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The Auditory Steady-State Response: Full-Term and Premature Neonates

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Abstract

Two studies were aimed at developing the auditory steady-state response (ASSR) for universal newborn hearing screening. First, neonates who had passed auditory brainstem response, transient evoked otoacoustic emission, and distortion-product otoacoustic emission tests were also tested with ASSRs using modulated tones that varied in frequency and level. Pass rates were highest (> 90%) for amplitude-modulated tones presented at levels ≥ 69 dB SPL. The effect of modulation frequency on ASSR for 500- and 2000-Hz tones was evaluated in full-term and premature infants in the second study. Full-term infants had higher pass rates for 2000-Hz tones amplitude modulated at 74 to 106 Hz compared with pass rates for a 500-Hz tone modulated at 58 to 90 Hz. Premature infants had lower pass rates than full-term infants for both carrier frequencies. Systematic investigation of ASSR threshold and the effect of modulation frequency in neonates is needed to adapt the technique for screening.

Key Words: Auditory evoked potentials, auditory threshold, newborn infant

Abbreviations: ABR = auditory brainstem response; AM = amplitude modulation; ASSR = auditory steady state response; CF = carrier frequency; c-ABR = click-evoked auditory brainstem response; DPOAE = distortion-production otoacoustic emission; EOAE = evoked otoacoustic emission; FM = frequency modulation; MSC = magnitude squared coherence; MF = modulation frequency; PC = phase coherence; PC^2 = phase coherence squared; SNR = signal-to-noise ratio; tb-ABR = toneburst-evoked auditory brainstem response; TEOAE = transient evoked otoacoustic emission

Sumario

Dos estudios fueron enfocados al desarrollo de la prueba de respuestas auditivas de estado-estable (ASSR) para tamizaje auditivo universal de recién nacidos. Primero, neonatos que habían aprobado evaluaciones de respuestas evocadas de tallo cerebral, de emisiones otoacústicas evocadas por transientes y de emisiones otoacústicas por productos de distorsión, fueron también evaluados por ASSR utilizando tonos modulados que variaban en frecuencia e intensidad. Las tasas de aprobación fueron más altas (> 90%) para tonos de amplitud modulada presentados a niveles de > 69 dB SPL. El efecto de la modulación de la frecuencia sobre los ASSR, para tonos de 500 y 2000 Hz, fue evaluado en niños prematuros y de término en el segundo estudio. Los infantes de término obtuvieron mayores tasas de aprobación para la prueba para tonos de 2000 Hz con amplitud modulada entre 74 a 106 Hz, comparadas con aquellas para tonos modulados de 500 Hz entre 58 y 90 Hz. Los niños prematuros tuvieron tasas de aprobación menores que los infantes de término para ambas frecuencias portadoras. Se necesita una investigación sistemática sobre los umbrales para ASSR y sobre el efecto de la modulación de la frecuencia para adaptar esta técnica a procedimientos de tamizaje

Palabras Clave: Potenciales evocados auditivos, umbral auditivo, niño recién nacido

Abreviaturas: ABR = respuesta auditiva del tallo cerebral; AM = modulación de la amplitud; ASSR = respuesta auditiva de estado-estable; CF = frecuencia portadora; c-ABR = respuesta auditiva del tallo cerebral evocada por click; DPOAE = emisión otoacústica por producto de distorsión; EOAE = emisión otoacústica evocada; FM = modulación de la frecuencia; MSC = coherencia de magnitud al cuadrado; MF = frecuencia de modulación; PC = coherencia de fase; PC^2 = coherencia de fase al cuadrado; SNR = tasa de relación señal/ruido; tb-ABR = respuesta auditiva de tallo cerebral evocada por burst tonal; TEOAE = emisión otoacústica evocada por transientes

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Newborn hearing screening tests using evoked otoacoustic emissions (EOAEs) or auditory brainstem responses (ABRs) were recommended by the U.S. National Institutes of Health in 1993, and there has been widespread adoption of this mandate across the United States and in Europe. Several large-scale studies have been completed that evaluated EOAE (Kennedy, 1999) or automatic ABR (Mason et al, 1998; Mason and Herrmann, 1998) technologies or both (Norton et al, 2000a) for newborn hearing screening. Norton and colleagues (2000b) showed that there was no difference in test performance for detecting hearing loss of 30 dB or greater at 2 to 4 kHz when an automatically detected click-evoked ABR (c-ABR) and EOAEs were compared. This study also showed that c-ABR had better performance characteristics than EOAE for detecting hearing when 1 kHz was used in the pure-tone average (Norton et al, 2000a). EOAE tests, however, are often thought to have some advantages in screening owing to their presumed greater frequency and place specificity in comparison with c-ABR.

Rickards and colleagues (1994) showed that auditory steady-state responses (ASSRs) could be recorded from full-term neonates using amplitude-modulated (AM) + frequency-modulated tones at 500, 1500, and 4000 Hz. They established ASSR thresholds for full-term infants and, importantly, showed that there were modulation frequencies (MFs) that were associated with greater "response efficiencies," a measure taking into account the response amplitude and phase coherence (PC). The MFs yielding the highest efficiencies increased with carrier frequency (CF), from 72 Hz for a CF at 500 Hz to 97 Hz for a CF at 4000 Hz.

