Effects of Repetition Rate, Phase, and Frequency on the Auditory Brainstem Response in Neonates and Adults

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Abstract
This study evaluated the effects of stimulus repetition rate, phase, and frequency on the auditory brainstem response (ABR) in normal-hearing neonates and adults. In both neonates and adults, the results clearly showed large ABR wave V latency differences between condensation and rarefaction for low-frequency stimuli. Phase dependent latency effects are believed to be a result of the phase-sensitive low-frequency neurons. Increasing stimulus repetition rate produced greater wave V latency shift in neonates than in adults. The consequences of rate changes were independent of stimulus phase and frequency.

Key Words: Auditory brainstem response (ABR), frequency, phase, repetition rate, single-cycle sinusoids, wave V latency

The auditory brainstem response (ABR) is a transient response reflecting predominantly neural activity synchronized to the onset of the stimulus (Picton et al, 1974). Stimulus properties such as stimulus phase and repetition rate exert profound effects on ABR latencies and amplitudes. In addition, a subject-related variable such as age seems to influence the outcome of ABR recording (Stockard et al, 1979).

Considerable debate has occurred regarding the effects of stimulus phase/polarity on the ABR. The phase of an acoustic stimulus refers to the initial direction of the transducer diaphragm and the resultant direction of the sound wave produced in the outer ear canal. The initial phase of the stimulus is referred to as either condensation (C) or rarefaction (R), depending on the movement of the transducer diaphragm. Movement of the diaphragm toward the tympanic membrane produces a positive pressure wave, also known as “C” phase. A pressure wave in a negative direction, also known as “R” phase, is produced by a movement of the transducer diaphragm away from the tympanic membrane (Cann and Knott, 1979).

Electrophysiologic studies exist that demonstrate the phase-locking ability of auditory neurons (Rose et al, 1967; Johnson, 1980). This phase-locking function seems to be predominantly low-frequency dependent and is reduced or insignificant for frequencies above 2000 Hz. Furthermore, at low frequencies, the R phase of the stimulus is considered excitatory while the C phase is inhibitory (Peake and Kiang, 1962).

In normal-hearing subjects, there is a lack of consensus on whether any phase effects exist and, if they exist, on the degree and direction of phase effects on ABR latencies. Some studies report no effect of click polarity on ABR waveform latency peaks when averaged across sample subjects (Terkildsen et al, 1973; Rosenhamer et al, 1978). Other studies report shorter latencies for all ABR waveform peaks with R clicks (Ornitz and Walter, 1975). Still others report shorter latencies for all ABR waveform peaks with C clicks (Hughes et al, 1981; Pijl, 1987). Most of the investigators, however, have reported differential phase effects on the ABR...
waveform latency peaks (Coats and Martin, 1977; Stockard et al, 1978; Borg and Lofqvist, 1981; Emerson et al, 1982). Subject age and stimulus repetition rate can influence the polarity-related effects. A greater wave I latency difference for C-R was reported (Stockard et al, 1979) for neonates (0.13 msec) when compared to adults (0.07 msec). With rapid click rates (e.g., 80/sec), an even longer latency for wave I (0.35 msec) is reported for C-R difference.

Gorga and Thornton (1989) relate the lack of consensus among investigators regarding phase effects on ABR to nonphysiologic factors such as differences in sample selection, recording protocols, and/or the calibration of stimulus phase. Furthermore, other nonphysiologic factors such as intensity differences as a function of stimulus polarity, significant after-ringing, and/or relatively enhanced amplitude displacement of the transducer diaphragm during the second half-cycle of the oscillation (Stockard et al, 1979; Arlinger, 1980; Hughes et al, 1981; Weber et al, 1981) also have been suggested as possible reasons for the reported ABR latency differences.

In addition, the effects of reversing the click phase on ABR latencies are expected to be minimal due to the relative short time intervals between the C and R phase clicks (Coats and Martin, 1977; Gorga et al, 1991; Orlando and Folsom, 1995). Studies of such parametric effects could be beneficial in suggesting procedural strategies that may enhance ABR recording. Sounds having greater duration than clicks have been used in this study to ascertain the role that frequency phase plays in the generation of scalp recorded ABR and to ascertain also how repetition rate interacts with stimulus phase, frequency, and age in evoking ABR waveforms. The objective of the present research, therefore, was to determine the effects of stimulus repetition rate, phase, and frequency on the ABR wave V latency in neonates and adults.

