J Am Acad Audiol 5: 110–118 (1994)

Paired Tone-Burst Study of Auditory Brainstem Response Adaptation in Guinea Pigs: Implications for Development of Multiple-Stimulus Methods

Curtin R. Mitchell*
Stephen A. Fausti†
Richard H. Frey‡

Abstract

In clinical testing using auditory evoked potentials, the practical length of a test session is limited. Thus, the amount of information that can be obtained during a routine test session is limited in electrocochleography and auditory brainstem testing. Attempts to obtain more information within a test session by increasing the stimulus repetition rate yields adapted responses. Multiple-stimulus methods that present sequences of stimuli at different frequencies and intensities can increase the efficiency of data collection while avoiding adaptation. This study was designed to investigate rapid adaptation of these early responses to enable more efficient data acquisition using multiple stimuli. Five experiments in guinea pigs using single and paired tone-burst stimuli are described. The intrapair time, frequency, and intensity were varied to determine when adaptation, measured by a latency delay, occurred. The effects of adaptation on waves I through IV are described. The differences in stimulus parameters that avoid adaptation can be determined from these experiments.

Key Words: Adaptation, auditory brainstem response (ABR), cochleography, frequency specificity, multiple stimuli

A major limitation of the clinical use of auditory evoked potentials is the practical length of the test session (Mitchell and Clemis, 1977; Jerger, Oliver, and Stach, 1985; Burkard, Shi, and Hecox, 1990; Hamill, Husslung, and Sammeth, 1991). In humans, responses to 1000 or more stimuli are usually necessary to obtain one response average; this requires 1.5 to 2 minutes. When both ears are tested at several intensities and frequencies, and duplicate averages to each stimulus are obtained, the length of a test session can be more than 90 minutes. This may exceed a person's ability to remain quiet and relaxed without sedation. Thus, the number of averages that can be obtained is limited, and the usefulness of routine evoked-potential testing is diminished.

If the stimulus repetition rate is increased in an attempt to obtain more averages within a test session, the response is degraded, due to adaptation (Spoor and Eggermont, 1971; Coats and Dickey, 1972; Thornton and Coleman, 1975; Mouney, Cullen, Gondra, and Berlin, 1976; Don, Allen, and Starr, 1977; Burkard et al, 1990). At stimulus rates faster than 10 per second, cochlear and brainstem responses exhibit adaptation, which is characterized by decreased amplitude and increased latency. Adaptation has been described as occurring in two phases, with rapid changes during the first few stimuli and slow changes thereafter (Sorensen, 1959; Spoor, 1965; Spoor and Eggermont, 1971). Recordings from single auditory neurons have shown two exponentially decaying time constants of adaptation that are similar to the rapid and slow

*Oregon Hearing Research Center and Department of Otolaryngology, Oregon Health Sciences University (OHSU); † Department of Veterans Affairs Medical Center and Department of Otolaryngology, OHSU, Portland, Oregon; and ‡Auditory Research Laboratory, Department of Veterans Affairs Medical Center, Portland, Oregon.

Reprint requests: Curtin R. Mitchell, Oregon Hearing Research Center, 3515 SW US Veterans Hospital Road, Portland, OR 97201

adaptation found in the compound action potential (Smith, Brachman, and Goodman, 1983; Westerman and Smith, 1984; Yates, Robertson, and Johnstone, 1985). The rapid adaptation of evoked potentials has been studied using both trains of stimuli (Spoor, 1965; Thornton and Coleman, 1975), as well as paired stimuli (Rosenzweig and Rosenblith, 1953; Kevanishvili and Lagidze, 1979; Hess and Ludin, 1987).

To overcome the limitations that adaptation imposes on evoked-potential testing, there has been renewed interest in methods for minimizing or avoiding adaptation. The use of multiple-intensity stimuli, used originally by Spoor (1974), has recently been shown to enable more efficient determination of click thresholds (Hamill, Yanez, Collier and Lionbarger, 1992). Another method using different frequency tone bursts in combination with high-pass masking has also demonstrated time savings (Hoke, Panter, Ansa, Lutkanhoner, and Herrmann, 1991). Mitchell (1991) and Fausti et al (1992, 1994) have demonstrated a method of presenting multiple stimuli of different frequencies and intensities to increase the efficiency of data collection while minimizing adaptation. The advantages of these multiple-stimulus techniques include both the ability to obtain more information within a test session and a reduction in test session length. These increases in efficiency can also enable more complex and sophisticated stimulus paradigms to be used, which can become the basis for new tests of auditory function.

The purpose of this study was to investigate the rapid adaptation of cochlear and brainstem responses in order to develop strategies that avoid adaptation. Time, intensity, and frequency were varied, and the amount of adaptation was determined by changes in latency.