These results were a starting point for two studies aimed at developing ASSRs for newborn hearing screening. The advantage of using ASSR over c-ABR would be its greater frequency specificity and a robust automatic detection algorithm. The advantage of using ASSR over EOAE would be that it would be less affected by external and middle ear status, which can disrupt the transmission of EOAE energy to the ear canal.

STUDY 1: TOWARD AN ASSR SCREENING TEST IN NEONATES

The focus of the first study was the effect of CF and stimulus level on the ability to obtain a statistically significant result (that is, a "pass") using the phase coherence squared (PC^2) automatic detection algorithm (Dobie and Wilson, 1993; Cone-Wesson et al, 2002). The questions asked were

1. What are the pass rates for ASSR tests that are varied by CF and stimulus level?
2. How long does it take to achieve a statistically significant ("pass") result for each CF and level combination when sampling the electroencephalogram (EEG) in 1.486-sec epochs?
3. What is the latency of the ASSR as estimated from phase angle data?

Method

The participants were 31 male and 51 female newborns who were recruited from the neonatal intensive care unit and well-baby nurseries at the Los Angeles County+University of Southern California Medical Center. They were tested as part of a larger study of newborn hearing screening technologies (Norton et al, 2000a). Forty-five infants were tested at 36 to 45 hours after birth, but 37 were tested at a mean age of 13 days after birth (range 4 to 120 days).

Infants were swaddled and tested in their isolettes during natural sleep, after obtaining informed consent from the parents. All parents were provided with information about normal hearing, speech, and language development during the first year of life, regardless of whether they decided to participate in this study.

Each infant was tested using a c-ABR, transient evoked otoacoustic emission (TEOAE), and distortion-product otoacoustic emission (DPOAE) prior to the ASSR test. For the c-ABR test, the stimulus was a 64 dB peSPL (nominally 30 dB nHL), and for TEOAE, the click level was 80 dB pSPL. DPOAEs were tested using primaries with an $f2:f1$ frequency ratio of 1.22 and $f1:f2$ levels at 65:50 dB SPL over an $f2$ frequency range of 1 to 6 kHz. ABRs were judged present if an Fsp test met a criterion of $p < .05$ significance (Sininger et al, 2000). EOAEs were judged normal when EOAE-to-noise ratios of 3 dB or greater were achieved in 4 out of 5 frequency bands. All infants who were recruited for this study of ASSR met the passing criteria for ABR, TEOAE, and DPOAE tests.

ASSRs were tested using AM tones at 250, 500, 1000, 2000, and 4000 Hz, with MFs of 87, 76, 83, 89, and 93 Hz, respectively. Stimulus levels were chosen to approximate levels needed to screen for mild or moderate hearing loss. Psychophysical thresholds for the test stimuli were determined for a panel of three normal-hearing adults, and the two test levels, 40 dB SL and 60 dB SL, were referenced to these results. The test levels used at each frequency were 61.5 and 81.5 dB SPL at 500 Hz, 52 and 72 dB SPL at 1000 Hz, 49 and 69 dB SPL at 2000 Hz, and 54.5 and 74.5 dB SPL at 4000 Hz (250-Hz tones were presented at –1.5 dB SPL for "no stimulus" control trials). Stimuli were presented through an EAR-3A insert transducer, calibrated in a Phonic Ear HA1-2-cc coupler. The order of stimulus frequency and level trials was randomized.

The EEG was sampled from electrodes placed at Cz and Mi. The samples obtained were 1.486 seconds in length, at an AD rate of 44.1 kHz. Samples were amplified with a gain of 86 dB via an Opti-Amp 3000D preamplifier (Intelligent Hearing Systems, Miami, Florida), bandpass filtered at 3 to 5000 Hz, and then converted to the frequency domain for analysis of phase characteristics.

Each CF × level test was considered a "trial," and there was one of three outcomes for each trial: pass, fail, or noise. EEG samples collected for a trial were subjected to analysis in the frequency domain, including an analysis of PC. The detection algorithm used for response detection was PC^2 (Dobie, 1993; Sininger and Cone-Wesson, 2001; Cone-Wesson et al, 2002). Trials meeting the PC^2 criterion of $p < .002$ within 64 samples were scored as a pass. By using this strict criterion, less than 2 of 1000 trials would result in a positive result if only noise (no response) were present. This strict criterion was adopted to minimize the chances that an infant with a hearing loss would yield a "false-positive" result. Trials in which the average noise levels were at –146 to –134 dB re 1 V and in which there was no statistically significant PC were scored as a fail. If there was no PC and the averaged noise levels exceeded –134 dB re 1 V, the trial was scored as noise. Scoring took place offline, after all trials had been completed.

Infants were tested while sleeping, immediately after the ABR, TEOAE, and DPOAE tests. A prototype of the ERA System (Appendix) was used to generate tones and acquire ASSRs.

Results

A total of 367 ASSR tests (trials) were completed for 87 infants; 40 were control trials. Seventy trials, including 16 controls, were scored as noise. Of the remaining trials, 239 met the passing criteria and 58 failed. Three of the remaining 24 control trials met the passing criteria and were false positives. Post hoc analyses of these false-positive trials showed them to be the result of artifact generated by the preamplifier when used with a low battery charge.

