/minus the modulation frequency. Thus, as shown in Figure 7, a 1000-Hz tone modulated at 85 Hz would contain energy at 915, 1000, and 1085 Hz. Because no energy is present at the modulation rate, interpretation of response presence/absence by the computer is less susceptible to stimulus artifact (assuming linear stimulus systems and appropriate EEG digitization; see below). Adding 10 to 25% frequency modulation results in somewhat larger ASSR amplitudes, but also complicates the stimulus spectra (Purcell and Dajani 2008). One possible reason most researchers studying the brainstem ASSR have used continuous stimuli (sine AM or AM/FM) may lie in a belief that these ASSRs are inherently different from the transient ABR. However, as discussed above, the 80-Hz ASSRs are brainstem responses and thus may show similar stimulus-response limitations as ABR wave V. For example, the transient ABR shows larger responses to stimuli with faster rise times (e.g., Stapells and Picton 1981); similarly, larger amplitude ASSRs are obtained using AM tones with more-rapid envelopes, such as brief-duration tones (Mo and Stapells 2008) or

exponential envelopes (John, Dimitrijevic and Picton 2002). Indeed, one recently introduced clinical ASSR system’s default stimuli are brief tones (4-8 ms duration), which may result in larger-amplitude ASSRs. However, to obtain a significant improvement in ASSR amplitude (compared to longer stimuli), durations must be reduced to quite brief (<4 cycles); such durations result in reduced frequency specificity as well as increased interactions (amplitude reductions) between responses to multiple simultaneous stimuli (Mo and Stapells 2008).

As noted above, stimuli with broader frequency spectra lead to larger amplitude ASSRs. AM/FM stimuli do show broader frequency spectra and result in larger amplitudes, and the small loss in frequency specificity has generally been considered acceptable. Some studies have investigated the use of stimuli with much broader frequency spectra (e.g., clicks or modulated noise), specifically for the purpose of newborn hearing screening (Cebulla, Sturzebecher, Elberling and Muller 2007; John, Brown, Muir and Picton 2004). The broad frequency spectra result in large-amplitude ASSRs, making response detection (and thus screening) much faster. However, as with the click-ABR, there is no frequency specificity to this screening. Research into the use of more frequency-specific stimuli for newborn screening is also underway (Cone-Wesson, Parker, Swiderski and Rickards 2002; John et al. 2004; Savio, Perez-Abalo, Gaya, Hernandez and Mijares 2006; Sturzebecher, Cebulla, Elberling and Berger 2006).

The Multiple ASSR Technique

A unique feature of the ASSR is that responses to multiple stimuli can be separated and independently assessed, all simultaneously. Because the ASSR to a stimulus presented at a specific modulation rate has its major response energy at exactly the stimulus modulation rate, it is possible to present several stimuli each with different carrier frequencies and, importantly, different modulation rates (Figure 7). Responses to each stimulus can then be evaluated by examining the response energy at each stimulus’ exact modulation rate. First demonstrated by Lins and Picton in 1995, this multiple-stimulus ASSR technique has subsequently been developed to allow assessment of responses from both ears and four carrier frequencies (i.e., eight different modulation rates) simultaneously. Research to date suggests that: (i) amplitudes are not reduced using the multiple-ASSR technique (compared to single stimuli) provided stimulus carrier frequencies (within an ear) are at least an oc-

tave apart in frequency and 60 dB SPL or less (Herdman and Stapells 2001; John, Lins, Boucher and Picton 1998); (ii) presenting multiple AM stimuli does not appear to reduce the frequency specificity of the stimulus-response pairing (Herdman, Picton and Stapells 2002; Herdman and Stapells 2003); (iii) at higher intensities (> 60 dB SPL), amplitudes decrease due to interactions between responses to the multiple stimuli (John et al. 1998; Picton, van Roon and John 2009; Wood 2009); and (iv) the multiple stimulus technique is more efficient (faster) than the single-stimulus technique, although not as much as initially expected. Especially for high intensities, the multiple-ASSR technique may be less efficient than the ASSR to single stimuli. Issues such as sloping audiograms, smaller amplitudes at some frequencies compared to others, and amplitude reductions due to interactions decrease the efficiency of the multiple stimulus technique such that it is, at best, only 1.5 to 3 times faster than the single-stimulus technique (Herdman and Stapells 2001, 2003; John, Purcell, Dimitrijevic and Picton 2002).

Although many clinical systems employing the multiple-ASSR are currently being marketed to clinicians, there are surprisingly few studies that have investigated the efficiency of the single versus multiple ASSR techniques. Our recent studies indicate that (i) normal infants show significant interactions with the multiple-ASSR, even at 60 dB SPL, but their thresholds are not affected and the multiple technique remains more efficient (Hatton and Stapells 2011), and (ii) stimuli with broader spectra, such as AM/FM, show significantly greater interactions, even at 60 dB SPL in adults, significantly reducing the efficiency of the multiple-ASSR technique (Mo and Stapells 2008; Wood 2009).¹¹

Frequency Specificity of the Brainstem ASSR

The *acoustic frequency specificity* of sinusoidally amplitude-modulated tones, even when combined with 10 to 25% frequency modulation (AM/FM), is reasonably narrow, a fact that is often touted as one advantage of the ASSR over the tone-evoked ABR. However, the *cochlear place specificity and the neuronal specificity* of the stimulus-response pairing must also be considered (Herdman et al. 2002; Picton, Dimitrijevic and John 2002). Use of

acoustically specific stimuli does not always translate into responses that are more frequency specific, for example, as noted above, although Blackman-windowed tones show better acoustic specificity, the brainstem responses to these stimuli have the same frequency specificity as do those to brief tones shaped by linear windows (Oates and Stapells 1997a, 1997b; Purdy and Abbas 2002). Research into the frequency specificity of the brainstem ASSR is quite limited. Nevertheless, using two distinct methods: (i) high-pass noise masking/derived response analyses in subjects with normal hearing (Herdman et al. 2002) and (ii) assessment of thresholds in individuals with steeply sloping SNHL (Herdman and Stapells 2003; Johnson and Brown 2005), results indicate the ASSR has reasonably good frequency specificity. However, ASSR frequency specificity was not as good as would be expected from the acoustic specificity of the AM stimuli, with the ASSR frequency specificity being very similar to that previously shown for the tone-evoked ABR (Herdman et al. 2002), a finding consistent with the view that ABR wave V underlies the 80-Hz ASSR. Importantly, no difference in ASSR frequency specificity was seen for responses to multiple versus single stimuli (Herdman et al. 2002; Herdman and Stapells 2003). It must be noted, however, that we currently know little of the frequency specificity of the brainstem ASSR to newer, more complex (compared to sinusoidal AM) stimuli, with no studies of the frequency specificity of brainstem ASSRs to exponential or brief-tone stimuli and only one such study for AM/FM stimuli (Johnson and Brown 2005).