METHOD

Recordings were obtained from nine guinea pigs (Topeka strain), weighing from 230 to 760 gm. The animals were anesthetized with allobarbital and urethane (60 and 240 mg/kg, respectively), injected intraperitoneally, with supplemental doses given as necessary. Differential recording electrodes were placed on the vertex (noninverting), below the ipsilateral ear (inverting), and on the hind leg (ground). A differential amplifier (Grass P15C) provided a filtered signal (300 to 3000 Hz) that was averaged on a computer (Macintosh II, using Lab VIEW® software).

Stimuli were tone bursts at 21 frequencies, from 1000 Hz to 32,000 Hz, in approximately ¼-octave steps. These tone bursts had a duration of 2 msec, with exponential rise–fall times of 1 msec and no plateau, and were produced by gating a continuous sine wave from a synthesizer (Hewlett-Packard 8904A) with an electronic switch (Coulbourn S8404 audio gate). To prevent AC cochlear potential contamination of wave I, the tone-burst stimuli were gated randomly with respect to phase. These electrical signals were transduced by a ½-inch Bruel & Kjaer condenser microphone, with acoustic tone bursts delivered to the ear through a closed system via a 3-cm sound cannula (Vernon, Katz, and Meikle, 1976). The sound cannula and a calibrated probe tube were held in the ear canal with a speculum throughout the testing session. In each ear tested, the system was calibrated by measuring the sound pressure level within 2 to 4 mm of the tympanic membrane with a calibrated probe tube. Averaged responses to 250 stimuli were obtained for each stimulus condition and then were immediately repeated. Tone bursts were presented singly and then in pairs. The intrapair interval, or time between the two stimuli of a pair, varied from 3 to 30 msec. The interpair or interstimulus interval was 100 to 110 msec maintaining a repetition rate of ≈ 10/sec.

Brainstem responses were recorded from surface electrodes using the method previously described by Mitchell and Fowler (1980). Positive response peaks were scored using the convention described by Mitchell and Fowler (1980) and Hunter and Willott (1987), with response latencies measured from the onset of each tone burst. At the shortest intrapair interval, 3 msec, responses from the first and second stimuli overlapped in time, producing a complex waveform consisting of late responses from the first stimulus and early responses from the second stimulus. An off-line subtraction technique was used to remove responses to the first stimulus from the complex waveform and allow scoring of responses to the second stimulus (Kevanishvili and Lagidze, 1979; Fowler and Swanson, 1988). Responses were scored in a single-blind manner (i.e., without reference to the stimulus conditions).

Rapid adaptation occurs when stimuli are presented with a short time interval between them. In the current study, single and paired stimuli were presented and the early responses, cochlear and brainstem waves I, II, III, and IV, were recorded. The adaptation, produced by a

stimulus, could be measured in two different ways: (1) the latency difference between the response obtained when a stimulus is presented singly and when it is presented as the second stimulus of a pair; or (2) the latency difference between the response to the first and second stimuli of a pair, (when both stimuli are the same). These two methods yielded the same results, because the response to a single stimulus and the first stimulus of a pair had the same latency. With the repetition rates used in the current study, the response to the first stimulus of a pair was not affected by the second stimulus (i.e. no backward masking, wrap-around, or other effects were detected). This was verified by recording responses to single and paired stimuli throughout this study. The effect on latency was of interest, because this is the primary measure used in clinical brainstem response testing.

Early responses consisting of cochlear and brainstem waves I through IV, which occur within the 10-msec period following a stimulus onset, were recorded to single and paired tone bursts. In the first experiment, both stimuli of each pair were at the same frequency and intensity while the time between them was varied. In the second and third experiments, the intensity of both stimuli was varied over a range of intensities while the time between them was maintained at either 3 or 10 msec. In the fourth and fifth experiments, the frequency of the second stimulus was changed while the time separation was maintained at 3 msec.

RESULTS

Experiment I. Paired Tones: Time Separation Varied

The purpose of this experiment was to determine the time between two stimuli where rapid adaptation occurs. The time between the first and second stimulus of the pair (intrapair time) was varied from 3 to 30 msec. While the intrapair time varied, both stimuli were maintained at the same frequency and intensity. The time between successive pairs (the interpair time) was held constant at 100 msec. A diagram of the responses to paired stimuli is shown in Figure 1.

Figure 2, *A* and *B*, shows data from stimulus pairs at 2 and 16 kHz, respectively. When the intrapair time was less than about 10 msec, the latency of the second response was delayed, due to adaptation produced by the first stimulus. Conversely, when the intrapair time was greater than 10 msec, the latencies of the first and second responses were not significantly different. Similar results were observed for tone-burst pairs at 4 kHz and 8 kHz.