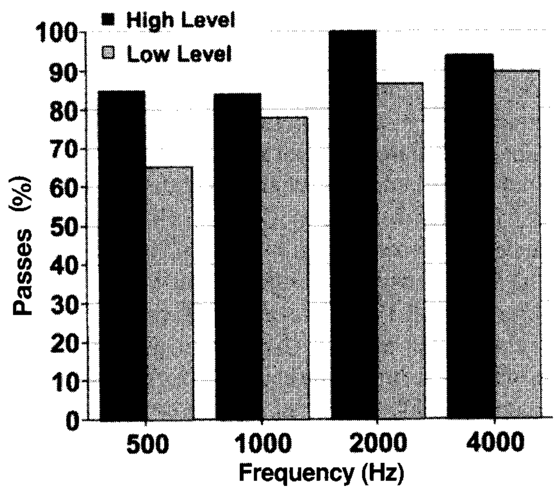

Figure 1 Pass rate for auditory steady-state response screening tests in newborns as a function of carrier frequency and level. Passes were determined by applying a phase coherence squared detection algorithm.

Pass rates varied with CF and level. This is illustrated in Figure 1. A 100 percent pass rate was achieved for 2000 Hz presented at 69 dB SPL and was still 86 percent at 49 dB SPL. For all CFs tested, the average pass rate for the higher stimulus level was 90 percent, and at the lower stimulus levels, the average pass rate was 79.5 percent.

For those trials that met the pass criterion, the number of samples needed to obtain a significant result was calculated based on a sample length of 1.49 sec/sample plus an 8-second presampling "conditioning" interval required by the software-hardware interface. On average, 44 seconds were needed for each screening trial, although the range was from 19.5 to 104 seconds. Differences in time were observed for both CF ($F = 3.384$, $df = 3$, $p < .01$) and for level ($F = 9.453$, $df = 1$, $p < .01$). Post hoc tests showed that the number of samples, and therefore time, needed to obtain a passing result was shorter for 1000- and 2000-Hz CFs in comparison with the 4000-Hz CF. Screening trials at the higher stimulus levels were passed an average of 7 seconds earlier in comparison with those at lower levels. There was no CF × level interaction. Table 1 lists the time required to achieve a passing result as a function of CF and level.

Table 1 Duration of Trial (Time, sec) Needed to Meet Pass Criterion, Period (msec), Phase Delay (Degree), and Estimated Latency (msec) of Auditory Steady-State Response as a Function of MF, CF, and Level

MF, Hz	*CF, Hz*	*Level, dB*	*Time, sec (SD)*	*Period, msec*	*Phase Delay, Degree*	*Latency, msec*
76	500	High	33.3 (16.8)	13.1	119	17.28
		Low	46.5 (22.7)		176	19.33
83	1000	High	31.5 (15.6)	12.0	148	16.88
		Low	31.6 (13.3)		176	17.80
89	2000	High	30.1 (14.6)	11.2	111	14.60
		Low	37.8 (21.0)		142	15.60
93	4000	High	36.1 (16.5)	10.7	67	12.60
		Low	44.6 (20.9)		101	13.60

Data are from study 1.
MF = modulation frequency; CF = carrier frequency.

Response latencies were estimated from the phase values used in the PC^2 analyses. Average latencies were calculated only for those responses that met the statistical criteria for a pass. The average phase delay between the MF and the response was calculated for each trial. For example, at 500 Hz, the MF was 76 Hz, which has a 13.1-msec period. The average phase delay for the high-level stimulus was 119 degrees. The estimated latency was calculated by multiplying the phase delay by the appropriate value for msec/degree and then by adding an amount equal to one full cycle of the MF. The results of the latency calculations are shown in Table 1. Latencies decreased with CF and increased inversely with level.

Discussion

The results of this study demonstrate that certain combinations of CF and level yield ASSR pass rates comparable to other newborn hearing screening tools and that the estimated latencies as a function of CF are similar to those found for toneburst-evoked ABR (tb-ABR). The data demonstrated that an ASSR screening test incorporating four frequencies could be completed for one ear in 3 minutes on average.

EOAE screening tests are sometimes preferred to c-ABR tests because the tests are quick, the results are presumed to be more frequency and place specific, and electrodes do not have to be applied to the scalp to obtain a response. The ASSR technique allows screening in the audiometric frequency range, from 500 to 4000 Hz, with results for one frequency obtained after 44 seconds of signal processing for each frequency tested. Although it is necessary to place electrodes on the scalp to record a response, electrode preparation time for technicians involved in newborn screening can generally be improved with practice (Sininger et al, 2000) and is not likely to be over a minute for more experienced technicians. EOAEs cannot be easily obtained for frequencies under 1500 Hz, at least in newborns tested in a screening context (Gorga et al 2000; Norton et al 2000b, 2000c), whereas with the ASSR technique, infant responses to 1000-Hz tones were not only easily obtained but appeared to show more robust signal-to-noise ratios (SNRs) than for 500- or 4000-Hz stimuli.

For the purposes of this study, the c-ABR, TEOAE, and DPOAE tests served as the gold standard against which the ASSR results could be compared, and only those infants who had met strict pass criteria for both c-ABR and two EOAE tests were included. The pass rate for ASSR trials varied with CF and with level. A 100 percent pass rate was achieved for a 2000-Hz tone modulated at 89 Hz, presented at a level of 69 dB SPL (5 dB higher than the peSPL of the click used for c-ABR). Pass rates increased with frequency for stimuli presented at the lower levels (52 to 61.5 dB SPL). Of course, the true performance of a newborn hearing screening tool must be determined with infants who have hearing impairment. This study, however, suggests that ASSR test specificity (ears passing when normal) at 2000 Hz compares favorably with the c-ABR and EOAE screening measures.