Calibration of Stimuli for the Brainstem ASSR

Similar to the long-duration pure-tone stimuli used for behavioral audiometry, the continuous nature of most ASSR stimuli makes them easy to measure using a sound-level meter set to “normal” (dB RMS) sound pressure level. Behavioral thresholds for continuous sinusoidal AM and AM/FM ASSR stimuli are close to those for long-duration pure tones, thus most studies (and ASSR systems) have calibrated these stimuli in dB HL (ANSI 1996). This is in contrast to the transient brief-tone stimuli used for the ABR, where calibrations are in dB “peak” or “peak-to-peak equivalent” SPL as well in dB “normal hearing level” (nHL). The nHL is employed because behavioral and ABR thresholds are elevated due to their brief duration (e.g., Stapells and Oates 1997). However, as shown below, ASSR thresholds (in dB HL) are also significantly elevated compared to normal be-

¹¹ Spectra for 100% AM/25% FM tones are about 3x wider (at -20 dB) than sine-AM and 2x wider than AM² stimuli (Wood 2009).

behavioral thresholds, especially in young infants. Interestingly, when expressed in dB peak-to-peak equivalent SPL, air-conduction ASSR thresholds in normal infants are within about 5 dB of those for the tone-evoked ABR (e.g., Rance et al. 2006). Thus, similar to the situation for the ABR, brainstem ASSR thresholds likely reflect a brief portion of the stimulus rather than the long-term RMS SPL of the whole stimulus. Another problem for the use of dB HL is that there remain large gaps in our understanding of the relationship between ASSR thresholds (in dB HL) and pure-tone behavioral thresholds (in dB HL), especially in infants with hearing loss. Caution is thus required when interpreting infant ASSR thresholds in “dB HL.”

The Problem of New ASSR Technology and Methodology

ASSR technology is quickly evolving and expanding. Fifteen years ago, there were no commercial clinical ASSR systems; 10 years ago, there were only two systems: the single-stimulus Viasys/GSI “Audera” (based on the Australian “ERA” system) and the multiple-stimulus Neuronic “Audix.” Today, there are many commercial ASSR systems available.¹² A looming concern is the lack of standardization among the different systems. Some of these systems are fairly closely based on the equipment (and thus techniques) used in much of the foundational ASSR research. However, many of the new systems employ new stimulation and analysis techniques that are quite different from published research. There are few published studies to support these changes or, when available, the research has only been carried out in adults with normal hearing. With differing methodologies, new systems and few published data (especially for infants with hearing loss), the current situation is one of “buyer beware” and caution must be advised. Individuals considering purchase of a particular ASSR system should ensure evidence (including clinical data) exists for that system’s methodology. Preferably, such data would be available in the peer-reviewed scientific literature, be obtained in the target population (infants, especially hearing-impaired infants) and (at least some) be at arms-length from manufacturers and patent holders.

Artificial ASSRs and Non-Auditory Responses

One clear example of the pitfalls of using of a “new” response or technique (in this case, the 80-Hz ASSR), new system, or new technology, is demonstrated by the

recent findings in our laboratory as well as others of spurious or artifactual ASSRs to high-intensity air- and bone-conduction stimuli (Gorga et al. 2004; Jeng et al. 2004; Narne, Nambi and Vanaja 2006; Picton and John 2004; Small and Stapells 2004).¹³ In these studies, clear “responses” were shown to be present for individuals who were deaf and could not hear the stimuli. Some of these artifactual ASSRs are now known to be due to high-amplitude stimulus artifact contaminating the recorded EEG, and aliasing to mimic physiologic responses (Picton and John 2004; Small and Stapells 2004). By changing the analog-to-digital (AD) rate, filtering the EEG, and alternating the stimuli, thus removing any aliased energy, we showed that *most* of these artifactual ASSRs disappeared (Small and Stapells 2004). This finding prompted an immediate change in at least one clinical ASSR system, but not until after many clinicians had reported ASSR responses to high-intensity stimuli for infants, some of which must have been due to technical error.

Although the artifactual ASSRs as a result of aliased stimulus artifact appear to have been solved through stimulus and analysis modifications—this has not been formally evaluated for many, if not most, clinical systems—there are, nevertheless, also physiologic but non-auditory ASSRs in individuals with severe or profound hearing loss (Narne et al. 2006; Small and Stapells 2004). In our 2004 study, we found that even when using an appropriate AD rate, anti-aliasing filter, and alternated-polarity stimuli, many of the deaf subjects still showed responses to 500- and 1000-Hz stimuli (no responses were seen at 2000 or 4000 Hz; Small and Stapells 2004). We suggested these responses might be vestibular in origin, as suggested by other studies using transient-evoked potentials (e.g., Cheng, Huang and Young 2003; Kato et al. 1998; Murofushi, Iwasaki, Takai and Takegoshi 2005; Papathanasiou et al. 2004; Sheykholsami, Kermany and Kaga 2000; Welgampola and Colebatch 2001). At this time, we do not have a method to differentiate the auditory and non-auditory (vestibular) responses in an ASSR recording, nor do we know how this finding will impact audiologic decisions. The responses occur in response to high-intensity stimuli,

¹² ASSR systems change and new systems appear regularly.

¹³ Another clear example was the development and marketing in the 1980s of a 40-Hz ASSR “objective infant audiometer” before infant studies demonstrated the 40-Hz ASSR was not easily recorded in infants.

usually low-frequency, for air-conduction stimuli (at least 100 dB HL; Gorga et al. 2004; Narne et al. 2006) and for bone-conduction stimuli (50 dB HL or higher; Narne et al. 2006; Small and Stapells 2004).