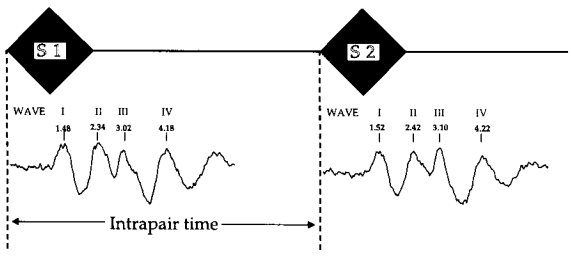

Figure 1 Diagram of the paired tone-burst (S1 and S2) stimuli and brainstem responses from each stimulus.

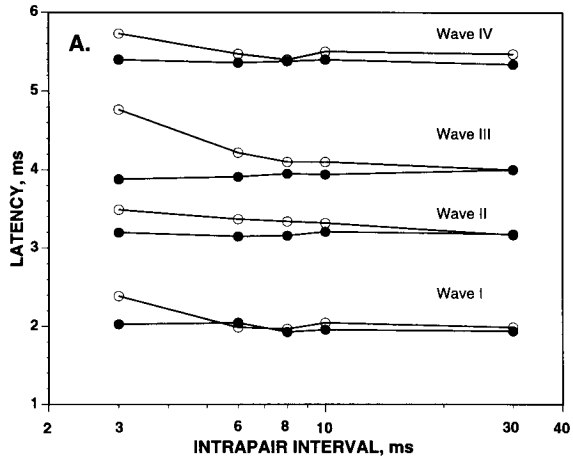

Figure 2 Latencies of cochlear (wave I) and brainstem (waves II–IV) responses to paired tone bursts when intrapair intervals were varied from 3 to 30 msec. Responses to first (line with closed dots) and second (line with open dots) tone bursts are shown. The time between stimulus pairs (interpair interval) was constant at 100 msec. *A*, Response latencies to paired 2-kHz tone bursts at 72 dB SPL. *B*, Response latencies to paired 16-kHz tone bursts at 70 dB SPL.

The latency delay of wave III appears dissimilar between 2 and 16 kHz in Figure 2, *A* and *B*. These results reflect the general observation that both waves II and III were more variable than I or IV. This variability was observed at different frequencies and intensities and in several different animals.

Experiment II. Latency-Intensity Functions: Ten-Msec Intrapair Interval

As shown in experiment I, the effects of adaptation are minimal when the time separation is 10 msec or greater. These data are limited to a few intensities, and it is important to know if minimal adaptation would be maintained throughout an intensity range. Therefore, in the second experiment, the intrapair interval was held constant at 10 msec while intensity was varied. The frequency and intensity of paired stimuli were always the same.

The latencies of the responses to the first and second stimuli of the pair over a wide range of intensities are shown in Figure 3. Latencies of waves I, II, and III were the same for both stimuli. However, wave IV, evoked by the second stimulus in the pair, was slightly delayed at all intensities except the lowest.

Thresholds shown in Figure 3, *A* and *B*, were determined as the lowest sound pressure level (SPL) where a response was detected. Threshold responses of each stimulus in the pair were the same at each frequency tested (2, 4, 8, and 16 kHz). Thus, it appeared that both the thresholds and latency-intensity functions were unaffected by the slight adaptation when intrapair intervals were 10 msec.

As previously mentioned, when intrapair times were greater than 10 msec, the effect on response latency was negligible. This was a consistent finding when both stimuli of a pair were at the same intensity. However, an effect was observed upon the amplitude of the second response at the 10-msec intrapair interval. Due to the greater variability of the amplitude, this effect was difficult to quantify. These data will be further analyzed and reported separately.

Experiment III. Latency-Intensity Functions: Three-Msec Intrapair Interval

The purpose of the third experiment was to explore adaptation as a function of intensity. Experiment I demonstrated that when the intrapair time is 3 msec, the response to the second stimulus is adapted. In experiment III,