One challenge in the design of an ASSR screening test is to determine normal threshold for newborns. Rickards and colleagues (1994) estimated ASSR threshold in newborns at 41, 24, and 34 dB HL for 500, 1500, and 4000 Hz, respectively. When expressed in SPL, these are at 52.5, 30.5, and 44.5 dB, considerably lower than thresholds found by Hyde and colleagues (1987) when thresholds in 4-month-old infants were estimated with toneburst ABR.

The Rickards and colleagues (1994) newborn thresholds are closer to tb-ABR thresholds in infants and young children determined by Stapells and colleagues (1995); however, the Rickards and colleagues (1994) ASSR thresholds are elevated compared with newborn tb-ABR threshold estimates determined by Sininger and colleagues (1997). Using the Rickards and colleagues (1994) values, the test levels used in the present study ranged from only 9 dB above threshold (500 Hz at 61.5 dB SPL) to 30 dB (4000 Hz at 74.5 dB) above the average threshold. Depending on the degree of hearing loss that is the target condition, levels considerably higher than those used in this may be suitable for screening purposes.

It is interesting to note that the shortest trial duration (fewest number of sweeps) to meet the pass criterion, the highest PC^2 values, and the largest SNRs were obtained at 1000 Hz. This is similar to Rickards and colleagues' (1994) findings that 1500 Hz resulted in the greatest "efficiency" quotient, a metric that took into account both the amplitude and the PC of the ASSR. Tb-ABRs at 1500 Hz also appear to have larger amplitudes compared with those for higher and lower frequencies (Sininger et al, 1997). It appears that AM tones in the mid-frequency range (1000 to 2000 Hz) evoke robust responses in newborns. The cochlear and neural bases of this mid-frequency advantage in newborns deserve more study.

Latency measures are used in ABR evaluations to characterize both the type and the degree of hearing loss and to help identify when an ABR has occurred; for example, visual detection methods often rely on observing an expected latency shift in the response as stimulus level is varied. Latency measures are less relevant for threshold estimation. The latencies estimated from the phase data in this study are in good agreement with tb-ABR latencies in young infants (Stapells et al, 1995). Also, there is an apparent shift in latency with stimulus level: latencies at the higher test levels are 1 to 2 msec shorter than those 20 dB lower. These latency shifts are characteristic of response properties seen in the tb-ABR.

The ASSRs for AM tones at MFs above 60 Hz show promise as a tool for newborn screening. ASSR pass rates were over 80 percent for all carrier frequencies and 100 percent for a 2000-Hz CF at 89 Hz at a level close to that of the c-ABR. ASSR tests are quick and frequency specific and employ an automatic detection algorithm, all of which are advantages for the screening hearing using an evoked potential technique. Further study of developmental and pathologic variables affecting the ASSR will increase the applicability and test performance of this screening tool.

STUDY 2: ASSRS IN NEONATES: EFFECT OF MODULATION FREQUENCY

When using evoked potentials to predict audiometric threshold, there is much to be gained by optimizing stimulus and recording parameters (Sininger and Cone-Wesson, 2001). One parameter to be considered is stimulus rate. Systematic investigations of stimulus rate on threshold, latency, and amplitude of the ABR have been conducted among normal-hearing individuals (Sininger and Don, 1989; Burkard et al, 1990) and those with various types of hearing loss (Fowler and Noffsinger, 1983). In general, as the rate of stimulation is increased, ABR latency increases, amplitude decreases, and therefore threshold increases. The effect of stimulus rate on threshold, however, may not be clinically significant if the rate is under 50/sec and the brainstem pathways are mature and intact (Sininger and Don, 1989). Rates of 30 to 60 stimuli per second are recommended for ABR threshold searching procedures. At these stimulus rates, the amplitude of the response is maintained, and the faster rates allow for a greater amount of averaging to take place, thus improving the SNR of the averaged response. In premature infants, stimulus rate has been shown to have a dramatic effect on the ABR latencies that may be increased by more than 1.5 msec as the rate is increased from 10 to 100/sec (Lasky, 1984).

Protocols for obtaining threshold estimates from ABRs must take into account the developmental and neurologic status of the patient before interpreting responses obtained at fast rates.

Like the ABR, the effects of MF on the ASSR appear to be age specific. Stapells and colleagues (1988) found that the ASSR could not be consistently evoked in sleeping infants at modulation rates of 9 and 59 Hz. The variability of the ASSR in sleeping infants and young children for low MFs has also been demonstrated by Aoyagi and colleagues (1994). Levi and colleagues (1993) investigated the effect of MF on the ASSR of 1-month-old infants tested while asleep. They used MFs at 10, 20, 30, 40, 50, and 80 Hz and CFs at 500 and 2000 Hz. The optimal MF was defined as that which gave the highest magnitude squared coherence (MSC) value, a statistic that takes into account the PC and amplitude of the ASSR. MSC increased with MF, and the highest values were obtained for 80 Hz. Rickards and colleagues (1994) also showed the effect of MF on the ASSR of full-term newborns. An "efficiency ratio" metric was used to evaluate the effect of MF, taking into consideration both the amplitude and PC of the response. The most efficient MFs were 72, 85, and 97 Hz for CFs of 500, 1500, and 4000 Hz, respectively. These studies show that MFs greater than 70 Hz can be used to evoke ASSRs in neonates and that the optimal MF for detection of an ASSR may vary with carrier frequency.