One drawback with ASSRs compared to transient-evoked ABRs is that ASSRs do not provide sensible time-domain waveforms to review when unexpected or questionable results are obtained. Sometimes, the time-domain waveforms can help differentiate auditory from non-auditory responses. Figure 8 shows ABR and ASSR results from an infant with profound hearing loss whose brainstem ASSR shows significant ($p < .05$) responses to 110 dB HL 500 to 4000 Hz air-conducted tones. However, his ABR waveforms to high-intensity air-conducted clicks and 2000-Hz brief tones are clearly abnormal, showing a clear early negative wave (3-4 ms post-stimulus) with no wave V following. Present even with alternating stimuli (i.e., not cochlear microphonic), this “N3” wave has been suggested to originate from stimulation of the vestibular system (Colebatch 2001; Kato et al.

1998; Murofushi et al. 2005; Papathanasiou et al. 2004), and is likely the cause of the low-amplitude but significantly present ASSRs. Current ASSR methodologies typically do not provide the ability to view resulting waveforms in the time domain, and the use of rapid multiple stimuli (and thus overlapping responses) make determination of response latency very complicated. This highlights the importance of the transient ABR when thresholds are elevated.

Brainstem ASSR Thresholds to Air-Conduction Stimuli

Adults with Hearing Loss

There are now many studies of 80-Hz air-conduction ASSRs in adults and older children with sensorineural hearing loss. Detailed review of these studies can be found in the recent chapter by Vander Werff and colleagues (Vander Werff, Johnson and Brown 2008) as well as the 2007 meta-analyses by Tlumak and colleagues (Tlumak, Rubinstein and Durrant 2007). For most studies, the ASSR threshold provided a good-to-excellent prediction of pure-tone behavioral threshold, with correlations between ASSR and behavioral thresholds typically in the .8 to .95 range for 1000 to 4000 Hz, and .7 to .85 range for 500 Hz. The slightly poorer correlation at 500 Hz has been suggested to be due to reduced neural synchrony for responses to 500-Hz stimuli (e.g., Lins et al. 1996), although the lower correlations could also be due to some studies having relatively few 500-Hz thresholds in the severe/profound range (i.e., a restriction of range problem). Nevertheless, 500-Hz ASSR thresholds do appear to be 5 to 10 dB worse than other frequencies, similar to those for the ABR (Stapells 2000b; Vander Werff et al. 2008). As shown on the top of table 6, Tlumak and colleagues’ recent meta-analysis of nine studies showed mean difference scores (ASSR threshold minus behavioral threshold) for hearing-impaired adults ranging from 8 to 14 dB, with individual studies showing standard deviations ranged from 7 to 18 dB (Tlumak et al. 2007). Some data suggest greater error (larger standard deviations) in estimating mild compared to more-significant hearing loss, especially at 500 Hz (D’Haenens et al. 2009; Rance et al. 2005). Studies using longer recording times (i.e., more averaging and thus lower residual EEG noise) tend to report better accuracy (Luts and Wouters 2004; Picton et al. 2005; Vander Werff et al. 2008). In addition to estimating thresholds for individual frequencies reasonably accu-

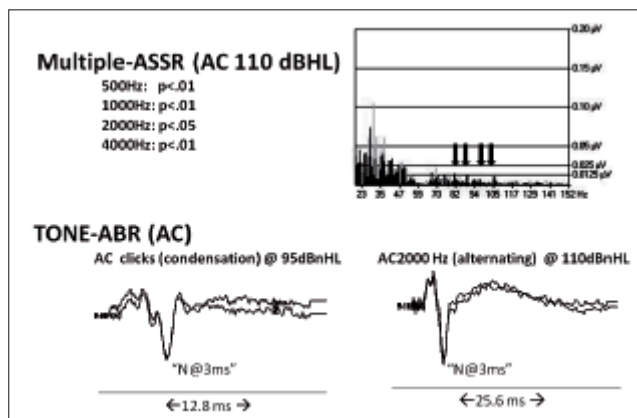


Figure 8. Air-conduction ASSR (top panel) and ABR (bottom panel) results in a 19-month-old infant with severe-profound bilateral sensorineural hearing loss. The multiple-ASSR showed small-amplitude statistically significant responses (arrows) in response to all four frequencies presented at the system’s maximum intensity. The click-evoked (bottom left) and tone-evoked (bottom right) ABR waveforms show a large negative wave at approximately 3 to 4 ms following stimulus onset, with no clear waves V present. This “N3” wave is neural (i.e., not cochlear microphonic), as it remains present with the alternating-polarity tonal stimuli. N3 has been suggested to reflect a brainstem response originating from stimulation of the vestibular system. The presence of the significant ASSRs is likely due to repetition of the N3 to each stimulus modulation cycle—amplitudes are likely reduced due to a combination of: (i) response refractoriness due to high modulation rates and multiple simultaneous stimuli, and (ii) ASSR analysis focuses on energy at the modulation rate, which is lower than this short-latency response. These abnormal, vestibular, results are clearly evident in the time-domain waveforms of the ABR. It is much more difficult to differentiate vestibular from near-threshold auditory responses using current ASSR methodology (i.e., using frequency-domain analyses and/or multiple stimuli). Results obtained in collaboration with Renée Janssen.

Table 6. Air-conduction brainstem ASSR thresholds and maximum “normal” levels (in dB HL) in infants and young children with normal hearing. Adult results from Tlumak et al. (2007) meta-analysis are shown for comparison.

AC ASSR study	STIM	Age	500		1000		2000		4000	
			Mean ±SD	Norm MAX	Mean ±SD	Norm MAX	Mean ±SD	Norm MAX	Mean ±SD	Norm MAX
<i>Tlumak et al., 2007</i> (Meta-analyses of adult data)	M	ADULT	17±12		13±12		11±10		15±10	
Lins et al., 1996 (Ottawa data)	M	1-10 mos	45±13	48	29±10	43	26±8	41	29±10	40
Cone-Wesson, Parker et al., 2002	S	<4 mos		>71		>72		50		54
John, Brown et al., 2004 (older group)	M	3-15 wks		>46		>50		>50		40
Rance et al., 2005 †	S	1-3 mos	32±8	52	33±7	47	24±6	40	28±8	43
Swanepoel & Steyn, 2005	M	3-8 wks	37±8	50	34±10	>50	34±11	>50	30±11	40
Luts et al., 2006	M	<3 mos	42±10	>44	35±10	>50	32±10	42	36±9	44
Rance & Tomlin, 2006	S	6 wks	40±7	50					33±8	40
Van Maanen & Stapells, 2009	M	≤6 mos	39±7	49	33±5	45	29±7	36	24±10	32
Van Maanen & Stapells, 2009	M	6.1-66 mos	41±7	49	37±11	45	31±8	36	22±10	32

STIM: S = single-stimulus ASSR; M = multiple-stimulus ASSR; Norm MAX: Maximum intensity (in dB HL) to be considered “normal” (i.e., level required for 90-95% response presence); Mean ±SD: Mean threshold in dB HL and standard deviation; Results rounded off to closest decibels; † calculated from Figure 1 of Rance et al., 2005.

rately in adults, the brainstem ASSR also appears to accurately estimate audiometric shape/configuration, as demonstrated by presentation of individual audiograms (e.g., Aoyagi et al. 1994; Herdman and Stapells 2003) and through formal statistical analyses (Herdman and Stapells 2003; Perez-Abalo et al. 2001). Thus, at least for adults with sensorineural hearing loss, the 80-Hz ASSR provides a reasonably good estimate of behavioral threshold. Interestingly, these ASSR difference scores are very similar to those shown in table 2 for the tone-ABR (Stapells 2000b).