**METHOD**

**Subjects**

Ten full-term neonates and 10 healthy, young adults served as subjects. All neonates were tested during natural sleep and met the following criteria: (1) normal, full-term gestational age between 38 to 42 weeks; (2) APGAR scores greater than or equal to 8 at 1 and 5 minutes postparturition; (3) physically and neurologically normal with external auditory canals free from obstruction based on an otoscopic examination by a licensed neonatologist; (4) negative family history of hearing loss and free from risk of hearing loss (Joint Committee on Infant Hearing, 1995); (5) informed signed consent from the parent(s) for participation as a subject; and (6) less than 72 hours postpartum age at the time of ABR testing.

All 10 adult subjects were tested either in natural sleep or in a relaxed awake state and met the following criteria: (1) physically and neurologically normal based on subject interview; (2) negative family history of hearing loss and neurologic problems; (3) external auditory canals free from obstruction based on an otoscopic examination; and (4) normal hearing sensitivity (-10–15 dB HL) at octave frequencies from 0.25 to 8.0 kHz and normal tympanometric findings (re ANSI, 1969).

**Stimuli**

Acoustic stimuli consisted of single-cycle, Blackman gated sinusoids at 0.25 and 2.0 kHz at two repetition rates: 11.1 and 55.5/sec. C and R signals of all two frequencies and repetition rates were randomly presented at 75 dB nHL. Acoustic polarity was initially determined by coupling the earphone to the sound level meter (SLM), routing the AC output from an SLM to an oscilloscope. The initial portion of the sinusoid was characterized either by a positive or a negative-going zero crossings on an oscilloscope for C and R stimuli, respectively. After checking for stimulus polarity, the stimulus repetition rate and frequency were measured from the oscillographic display. For two repetition rates (11.1 and 55.5/sec), the time interval between identical points on successive stimuli was measured at 90.09 and 18.01 msec, respectively. The frequency calibration for 0.25 and 2.0 kHz stimuli was established by measuring one cycle duration on the oscillographic sweep at 4 and 0.5 msec, respectively. Stimuli were delivered via a tube phone (Etymotic, ER-3A).

**Procedures**

Two channel ABRs were measured between gold-plated disc electrodes affixed to the vertex and the ipsilateral and contralateral earlobes. All three electrodes were referred to a ground electrode placed at the high forehead. Impedance among all four electrodes was always less than 3.0 kohms and differences among electrodes were always less than 1.0 kohm. Baseline imped-
ance values were monitored throughout testing to ensure consistency of recording. The EEG activity was amplified (100,000) and filtered (0.1 to 3.0 kHz) using a Biologic Navigator Evoked Potential System. The recording time base was 15 msec. For each test condition, responses to 2048 stimulus presentations were included in each averaged response, which was replicated once.

RESULTS

Averaged Waveforms

Figure 1 (A and B) illustrates the ABR waveforms from one neonate for 75 dB nHL at two rates to 2.0 and 0.25-kHz tone bursts. In each panel, the top two superimposed traces represent the responses obtained for R stimuli and the bottom two superimposed traces represent the responses obtained for C stimuli. Clearly, response latency depends on stimulus phase and frequency. Well-formed ABR waveforms were observed at both frequencies for C and R stimuli. However, there were notable waveform differences. Whereas the ABR morphology for the C and R stimuli is essentially similar for the high-frequency stimuli (see Fig. 1A), substantial latency differences can be observed between C and R responses for low-frequency stimuli (see Fig. 1B). Furthermore, increasing the rate from 11.1 to 55.5/sec resulted in prolongation of the ABR wave V latency (see Fig. 1A and B).

Figure 2 (A and B) illustrates the ABR waveform from one adult subject in response to 75 dB nHL (2.0-kHz tone burst) at two repetition rates. Within each panel, the top two superimposed traces represent responses to rarefaction (R) stimuli, the bottom two superimposed traces represent responses to condensation (C) stimuli. B, the same except that stimulus is 0.25-kHz tone burst. ABR wave V peaks are labeled with triangles.