If ASSRs are to be used for estimation of audiometric threshold in young infants or in newborn hearing screening, it is also crucial to determine pathologic variables (apart from hearing loss) that affect the ASSR such as neurologic insult or developmental delay. The aim of this study was to determine the MF-CF combinations that would yield the highest rate of responses meeting the PC^2 detection criteria (i.e., a "pass"), thus indicating optimization of stimulus parameters. The second aim was to determine how ASSRs in preterm infants differed from those of full-term infants to evaluate the effect of neurologic status on the ASSR.

Method

Participants

Two groups of infants participated in the study: the first group was recruited on the basis of a normal birth history, without risk indicators for hearing loss, and had 19 term (38 to 41 weeks gestational age) infants (9 females). The second group was recruited on the basis of prematurity, with gestational ages ranging from 23 to 34 weeks (mean = 29 weeks), and consisted of 11 infants (8 females). The normal term infants were tested within 72 hours of birth. The age at the time of testing for the premature group ranged from 4 to 123 days (mean 55 days), with all premature infants tested after they had achieved a gestational age of at least 31 weeks. All premature infants had been confined to a neonatal intensive care unit or special care nursery for varying periods of time but were in an open cot and breathing room air when tested (although 4 infants continued to receive oxygen therapy on a regular schedule).

Stimuli and ASSR Recording Procedures

Tones at 500 and 2000 Hz were presented at 66 and 56.5 dB SPL, respectively, through Etymotic Research ER-3a tubephones coupled to the ear with a small rubber nipple. The tones were calibrated using a Bruel and Kjaer Model 2209 SPL meter, with a Phonic Ear HA-1 2-cc coupler. The 500-Hz tone underwent 100 percent AM at 58 to 90 Hz varied in 4-Hz steps, whereas at 2000 Hz, the range of MFs tested was 74 to 106 Hz, in 4-Hz steps. The order of CF and MF presentation was randomized across the subjects. ASSRs were recorded using gold-cup electrodes placed at the vertex and ipsilateral earlobe or mastoid and led to an Intelligent Hearing Systems Opti-Amp 3000D preamplifier interfaced with a custom-built processor and desktop computer that controlled stimulus generation and data acquisition. EEG samples of 1486 msec in length, sampled at 44.1 kHz, were filtered at 3.0 to 5000 Hz and amplified with a gain of 86.9 dB. Sixty-four samples of 1486 msec each for each CF-MF combination were subjected to analysis using a PC^2 algorithm. The results (pass versus fail) were determined on the basis of the PC^2 algorithm reaching a statistical significance of $p < .002$.

DPOAEs were also obtained for each infant using an ILO-92 Otoacoustic Emission Analyser. Primary tones f1 and f2 were presented at a sound pressure level of 65 and 50 dB, respectively, with an f2:f1 frequency ratio of 1.22. Responses were recorded between 1500 and 6000 Hz, with a frequency resolution of four points per octave to form a "DP-gram." Emissions that were 3 dB or more above 2 SD of the averaged noise floor were considered valid. A "pass" response was a DP-gram that had valid responses at each test frequency in the DP-gram.

Procedure

Infants were swaddled and tested in their isolettes during natural sleep after obtaining informed consent from the parents. All parents were provided with information about normal hearing, speech, and language development during the first year of life, regardless of whether they decided to participate in this study. A small storage room in the vicinity of the nursery was used as a test facility.

Results

DP-grams were completed in 16 of 19 full-term infants and in 8 of 11 preterm infants.

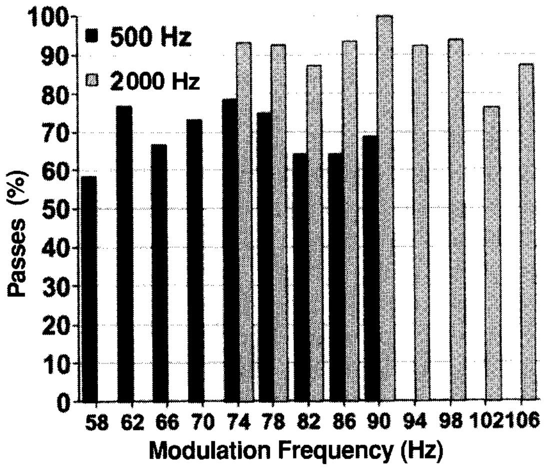

Figure 2 Pass rate for auditory steady-state response screening tests in full-term newborns as a function of modulation frequency and frequency. Passes were determined by applying a phase coherence squared detection algorithm.

Tests were not completed when there was excessive noise or a poor response state or when the ear canal was too small to obtain an adequate probe fit. The 16 full-term infants tested met the DP-gram pass criteria; however, only 4 of 8 preterm infants tested had responses that met the criteria.