Given that, as noted above, conductive loss is very common in young infants, it is surprising that there appears to be only one published study of the AC ASSR in adults with true conductive loss (D’Haenens et al. 2009) and none studying individuals with mixed loss. An additional two studies have recorded ASSRs in adults with *simulated* conductive loss (produced by blocking the tubes of insert earphones; Dimitrijevic et al. 2002; Jeng et al. 2004). Overall, results suggest that difference scores (AC-ASSR minus behavioral thresholds) are somewhat larger in conductive loss than in SNHL. However, given that the results include only seven adults

with true conductive loss (D’Haenens et al. 2009), more research is clearly required.

A number of studies have suggested that, compared to the ABR, the ASSR provides a better indication of residual sensitivity in individuals with profound hearing loss (Rance and Briggs 2002; Rance, Dowell, Rickards, Beer and Clark 1998; Rance and Rickards 2002; Rance, Rickards, Cohen, Burton and Clark 1993; Stueve and O’Rourke 2003; Swanepoel and Hugo 2004; Swanepoel, Hugo and Roode 2004). That is, ASSRs are present (especially for lower frequencies) when the ABR is absent. Although this may indeed be a real phenomenon, there are a number of issues with this suggestion: (i) Most studies used clicks to evoke the ABR. Clicks spread their energy over a wide frequency range (e.g., 100-8000 Hz), rather than concentrating their energy into a specific frequency region as do sinusoidal AM tones. The click-evoked ABR is well-known not to provide an accurate assessment for specific frequencies, especially for low frequencies. This is even worse when high-pass EEG filter settings of 100 Hz or higher are used (e.g., Stapells and Oates 1997), which is the case of many of the above studies. Another problem is that the maxi-

imum click intensity of most studies was only about 90 dB nHL compared to 120 dB HL for the ASSR. Thus, for these two reasons (frequency spread and maximum intensity), the ASSR and ABR data have not been compared when the stimuli have equivalent energy at the frequency of interest. (ii) The studies that compared 500-Hz tone-evoked ABR and the ASSR also had issues, such as: lower maximum intensities for the ABR tones (in dB nHL) than the ASSR stimuli (in dB HL), incorrect (100 Hz) high-pass EEG filters, and waveform interpretation concerns (e.g., figures show clear ABR to 500 Hz but were indicated as “absent”). (iii) Finally, and importantly, at least some of the ASSRs to high-intensity stimuli may have been artifactual, either due to stimulus artifact contamination or to a non-auditory physiologic response as previously discussed and shown in Figure 8 (Gorga et al. 2004; Jeng et al. 2004; Narne et al. 2006; Picton and John 2004; Small and Stapells 2004).

In summary, although the ability to assess profound hearing losses is stated as a feature of the ASSR and an advantage over the ABR, there has yet to be an appropriate comparison which controls stimulus energy or artifactual (or non-auditory) responses. Further research and careful thought is required. Finally, it must be reiterated that presentation of high-intensity continuous tones for prolonged periods (at least 5 to 10 minutes may be required to reduce response noise below that required to state “no response”) may result in noise-induced trauma to hair cells. Rest time for the cochlea must be provided by interrupting the stimuli.

Young Infants with Normal Hearing

As discussed above and shown in table 1, there is a fairly reasonable database for the ABR to air-conducted brief tones thresholds in normal infants, as well as consensus as to what should be the criteria for “normal” in clinical testing (Stapells 2000a, 2000b). The normative database for infant brainstem-ASSR thresholds is less well understood, and more recent. As noted above, the issue for ASSR is complicated further because studies have used differing stimulus (e.g., single versus multiple) and analysis (e.g., signal-to-noise and noise criteria, and thus recording time) techniques. Nevertheless, there are now many studies providing normative thresholds for infants. Figure 7B presents air-conduction results for a normal 11-week-old infant, showing multiple ASSR thresholds of 46, 29, 24, and 2 dB HL at 500, 1000, 2000, and 4000 Hz, thresholds which are quite different from those of adults (table 6, top line). Table 6 presents

a detailed summary of normal infant thresholds from eight studies: mean infant thresholds (in dB HL) across studies range from 32 to 45, 29 to 37, 26 to 34, and 22 to 36 dB HL for 500, 1000, 2000, and 4000 Hz, respectively, most (85%) with standard deviations ≤ 10 dB. Importantly, infant air-conduction ASSR thresholds (uncorrected for ear-canal differences) are elevated relative to those of adults by about 20 dB for 500 to 2000 Hz, and by 10 to 15 dB for 4000 Hz. Thresholds appear to be even more elevated in very young infants (especially less than age 3-6 weeks; John et al. 2004; Rance and Tomlin 2006; Rance et al. 2006; Savio, Cardenas, Perez Abalo, Gonzales and Valdes 2001); in our recent study, however, we did not find a difference in thresholds between younger (≤ 6 months) and older (6.1-66 months) infants (van Maanen and Stapells 2009).¹⁴ Interestingly, the higher ASSR threshold in infants compared to adults contrasts with the similar tone-ABR thresholds (in dB nHL) for the two age groups (see table 1). Rance and colleagues recently compared tone-ABR and ASSR thresholds in very young infants and showed elevated ASSR thresholds in 1-week-old infants that improved over at least six weeks; tone-ABR thresholds, however, were better (lower) than the ASSR thresholds and did not change over the first six weeks of life (Rance et al. 2006). The reasons for these differences are not clear; one possible explanation is that very young auditory systems have reduced abilities to process the very rapid modulation rates (80-110 Hz) used for the brainstem ASSR, whereas the relatively slower rates (30-50/s) for the tone-ABR pose no problem (Burkard, Shi and Hecox 1990; Lasky 1991; Rance 2008a). Until recently, there has been little discussion in the literature concerning what constitutes a “normal” ASSR threshold in infants (i.e., above what intensity should an infant’s thresholds be considered “elevated”). Given that mean AC-ASSR thresholds in normal infants are significantly elevated relative to adults (see Table 6), clearly one cannot use the “normal” levels typically used for adults (i.e., one cannot use 20 to 25 dB HL as criterion for normal). To establish the criterion for “normal” for clinical testing, one does not use the mean or median thresholds (at which only ~50% of normal infants will demonstrate a response). Rather, the “normal” criterion must be a level where at least 90 to 95% of infants should