Figure 2 (A and B) illustrates the ABR waveform from one adult for 75 dB nHL at two rates to 2.0- and 0.25-kHz tone bursts. In each panel, the top two superimposed traces represent the responses obtained for R stimuli and the bottom two superimposed traces represent the responses obtained for C stimuli. Again, clear ABR waveforms were observed for both frequencies for C and R stimuli. Similar to those for neonates, the morphology of the ABR waveform for the C and R stimuli is essentially the same for the high-frequency stimuli (see Fig. 2A). However, substantial latency differences can be observed between the C and R responses for low-frequency stimuli. Again, as seen in neonates, increasing the rate from 11.1 to 55.5/sec resulted in prolongation of the ABR wave V latency (see Fig. 2A and B).

Statistical Analysis

Figure 3 (A and B) illustrates average ABR wave V latencies (± 1 standard deviation) as a function of repetition rate, phase, and frequency in neonates and adults. Intersubject latency variability, as indicated by the bars, is much greater in neonates than in adults for lower than for higher frequencies. A multivariate analysis of variance (MANOVA) for repeated measures was performed. A post hoc Tukey's multiple comparison test on all of the interaction effects was calculated with the statistical significance level set at .05.
effect showed that the ABR wave V latency shift with increases in repetition rates is significantly greater (0.75–0.9 msec) in newborn neonates than in adults (0.3–0.5 msec). The rate × frequency and rate × frequency × age interaction effects on ABR wave V latency were insignificant.

Phase Effects

With few exceptions, in both neonates and adults, the R stimuli at 0.25 kHz elicited shorter absolute ABR wave V latencies. The MANOVA results revealed a significant interaction effect between phase and frequency (see Table 1). A post hoc analysis on the interaction effect showed that the phase effect on ABR wave V latency produced significantly shorter latencies (0.75–1 msec) to R stimuli at low frequency. However, the phase effect on ABR wave V latency was not significant for the high-frequency stimuli. The phase × rate, phase × age, phase × rate × frequency, phase × frequency × age, and phase × rate × frequency × age interaction effects on ABR wave V latency were insignificant.

Frequency and Age Effects

The results of the MANOVA (see Table 1) uncovered a significant interaction between frequency and age. A post hoc analysis on the interaction effect showed significantly shorter ABR wave V latencies (1.25–1.5 msec) in adults than in neonates.

DISCUSSION

The results of this investigation clearly show that large ABR wave V latency differences occur as a result of stimulus phase reversal for low-frequency stimuli in both neonates and adult subjects. For the high-frequency stimuli, subjects were likely to demonstrate shorter latencies with either R or C stimuli. Single-cycle sinusoids were used to produce place-specific excitation in the cochlear partition. The frequency content of the signal produces, as would be expected, a certain space-time pattern of basilar membrane motion, which in turn activates specific sets of neural elements (Don and Eggermont, 1978). Although few experiments have shown place-specific excitation at low levels of sound stimulation, basal spread of excitation seems to occur for relatively moderate to high levels of sound stimulation (Klein and Teas, 1978; Stapells and Picton, 1981; Gorga et al, 1988).
With few exceptions, in both neonates and adults, the phase effects on ABR wave V waveforms produced shorter latencies to R stimuli for low-frequency (0.25 kHz) stimuli. Again, in the majority of subjects, the phase effect was not apparent for the high-frequency (2.0 kHz) stimuli. Our findings in the present study are in good agreement with the previous results (Ornitz et al, 1980; Moller, 1986; Gorga et al, 1991; Fowler, 1992; Orlando and Folsom, 1995), which have shown larger latency differences as a function of phase reversal for low-frequency stimuli. These phase-related latency changes that are observed for low-frequency stimuli seem to be a result of phase-locking neurons tuned to low-frequency stimuli (Rose et al, 1974; Gorga and Thornton, 1989). It is presumed that the phase-dependent neural responses may be delayed by one-half period of the stimulus waveforms (Brama and Sohmer, 1977).

In this study, for both neonates and adults, the C-R latency difference (0.75-1.0 msec) was less than the predicted latency difference for the C and R stimuli. A possible explanation for the minimal C-R latency difference is the basal spread of excitation at high-level stimuli (75 dB nHL) being used in our study. Salt and Thornton (1984) and Beattie and Boyd (1984) reported no systematic increase in C-R latency difference with an increase in stimulus rise time. In their study, however, increasing the stimulus rise time at a high-intensity level could not have minimized either basalward spread of excitation or increases in traveling wave velocity (Hecox and Deegan, 1983; Neely, 1990). The lack of C-R latency difference for the 2.0-kHz stimulus is most likely caused by an inability to resolve the relatively short temporal onset differences with the volume-conducted far-field ABR recording (Orlando and Folsom, 1995).