Effect of Carrier and Modulation Frequency on Pass Rate: Full-Term Infants

There was a significant effect ($\chi^2 = 18.9$, $p < .01$) of CF on pass rate, with 69.8 percent of trials (90/129) at 500 Hz and 90.7 percent of trials (127/140) at 2000 Hz meeting the pass criterion. The effect of MF on the pass rate for a 500-Hz CF is shown in Figure 2. This figure shows that pass rates are highest for MFs in the 70- to 78-Hz range, with the lowest pass rate at 58 Hz (58.3%) and the highest at 74 Hz (78.6%). Statistical analysis (chi-square test) of the pass rate as a function of MF did not achieve significance, however. The effect of MF (varied from 74 to 106 Hz in 4-Hz steps) on pass rate at 2000 Hz is also shown in Figure 2. A 100 percent pass rate was obtained at 90 Hz, but at 102 Hz, only 76.5 percent of trials were passes. The 2000-Hz CF produced a high pass rate regardless of MF, falling below 90 percent only at 82, 102, and 106 Hz. As in the case of 500 Hz, no statistically significant effect of MF on pass rate was found for this range.

Table 2 Signal-to-Noise Ratio (SNR) as a Function of Infant Group (Full Term or Premature), Carrier Frequency, and Test Result (Pass-Fail)

Group	*Carrier Frequency, Hz*	*Result*	*SNR**	*SD*
Full term	500	Pass	2.59	6.24
Full term	500	Fail	−12.44	4.48
Full term	2000	Pass	3.51	5.83
Full term	2000	Fail	−11.73	3.34
Premature	500	Pass	1.67	5.91
Premature	500	Fail	−16.43	5.37
Premature	2000	Pass	2.74	6.82
Premature	2000	Fail	−10.11	3.50

Data are from study 2.

*Signal and noise levels were measured in decibel attenuation re 1 μV.

Pass Rate and Signal-to-Noise Ratio

Amplitude-based artifact rejection is conventionally used to reduce the effect of myogenic or electrical noise on the averaged response (Hyde, 1994). The advantage of this method is that large electric events that could not possibly be neural responses are eliminated from the average. The disadvantage, however, is that some response may be rejected at the same time as the artifact; thus, data acquisition time is increased. Methods for estimating noise in an averaged response exist (Don and Elberling, 1994), and conventional averaging can take place until either a criterion estimate of the SNR is reached or until noise estimates reach a very low level. Online amplitude-based artifact rejection was not employed in this study; however, trials were excluded from post hoc analyses on the basis of excessive noise. Of 295 trials, 26 were not included in the previous data analyses because of excessive noise. For the remaining trials, all sample vectors were normalized (in length) to unity for the PC^2 analysis. This served to reduce the effect of large out-of-phase vectors containing noise on the statistical significance of PC for the trial. The magnitudes of all sample vectors were stored, so it was possible to estimate the level of the signal (response) and noise. Noise estimates were no higher in trials that did not meet the pass criterion compared with those that did. Table 2 shows the mean SNR as a function of CF and test result (pass versus fail).

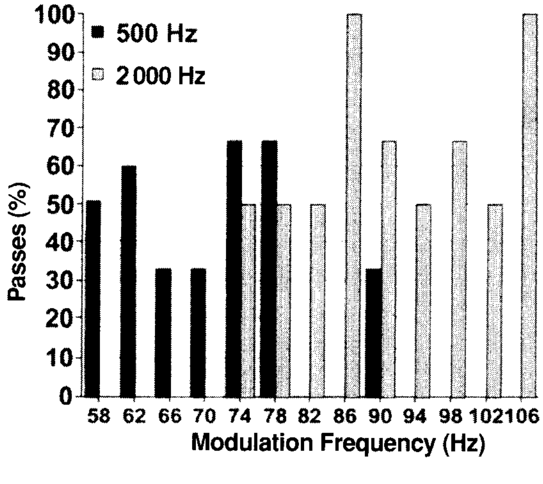

Figure 3 Pass rate for auditory steady-state response screening tests in premature newborns as a function of modulation frequency and frequency. Passes were determined by applying a phase coherence squared detection algorithm.

Preterm Infants

Pass rates for ASSR trials as a function of CF and MF were also determined for preterm infants (Fig. 3). The overall pass rate was 40.7 percent (11/27) for 500 Hz and 62.5 percent (15/24) for 2000 Hz. These results are considerably poorer than those obtained from full-term infants. The MFs associated with the highest pass rates for a 500-Hz CF were 74 and 78 Hz, with 2 of 3 trials passing. At 2000 Hz, 90, 98, and 106 Hz demonstrated pass rates above 50 percent. Noise estimates were carried out for preterm infants as they were for full-term infants. Twenty-three of 74 trials in preterm infants were indeterminate (and not included in analyses) because of excessive noise levels. Although there were infants who failed ASSR trials because noise levels were high, overall, the noise levels for trials that met the pass or fail criteria in preterm infants did not differ from those found in full-term infants. SNRs for premature infants are shown in Table 2 as a function of CF and test result.

Discussion

ASSR is most detectable at 40 Hz in awake adults (Cohen et al, 1991; Dobie and Wilson, 1998), and for sleeping infants and children, MFs greater than 70 Hz are optimal (Aoyagi et al, 1993, 1994; Levi et al, 1993; Rickards et al, 1994). This study expands on that work and also demonstrated that ASSR in preterm infants may differ substantially from those in a full-term infant.