¹⁴ The thresholds reported above are in dB HL re: ANSI 1996, and are not levels measured in the ear-canal, which change due to maturation of the ear canal (Bagatto, Seewald, Scollie and Tharpe 2006; Rance and Tomlin 2006; Seewald, Moodie, Scollie and Bagatto 2005; Sininger, Abdala and Cone-Wesson 1997).

show a response at that level. Table 6 thus also presents “normal” levels for infant AC-ASSRs from nine studies. Considering these published results as well as our recent data, we recently recommended infant normal AC-ASSR levels of 50, 45, 40, and 40 dB HL for 500, 1000, 2000, and 4000 Hz, respectively, provided low-noise ASSR recordings are obtained in a quiet sound booth (table 8; van Maanen and Stapells 2009, 2010).¹⁵

Young Infants with Hearing Loss

Perhaps the greatest concern for clinical implementation of ASSRs is that there are very few studies of ASSR thresholds in infants with hearing loss where ASSR thresholds have been compared with gold-standard frequency-specific measures of their actual thresholds (i.e., behavioral audiometry or tone-ABR). Although several studies of ASSR thresholds in children exist, the majority of these either compare ASSR only to click-ABR thresholds; some study older children (e.g., 13 years old); and others have technical problems, especially with their tone-ABR methodology (for review see Stapells, Herdman, Small, Dimitrijevic and Hatton 2005). Table 7 lists those studies that have published difference scores (AC-ASSR thresholds minus frequency-specific behavioral or tone-ABR thresholds) in infants and young children with hearing loss. The studies by Rance and colleagues, using the single-stimulus ASSR technique, have provided the largest sample size (285 with normal hearing and 271 with sensorineural hearing loss; Rance et al. 2005). Three other studies used the multiple-ASSR technique and have a total sample size of approximately 120 ears (Han, Mo, Liu, Chen and Huang 2006; Luts, Desloovere and Wouters 2006; van Maanen and Stapells 2010).¹⁶ Han and colleagues’ study is one of the first hearing-impaired infant threshold studies to record ASSRs to multiple brief-tone stimuli (in contrast to the more-common sinusoidal AM or AM/FM stimuli).

As is the case with adult ASSR data, assessment of infants and children with conductive loss has received little attention. There appears to be only one study of AC-ASSR thresholds in children with conductive loss (Swanepoel, Ebrahim, Friedland, Swanepoel and Potts 2008), and none for children with hearing loss of mixed origin. Although the results are promising, in Swanepoel and colleague’s study (using the single-stimulus ASSR), the “conductive loss” group had no confirmation of the conductive component by frequency-specific air- and bone-conduction behavioral or tone-ABR thresholds, relying, instead, on air-conducted click-ABR, EOAE, tym-

Table 7. Air-conduction brainstem ASSR minus behavioral threshold difference scores (in dB) in infants and young children (<7 yrs) with hearing loss. Adult results from Tlumak et al. (2007) meta-analysis are shown for comparison.

AC ASSR STUDY	STIM	Age	500	1000	2000	4000
<i>Tlumak et al., 2007</i>			14±13	10±13	9±12	8±13
<i>(Meta-analyses of adult data)</i>	M	Adults	(327)	(330)	(328)	(329)
Rance & Briggs, 2002 †	S	1-8 mos	6±9 (160)	6±7 (232)	4±8 (125)	3±11 (131)
Han et al., 2006	M	6-60 mos	15±9 (46)	9±8 (45)	8±8 (42)	11±9 (27)
Luts et al., 2006	M	0-50 mos	8±13 (12)	6±15 (25)	7±13 (25)	9±12 (20)
Van Maanen & Stapells, 2010 ‡	M	1-79 mos	14±9 (50)	13±9 (52)	9±9 (54)	-2±10 (56)

Difference score (dB) = air-conduction ASSR threshold minus pure-tone behavioral threshold; Mean (dB) ± standard deviation. Results rounded off to closest decibels. Number of ears in parentheses; † Rance and colleagues (2005) updated their 2002 results with additional infants; however, no difference scores were provided; ‡ Behavioral threshold estimated from tone-ABR threshold using Stapells (2000b) meta-analysis difference scores (Table 2).

panograms, and otoscopy, none of which can provide an estimate of the amount of a conductive component.

Although the data to date are somewhat limited, especially for the multiple-ASSR, the results in Table 7 provide preliminary difference scores (i.e., corrections) to convert ASSR thresholds to EHL. Conservative AC-ASSR to EHL corrections (i.e., corrections less likely to over-estimate the amount of hearing loss) appear to be about 10 to 15 dB (see table 8). These corrections apply to young children with SNHL and will require elaboration and confirmation through further research.¹⁷

¹⁵ Interestingly, considered in ppe SPL, these normal ASSR levels are close, within 10 dB, to those recommended for the tone ABR.

¹⁶ A recent study by Alaerts and colleagues (Alaerts, Luts, Van Dan, Desloovere and Wouters 2010) obtained both multiple-ASSR and follow-up behavioral thresholds in 50 young infants. However, details were not provided concerning (i) how many of these had hearing loss, (ii) the type and range of hearing loss, or (iii) the corresponding behavioral thresholds. It is also not clear if any of the infants (with normal or impaired hearing) were included in the earlier study (Luts et al. 2006) published by this research group.

¹⁷ In reviewing the AC-ASSR normal levels (Table 6) and the difference scores with hearing loss (Table 7), it becomes clear that current information makes separation of normal hearing and mild hearing loss difficult, especially at 500 Hz. For example, even a 20 dB correction factor applied to the normal level of 50 dB HL at 500 Hz results in a predicted behavioral threshold of 30 dB HL, a result still in the elevated range.