Although the majority of both neonates and adults show shorter absolute ABR wave V latencies for the low-frequency R stimuli, a few neonates and adult subjects show shorter latencies for the low-frequency C stimuli. Findings of shorter latencies for C stimuli in our present study are few: 20 percent in adults and 30 percent in neonates. These findings are consistent with previous findings, which have reported shorter latencies for C stimuli in 10 percent to 30 percent of the subjects (Coats and Martin, 1977; Stockard et al, 1979; Borg and Lofqvist, 1981; Orlando and Folsom, 1995). In addition to nonphysiologic factors such as intensity, frequency, sample selection, recording protocols, and calibration of stimulus phase (Gorga and Thorton, 1989), the intersubject variability might be a result of physiologic factors such as variations in middle ear transfer function and inner ear mechanics (Dallos, 1975; Borg et al, 1982; Gerull et al, 1986; Brenkman et al, 1987).

Furthermore, the analysis of data revealed a significant interaction effect between repetition rate and age. The rate-dependent change on wave V latency was significantly greater in newborn neonates (0.75-0.9 msec) than in adults (0.3-0.5 msec). The latency changes with repetition rate were independent of the stimulus phase and frequency. These findings are in good agreement with the previous results (Stockard et al, 1979; Despland and Galambos, 1980; Lasky, 1984), which have shown that greater latency shifts in newborn neonates occur as the repetition rate of the stimulus is increased. This age-related difference in latency-rate functions has obvious clinical implications for interpreting developmental change in the ABR waveforms. The younger the subject, the longer the expected ABR latencies to the same auditory stimulus (Schulman-Galambos and Galambos, 1975; Starr et al, 1977). Prolonged neural transmission time in younger subjects, due to incomplete myelination and decreased synaptic efficiency, is considered to be the neurophysiologic basis for these rate-age-latency interactions (Hecox, 1975; Pratt and Sohmer, 1976; Lasky, 1984).

The frequency effects on ABR waveforms in both the neonates and adults have shown shorter wave V latencies to a 2.0-kHz tone burst than to a 0.25-kHz tone burst. In addition, the analysis of data showed a significant interaction between frequency and age. As expected, independent of stimulus frequency, the ABR wave V latencies were shorter (1.25-1.5 msec) in adults than in neonates. The frequency content of the signal produces, as would be expected, a certain space-time pattern of basilar membrane motion, which in turn activates specific sets of neural elements (Don and Eggermont, 1978). The results are also in consonance with previous results (Stapells and Picton, 1981; Gorga et al, 1988, 1991; Parthasarathy and Moushegian, 1993).

CONCLUSIONS

First, in both neonates and adults, large ABR wave V latency differences occur as a result of stimulus phase reversal for low-frequency (0.25 kHz) stimuli. With few exceptions, R stimuli elicited shorter ABR wave V latencies. However, minimal ABR wave V latency differences occurred as a result of stimulus phase reversal...
for high-frequency (2.0 kHz) stimuli. Findings from our study are supported by data from subjects with high-frequency sensorineural hearing loss who demonstrate significant C-R differences for clicks (Coats and Martin, 1977; Pijl, 1987). It is hypothesized that subjects with high-frequency sensorineural hearing loss receive greater contribution to the ABR from the phase-sensitive low-frequency neurons (Gorga et al, 1991). Considering the large C-R differences expected for low-frequency stimuli in normal-hearing subjects or in subjects with high-frequency sensorineural hearing loss (Borg and Lofqvist, 1981; Borg et al, 1982; Pijl, 1987), summing or alternating the stimulus polarity in clinical ABR application is not recommended. Based on our results, the need for independent norms for different stimulus polarity for neonates and adults is strongly recommended. In both neonates and adults, the use of single-polarity stimuli or separate averaging for each polarity is recommended.

Second, compared to adults, greater ABR wave V latency shift occurs in neonates as a result of increase in repetition rate. The latency changes with repetition rate are both phase and frequency independent. Finally, compared to adults, neonatal ABR wave V latencies at 0.25 and 2.0 kHz are longer with greater variability to a 0.25-kHz tone burst. The present research study should be replicated in both normal and sensorineural hearing loss subjects using different sound intensities, repetition rates, and age groups. Aspects pertaining to ABR morphologic differences as a function of changes in stimulus repetition rate, phase, and frequency in different age groups warrant further investigation.

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REFERENCES