Pass rates for tests using a 500-Hz CF are lower than for 2000-Hz CF. This has implications for both screening and diagnostic applications of the ASSR. The levels in this study were deliberately set to be lower than those that would typically be used in a screening test to test the hypotheses regarding MF. If levels were > 30 dB re threshold, it would not have been possible to determine the significance of MF. At 500 Hz, the test level was 15 dB above mean neonatal ASSR threshold as determined by Rickards and colleagues (1994). ASSR thresholds in normal newborns for 2000-Hz AM tones have not yet been determined, but a level of 52.5 dB SPL is approximately 20 dB above ABR threshold determined for 2000-Hz tone bursts. A pass rate of 78.6 percent was achieved at a 74-Hz MF for 500 Hz but fell to a low of 69.7 percent for a 58-Hz MF. At 2000 Hz, the overall pass rate was at 91 percent, but at 102 Hz, the pass rate was only 76.5 percent. Although ASSR threshold was not tested in this study, the difference in pass rate as a function of CF suggests that thresholds at 500 Hz are elevated with respect to 2000 Hz. Poorer responses at 500 Hz compared with 2000 Hz may occur owing to developmental effects of the external auditory meatus and middle ear system. Levi and colleagues (1993) showed that when the sound pressure level of AM tones was measured in the infant ear canal and compared to coupler measures, the coupler overestimated the sound pressure level of the low-frequency tone. Keefe and Levi (1996) have also shown that the power absorption of the middle ear is less for low frequencies compared with high-frequency tones. Sininger and colleagues (1997) showed a differential effect of frequency when sound pressure levels were measured in the ear canal of newborn infants. The underlying factors for ASSR threshold or detectability differences as a function of CF in newborns need further investigation.

Within the range of MFs tested, there was no statistically significant effect of MF on ASSR detectability for full-term infants. There are peaks in the MF transfer function revealed by ASSRs (Cohen et al, 1991; Rickards et al, 1994), but the effect of maturation on these transfer functions has not been explored past the age of 1 month (Levi et al, 1993).

Premature infants proved to have very poor pass rates for ASSR. It was not possible to rule out hearing loss (either conductive or sensorineural) as a cause in some infants because only 8 of 11 could be tested with

DPOAEs, and of those 8 tested, only 4 had acceptable responses. The presence of DPOAE, indicating normal middle ear and outer hair cell function, did not always correspond with the ASSR result. Even if the increased rate of conductive and sensorineural hearing loss among premature infants (Cone-Wesson et al, 2000) is factored in, the pass rates for ASSR tests were lower than expected. Because stimulus rate has a profound effect on ABR for premature infants or others with neural compromise (Cone-Wesson and Spingarn, 1993), the present data suggest that ASSRs could be affected in this population. The data obtained in this study are preliminary in nature but suggest a conservative approach to the use of ASSR for hearing estimation when neurologic or developmental status is compromised.

Separating the signal (response) from the background EEG and myogenic noise is the basis of signal processing and response detection. Although online amplitude-based artifact rejection was not used during data acquisition, trials that had excessive noise were eliminated from the post hoc analyses (including determination of pass-fail rates as a function of MF). Noise levels did not vary for pass versus fail trials, nor did they vary for the full-term versus premature groups, although a higher percentage of trials from premature infants was excluded from analyses owing to noise. Weighted averaging has been used in conjunction with MSC to improve the detectability of the ASSR (Dobie and Wilson, 1998). Parametric investigation of both the (ASSR) signal and noise in the target population for clinical tests (infants and children) will lead to improved methods of signal processing and response detection.

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REFERENCES

Aoyagi M, Kiren Y, Yutaka S, et al. (1993). Optimal modulation frequency for amplitude modulation following response in young children during sleep. *Hear Res* 65:253–261.

Aoyagi M, Kiren T, Furuse H, et al. (1994). Effects of aging on amplitude modulation-following response. *Acta Otolaryngolog Suppl (Stockh)* 511:15–22.

Burkard R, Shi Y, Hecox K. (1990). A comparison of maximum length sequences for the derivation of brain-stem auditory-evoked responses at rapid rates of stimulation. *J Acoust Soc Am* 87:1656–1664.

Cohen LT, Rickards FW, Clark GM. (1991). A comparison of steady state evoked potentials to modulated tones in awake and sleeping humans. *J Acoust Soc Am* 90:2467–2479.

Cone-Wesson B, Spingarn A. (1993). Effects of maternal cocaine abuse on neonatal auditory brainstem responses. *Am J Audiol* 2:48–54.

Cone-Wesson B, Vohr BR, Sininger YS, et al. (2000). Identification of neonatal hearing impairment: infants with hearing loss. *Ear Hear* 21:488–507.

Cone-Wesson B, Dowell RC, Tomlin D, et al. (2002). The auditory steady state response part I: comparisons with auditory brainstem response. *J Am Acad Audiol* 13:173–187.

Dobie RA. (1993). Objective response detection. *Ear Hear* 14:31–35.

Dobie RA, Wilson MJ. (1993). Objective response detection in the frequency domain. *Electroencephalogr Clin Neurophysiol* 88:516–524.