Brainstem ASSRs to Bone-Conduction Stimuli

ASSRs to bone-conduction stimuli have not been thoroughly investigated. Several studies have reported bone-conduction ASSR thresholds in adults with normal hearing (Dimitrijevic et al. 2002; Jeng et al. 2004; Lins et al. 1996; Small and Stapells 2005, 2008b, 2008c). Four studies have assessed the presence of spurious ASSRs in adults with severe/profound SNHL (Gorga et al. 2004; Jeng et al. 2004; Narne et al. 2006; Small and Stapells 2004). One study has assessed bone-conduction ASSRs in adults with simulated conductive loss (Jeng et al. 2004). Recently, we studied the multiple-ASSR in adults with bone-conduction thresholds elevated either by masking noise or by SNHL. We found reasonably high correlations (.8-.9) between BC-ASSR and BC behavioral thresholds at 1000, 2000, and 4000 Hz, and somewhat poorer (.7-.8) correlations at 500 Hz. We concluded that, at least for 1000 to 4000 Hz, the BC-ASSR should provide reasonable estimates of bone-conduction thresholds (Ishida et al. 2011). However, results from infants with hearing loss are still required to confirm appropriate normal levels and determine corrections.

Our recent research has investigated the maturation of BC-ASSR thresholds in groups of premature infants, young infants, older infants as well as adults (Small et al. 2007; Small and Stapells 2005, 2006, 2008b, 2008c). A detailed summary of our infant BC-ASSR research can be found in Small and Stapells (2008a). As shown earlier by ABR research, infant thresholds to bone-conduction stimuli are significantly different from those of adults, especially in the low frequencies. Young infants low-frequency BC-ASSR thresholds are better (i.e., lower dB HL) than those of older infants; similarly, older infants' low-frequency BC-ASSR thresholds are better than those of adults. Thus, BC stimuli in infants are effectively more intense than the same stimuli in adults, likely due to infant skull maturation and other issues (reviewed in Small and Stapells 2008c). Overall, low-frequency BC thresholds increase (become worse) by about 15 to 20 dB from infancy to adulthood. ASSR thresholds to 2000- and 4000-Hz BC stimuli show little or no change (Small and Stapells 2008c). Additionally, young infant ASSR thresholds to 500- and 1000-Hz BC stimuli are better than those to 2000- and 4000-Hz BC stimuli (Small and Stapells 2008b, 2008c). These patterns are clearly different than those for air-conduction stimuli, and indicate that "normal levels" and BC-ASSR-to-behavioral correction factors must be determined from infant data. The existing infant data are currently limited to research in our lab; based on this re-

search, we have recommended normal BC-ASSR levels of 30, 20, 40 and 30 dB HL for infants aged 0 to 11 months, and 40, 20, 40, and 30 dB HL for infants aged 12 to 24 months (see table 8; Small and Stapells 2008a).¹⁸

We have also investigated methodological issues such as: (i) bone oscillator placement (mastoid versus upper temporal bone versus forehead), (ii) bone oscillator coupling technique (handheld versus elastic band), and (iii) the occlusion effect (Small et al. 2007). These infant studies indicate that: (i) forehead placement should be avoided as thresholds are elevated; upper temporal bone and mastoid results are similar although upper temporal bone may be easier to accomplish; (ii) either hand-held or elastic band may be used, provided individuals are adequately trained, and (iii) as infants do not demonstrate an occlusion effect, insert earphones may be left an infant's ear canal during testing with no correction required.

Similar to the ABR, two-channel EEG recordings of infants' brainstem ASSRs also show significant ipsilateral/contralateral asymmetries, with the responses larger and earlier (in latency) in the EEG channel ipsilateral to the stimulated ear (Small and Stapells 2008b). Our preliminary research suggests these asymmetries may be useful in determining which cochlea is responding to bone-conduction stimuli, as is currently possible with two-channel recordings of the ABR. However, further research is required, especially in infants with hearing loss, before these ASSR ipsilateral/contralateral asymmetries can be used clinically. Currently, there are no bone-conduction ASSR studies in young infants with hearing loss. Swanepoel and colleagues recently published the first study to assess bone-conduction ASSRs in young children (mean age: 3.6 years) with elevated air-conduction click-ABR thresholds (Swanepoel et al. 2008). They also reported possible "spurious" responses using the single stimulus system, with results suggesting more spurious responses than studies using the multiple-ASSR technique (Jeng et al. 2004; Small and Stapells 2004). Unfortunately, as noted above, Swanepoel and colleagues did not confirm the hearing status or levels of their subjects. Additional research comparing BC-ASSR thresholds in infants with hearing loss confirmed by behavioral (or tone-ABR) thresholds to air- and bone-conduction stimuli is required.

¹⁸ We have also recommended normal levels of: (i) 30, 30, 50+, and 50 dB HL for premature infants (Small and Stapells 2006), and (ii) 40, 30, 30 and 20 dB HL for adults (Ishida et al. 2011).

Current Status of the ABR and ASSR for Frequency-Specific Threshold Assessment in Infants and Young Children

As the preceding review indicates, using the 80-Hz ASSR to estimate hearing threshold in infants is very promising; however a number of important concerns remain. These concerns include: (i) New stimulus parameters and/or new analysis methods as well as new clinical systems have received little assessment, with few peer-reviewed data supporting their use clinically, especially for infants with hearing loss. (ii) Data for ASSR estimation of threshold in infants with hearing loss are limited to air-conduction thresholds in infants with sensorineural hearing loss. No data exist for infants with conductive or mixed hearing loss where ASSR thresholds have been compared with gold-standard behavioral and/or tone-evoked ABR thresholds. (iii) Very limited data of the bone-conduction ASSR, especially for infants with hearing loss. (iv) The relationship of ASSR thresholds in individuals with profound hearing loss is not adequately studied. The impact of non-physiologic (artificial) or non-auditory physiologic (e.g., vestibular) “spurious” responses on results, especially in those with profound loss remains unclear.

Without resolution of these issues, it remains premature to recommend the use of ASSRs as the primary electrophysiologic measure for threshold estimation in infants. Given the current rapid pace of ASSR research, the much-needed results *may* be available within a few years—when considering the results of future ASSR studies, clinicians must critically appraise them to ensure they involved infants with hearing loss confirmed using frequency-specific gold-standard methods (i.e., behavioral or tone-ABR thresholds using air- and bone-conduction stimuli). Until then, only the tone-evoked ABR has the sufficient research, clinical database, and clinical history to recommend it as the *primary* technique for threshold estimation in young infants. Only the tone-evoked ABR can provide both the air- and bone-conduction results required for early intervention for children with conductive, mixed and sensorineural hearing loss. Except when air-conduction thresholds are normal, the ASSR is thus only appropriate if used *in conjunction with* the tone-evoked ABR.