Dobie RA, Wilson MJ. (1998). Low-level steady-state auditory evoked potentials: effects of rate and sedation on detectability. *J Acoust Soc Am* 104:3482–3488.

Don M, Elberling C. (1994). Evaluating residual background noise in human auditory brainstem responses. *J Acoust Soc Am* 96:2746–2757.

Fowler CG, Noffsinger D. (1983). Effects of stimulus repetition rate and frequency on the audiory brainstem response in normal, cochlear-impaired and VIII nerve/brainstem-impaired subjects. *J Speech Hear Res* 26:560–567.

Gorga MP, Norton SJ, Sininger YS, et al. (2000). Identification of neonatal hearing impairment: distortion product otoacoustic emissions during the perinatal period. *Ear Hear* 21:400–424.

Hyde M. (1994). Signal processing and analysis. In: Jacobson JT, ed. *Principles and Applications in Auditory Evoked Potentials*. Boston: Allyn and Bacon, 47–83.

Hyde ML, Matsumoto N, Alberti PW. (1987). The normative basis for click and frequency-specific BERA in high-risk infants. *Acta Otolaryngol (Stockh)* 103:602–611.

Keefe DH, Levi E. (1996). Maturation of the middle and external ears: acoustic power-based responses and reflectance tympanometry. *Ear Hear* 17:361–373.

Kennedy CR. (1999). Controlled trial of universal neonatal screening for early identification of permanent hearing impairment: coverage, positive predictive value, effect on mothers and incremental yield. Wessex Universal Neonatal Screening Trial Group. *Acta Paediatr Suppl* 88:73–75.

Lasky RE. (1984). A developmental study on the effect of stimulus rate on the auditory evoked brain-stem response. *Electroencephalogr Clin Neurophysiol* 59:411–419.

Levi EC, Folsom RC, Dobie RA. (1993). Amplitude-modulation following response (AMFR): effects of modulation rate, carrier frequency, age and state. *Hear Res* 68:42–52.

Mason JA, Herrmann KR. (1998). Universal infant hearing screening by automated auditory brainstem response measurement. *Pediatrics* 101:221–228.

Mason S, Davis A, Wood S, Farnsworth A. (1998). Field sensitivity of targeted neonatal hearing screening using the Nottingham ABR screener. *Ear Hear* 19:91–102.

National Institute on Deafness and Other Communication Disorders. (1993). *National Institutes of Health Consensus Statement: Early Identification in Hearing Impairment in Infants and Young Children*. Bethesda, MD: National Institute on Deafness and Other Communication Disorders.

Norton SJ, Gorga MP, Widen JE, et al. (2000a). Identification of neonatal hearing impairment: a multicenter investigation. *Ear Hear* 21:348–356.

Norton SJ, Gorga MP, Widen JE, et al. (2000b). Identification of neonatal hearing impairment: evaluation of transient evoked otoacoustic emission, distortion product otoacoustic emission, and auditory brain stem response test performance. *Ear Hear* 21:508–528.

Norton SJ, Gorga MP, Widen JE, et al. (2000c). Identification of neonatal hearing impairment: transient evoked otoacoustic emissions during the perinatal period. *Ear Hear* 21:425–442.

Rickards, FW, Tan LE, Cohen LT, et al. (1994). Auditory steady-state evoked potential in newborns. *Br J Audiol* 28:327–337.

Sininger YS, Don M. (1989). Effects of click rate and electrode orientation on threshold detectability of the auditory brainstem response. *J Speech Hear Res* 32:880–886.

Sininger YS, Abdala C, Cone-Wesson B. (1997). Auditory threshold sensitivity of the human neonate as measured by the auditory brainstem response. *Hear Res* 104:27–38.

Sininger YS, Cone-Wesson B, Folsom RC, et al. (2000). Identification of neonatal hearing impairment: auditory brain stem responses in the perinatal period. *Ear Hear* 21:383–399.

Sininger YS, Cone-Wesson B. (2001). Threshold prediction with auditory brainstem response and steady-state evoked potentials: hearing assessment of infants and young children. In: Katz J, Burkhard RF, Medwetsky L, eds. *Katz Handbook of Clinical Audiology*. 5th Ed. Baltimore: Lippincott, Williams and Wilkins, 298–322.

Stapells DR, Galambos R, Costello JA, Makeig S. (1988). Inconsistency of auditory middle latency and steady-state responses in infants. *Electroencephalogr Clin Neurophysiol* 71:289–295.

Stapells DR, Gravel JS, Martin BA. (1995). Thresholds for auditory brainstem responses to tones in notched noise from infants and young children with normal hearing or sensorineural hearing loss. *Ear Hear* 16:361–371.

APPENDIX

ERA System Specifications

Stimulus generation and data acquisition are programmed on a Motorola DSP56002FC66 processor and interfaced with a personal computer running a Windows operating system at 66 MHz or higher. The EEG is recorded using scalp electrodes placed at the vertex and ipsilateral earlobe or mastoid and is led to an Intelligent Hearing Systems Opti-Amp 3000D preamplifier. EEG samples of 1486 msec in length, sampled at 44.1 kHz, are filtered at 3.0 to 5000 Hz and amplified with a gain of 70 dB. Up to 64 samples of 1486 msec each are subjected to a fast Fourier analysis and the coherence evaluated using the PC^2 algorithm (Dobie and Wilson, 1993).