Currently, there are two ways the ASSR may be used in conjunction with the tone-ABR. First, the ASSR can be very fast as the first step in the diagnostic “ABR/ASSR” protocol, quickly determining whether elevated or nor-

mal thresholds are present, by recording responses to air-conduction stimuli at “normal” level. We have found the dichotic (two-ear) multiple stimulus ASSR to be very fast, requiring only about 4 to 6 minutes total in infants with normal hearing (Janssen and Stapells 2009; van Maanen and Stapells 2009). In normal infants, this is about 50 to 70% of the time required for the tone-ABR; in infants with elevated thresholds, we found the multiple-ASSR in this first step indicated “elevated” only slightly faster, requiring about 80 to 90% of the tone-ABR time (Janssen and Stapells 2009). If the AC-ASSR is absent at the normal levels (i.e., elevated thresholds are present), testing is then quickly switched to the tone-ABR using both bone-conduction and air-conduction stimuli. The second use of the ASSR involves threshold searches *after* required tone-ABR thresholds have been obtained; these ASSR thresholds can provide an important cross-check for the tone-ABR thresholds. The following section outlines our current recommended test sequence and the rationale behind it.

Protocols and the Sequence of Testing using the ABR/ASSR

It is essential to use a test sequence that is fast and efficient, and provides the greatest increase in clinical information with each successive step.¹⁹ Several principles guide the general strategy of stimulus conditions: (i) test time is limited—the infant may wake-up at any moment—so the most important question must be assessed first; (ii) the choice of stimulus condition should be based on what is the most probable outcome: for example, most infants coming to the diagnostic ABR stage after referral during the newborn period have normal hearing. This is usually due to a middle-ear disorder that has resolved since the screening referral, although screening errors also occur. Thus, starting at a low intensity (i.e., at the “normal” levels discussed above) will quickly obtain the necessary results for most infants; (iii) choice of stimulus condition should be based on provision of results that make a difference in management as well as information to the parents: for example, when no response is present at the air-conduction “normal” intensity, spending time collecting precise air-conduction threshold information is less useful than obtaining bone-

¹⁹ Greater detail of our protocols and their rationale are provided in the BCEHP and OIHP protocol documents (BCEHP 2008; OIHP 2008), as well as in the excellent chapter by Slinger and Hyde (2009).

conduction results, because air-conduction threshold in most infants with conductive hearing loss is a “moving target” (i.e., it changes over time). Having information about the type of impairment directs subsequent management (including medical management) and provides more certain information for the family; (iv) efficient strategies require clinicians to frequently switch ears and mode (AC versus BC) of stimulation—insert earphones should be placed in both ears at the beginning of testing, and the bone oscillator ready for application: for example, after obtaining a “no response” at the air-conduction screening intensity in the first ear, one should switch to the other ear rather than seek threshold. Otherwise, one may have spent time determining threshold for one ear, only to have the infant wake-up before determining that the other ear was normal (determined on a second ABR appointment). Obviously, it would have been better, both for management, and for the family, to know that at least one ear was normal.

For most infants, therefore, the diagnostic ABR/ASSR assessment should aim to answer the following three questions, in order of priority: (1) Is an ear’s AC threshold normal or elevated? Is the other ear’s AC threshold normal or elevated? (2) If elevated, is the elevation conductive in nature or is there a sensorineural component? (3) If elevated, what are the specific thresholds (AC and/or BC)? The first question is answered by testing each ear at the “normal” AC level; that is, the minimum level required to conclude normal thresholds for that ear. Results for 2000 Hz are typically obtained first, and this step does not normally involve a threshold search. If the baby wakes up at the end of this, the clinician is still able to state whether one or both ears’ thresholds are normal/elevated. If one has multiple-ASSR available, one can answer this question quite quickly by recording the ASSR to 500, 1000, 2000, and 4000 Hz air-conducted stimuli presented at the normal levels to both ears. Table 8 summarizes the normal levels currently recommended for AC (and BC) stimuli for tone-ABR and ASSR.

The second question is answered by BC testing (at the minimum “normal” BC level) of the ear(s) with AC elevation(s). This question currently can only be answered by the tone-ABR, given the current lack of BC-ASSR data. This step should occur as soon as both ears have been tested in step one at 2000 Hz and one or both ears show no-response (at the normal level). If the infant wakes up at the end of this bone-conduction stage, the clinician is able to state that the elevation in AC threshold is either conductive in nature or has a sensorineural, and thus permanent, component. As the majority of infants

referred from universal newborn hearing screening (UNHS) with elevated AC thresholds will turn out to have conductive losses, this procedure will most often quickly identify an infant’s elevation as conductive in nature, providing important information for subsequent management and for the parents.

The third question is answered by detailed determination of AC (and BC) thresholds. AC thresholds for each required frequency are required for subsequent interventions, including amplification (when chosen by the family) when sensorineural hearing loss is present. Currently, this information must be provided by the tone-ABR. Given the relatively few ASSR data for infants with hearing loss, and uncertainties concerning appropriate ASSR-behavioral corrections, any threshold information obtained using the ASSR should come after completing the tone-ABR.

The above does not clearly indicate the priority sequence of testing for stimulus frequencies. In general, greatest priority is given to 2000 Hz, and results for this frequency are normally obtained first. Next in priority is 500 Hz, then 4000 Hz following, and, if required, 1000 Hz following.²⁰ Prior information (excluding hearing screening results), history (e.g., ototoxic medications) and actual results obtained during the assessment may alter the relative priority of frequencies, but the above sequence should be appropriate for the majority of infants requiring diagnostic ABR/ASSR assessment. Selecting the frequency test order is less of an issue for threshold searches carried out using the multiple-ASSR, as results are obtained for four frequencies simultaneously.

Generally, regularly using intensity step-sizes smaller than 20 dB are inefficient; however, thresholds should be established using a *final* step-size of 10 dB (except, as noted above, when thresholds are greater than 70 dB nHL, where a 5 dB final step-size may be helpful). It is inefficient to routinely use a 5 dB step-size or test at levels below the 25 to 35 dB nHL normal levels (with perhaps the exception of ototoxic monitoring, the management of a “threshold” at the 25 to 35 dB nHL levels is unlikely to be different from a 10 to 20 dB nHL threshold; Slinger and Hyde 2009). Intensities tested should bracket threshold: for example, if no response is seen at 30 dB nHL (2000 Hz), choosing the

²⁰ Often, there is little gained in testing 1000 Hz if thresholds for 500 and 2000 Hz are within 20 dB of each other. Thus, testing at 1000 Hz should only be carried-out: (i) if 500 to 2000 Hz thresholds differ by more than 20 dB, or (ii) all other required testing has been completed (BCEHP 2008; OIHP 2008).

Table 8. Normal maximum levels and threshold correction factors for infant tone-ABR and ASSR thresholds

		500 Hz		1000 Hz		2000 Hz		4000 Hz	
		AC	BC	AC	BC	AC	BC	AC	BC
ABR	NORMAL MAX (dB nHL)	35	20	30-35	na	30	30	25	na
	EHL correction in dB (<i>mid-range, from Table 2</i>)	10	na	5	na	0	na	-5	na
	EHL correction in dB (<i>conservative</i>)	15	na	10	na	5	na	0	na
ASSR	NORMAL MAX (dB HL)	50	30	45	20	40	40	40	30
	EHL correction in dB † (<i>preliminary, conservative</i>)	10-20	na	10-15	na	10-15	na	5-15	na

NORMAL MAX = response must be present at this level to be considered normal; EHL = estimated behavioral hearing level; EHL correction: ABR (dB nHL) or ASSR threshold (dB HL) minus correction = estimated behavioral hearing threshold (in dB HL). “Conservative” ABR corrections used by BCEHP (2008) and OIHP (2008); na: not available or not applicable; † EHL correction factors for ASSR are preliminary. Further research is required.

next level to be 40 dB nHL will give little information if there is no response at 40 dB nHL. A better compromise is 60 dB nHL. If both 30 and 60 dB nHL at 2000 Hz have been tested (as well as BC 2000 Hz at 30 dB) before the infant wakes up, then we know the following: (i) an impairment exists for one or both ears, (ii) whether a sensorineural component exists, and (iii) whether the loss is mild/moderate (if 60 dB nHL response is present) or more severe (if 60 dB nHL is absent). Unfortunately, all too often, clinicians use smaller step-sizes, and follow a sequence which does not switch ears (and AC/BC mode), with the end result that the infant wakes up before a clear picture of the status of *both* ears, as well as the type and severity of loss, has been obtained (BCEHP 2008; OIHP 2008).

ABR (and ASSR) assessment of young infants can be seriously compromised by auditory neuropathy spectrum disorder and/or neurologic involvement (in such cases, especially in ANSD, ABR and ASSR thresholds typically do not reflect cochlear or behavioral sensitivity; BCEHP 2008; OIHP 2008; Rance 2005). As a rule, if a clinician sees a distinct wave that is clearly ABR wave V (to a brief tone of any frequency, whether AC or BC), then they can be reasonably confident that an elevated ABR threshold is *not* due to ANSD or neurologic dysfunction.

(Providing wave V is clear and the V/I amplitude ratio is normal, the finding of a prolonged wave I-V interpeak latency should not be interpreted as suggesting any threshold elevation is due to neurologic dysfunction.) On the other hand, the lack of a *clear* ABR wave V in any waveform, even at the highest intensity, may be the result of profound peripheral (conductive and cochlear) impairment *or* ANSD/neurologic dysfunction. In such a situation (no tone-ABR response with a clear wave V), the clinician must obtain recordings to high-intensity clicks (90-100 dB nHL, mono-polarity, ~19 per second rate). Unfortunately, with ASSR one does not have interpretable time-domain waveforms, thus for any elevated ASSR threshold, one requires confirmation by tone-ABR, and, if no clear wave V is present to the brief tones, by click-ABR.²¹

The question is often asked: “How much time will this tone-ABR testing require?” It definitely takes longer than a simple air-conducted click-evoked ABR; after all,

²¹ It also is important to obtain other measures of auditory responsivity to cross-check the ABR/ASSR results, especially evoked otoacoustic emissions and behavioral responses.

far more information is being sought. Because of this, clinicians must be skilled in carrying out and interpreting tone-ABR results, and they now must use appropriate and efficient test protocols. We recently reviewed 188 tone-ABR assessments (184 infants) carried out over a 20-month period in one of our clinical facilities utilizing tone-ABR protocols (BCEHP 2008) similar to the sequence outlined above, and found that on average, we had 58 minutes of test time for sedated infants, during which we obtained about eight “measures” (e.g., four thresholds in each ear). Non-sedated infants, all aged under 6 months, had an average of 49 minutes of test time, with six “measures” obtained. Importantly, we obtained at least six measures (e.g., three frequencies per ear) for most infants (>80%), thus providing the required information in one session for most infants (Janssen et al. 2010). An earlier study (using different protocols, including click-ABR) reported obtaining at least four threshold estimates for 88% of infants (Karzon and Lieu, 2006). Nevertheless, even with efficient protocols, there will be infants for whom complete information is not obtained within one test session, and a second test session will be required. Although sedation provides, on average, about nine additional minutes of test time, our experience is that non-sedated appointments are much easier and flexible to schedule (no evaluation or monitoring by medical personnel need be arranged), and are typically more accepted by families. Importantly, with today’s very early identification, many infants are now seen at a very young age when they sleep naturally, and sedation is rarely necessary or appropriate. There should be no hesitation in scheduling a second diagnostic ABR session.

What is the minimum information required from ABR/ASSR threshold assessment? Assuming results are deemed reliable and no neurologic/ANSD component to the threshold elevation is suspected (i.e., a clear wave V is present), then, at a minimum, a “complete” tone-ABR evaluation should provide, for each ear, AC thresholds for 500 and 2000 Hz (or, responses at the normal levels) and, if thresholds are elevated, BC tested at least for 2000 Hz and AC thresholds for 4000 Hz (BCEHP 2008; OIHP 2008). Normally, additional information (EOAE, immittance) is also obtained (Janssen et al. 2010), but these additional measures are usually obtained after the tone-ABR testing is completed (i.e., they should not take up ABR test/sleep time; BCEHP 2008). With this information, appropriate management can be initiated early, to be modified later as further information, especially behavioral thresholds, becomes available (Gravel 2002; JCIH 2007; Sininger 2003).

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