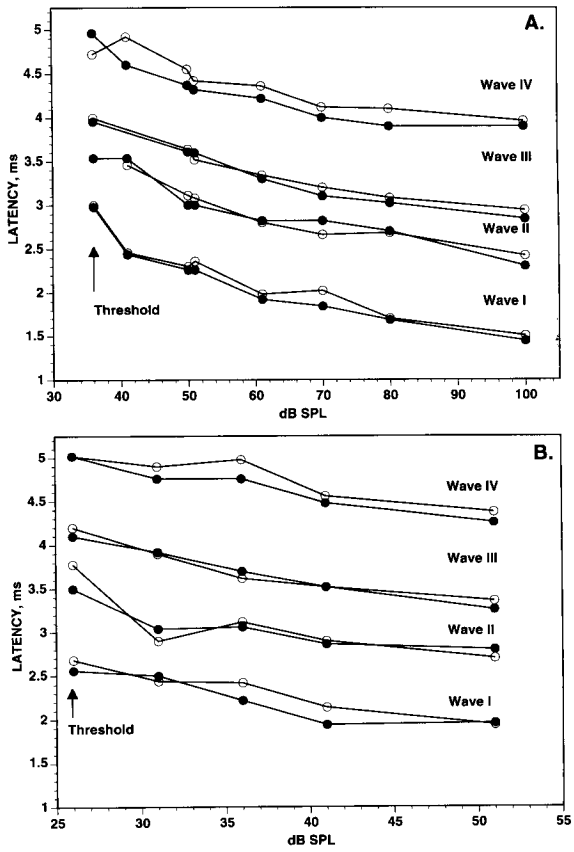

Figure 3 Response latency-intensity functions from first (line with closed dots) and second (line with open dots) tone bursts when the intrapair interval was held constant at 10 msec. *A*, Tone pairs at 4 kHz. *B*, Tone pairs at 8 kHz.

the intrapair time was held constant at 3 msec while the intensity of the stimulus pair was varied.

Responses to paired tone bursts at 4 and 16 kHz are shown in Figure 4, *A* and *B*, respectively. The delayed latencies of second responses are apparent at most intensities (open circles). Three observations regarding these delays are of interest. First, the delays are usually less for wave I than for later waves. Second, the latency delays are usually less near threshold than at higher intensities. Thresholds of the first and second stimuli were equal or within 5 dB, suggesting that adaptation may be less near threshold. Third, the latencies of waves II and III showed greater variability than the other waves. These observations were consistent at all frequencies (2, 4, 8, and 16 kHz).

Wave I thresholds were occasionally 5 to 10 dB higher than those for waves II and III. Wave IV, in a few cases, exhibited thresholds that were as much as 20 dB higher than the earlier waves. These threshold differences between

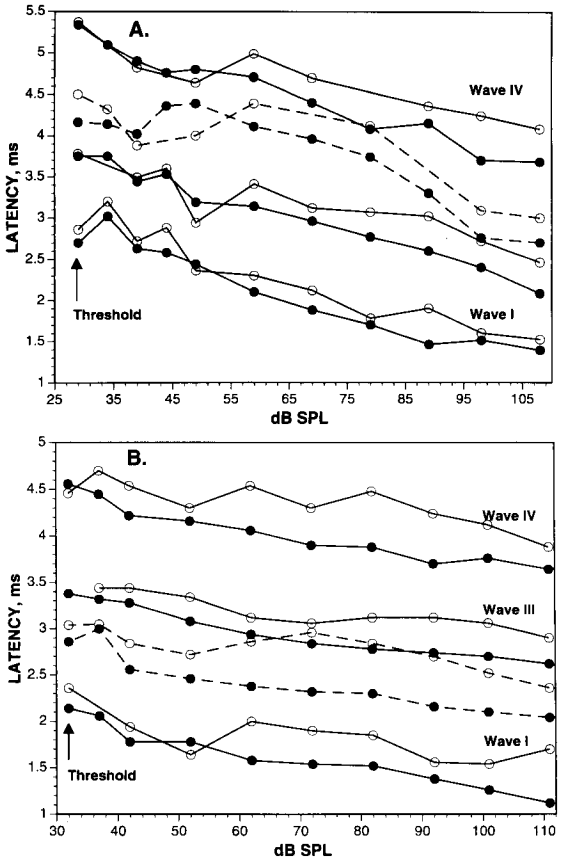

Figure 4 Latency-intensity functions from paired tone bursts when the interstimulus interval was held constant at 3 msec. *A*, Responses from the first (line with closed dots) and second (line with open dots) 4-kHz tone bursts. *B*, Responses from tone bursts at 16 kHz.

the different waves seemed unaffected by the intrapair interval. For example, when wave II was recorded at a lower intensity than wave I, there was no difference between the thresholds of the two stimuli. Thus, although threshold differences were found between the different waves, this did not change the general conclusion that adaptation has little effect on the threshold of a particular stimulus.

Experiment IV. Adaptation at Different Frequencies

The purpose of the fourth experiment was to determine the extent of rapid adaptation in the frequency domain. A method of avoiding adaptation by presenting a sequence of stimuli at different frequencies has been previously reported (Mitchell, 1991). In this method, it was assumed that if the frequency of a successive stimulus was different enough, then different populations of neurons would be stimulated, and adaptation would be minimized or avoided. In experiments I–III above, both stimuli of each pair were presented at the same frequency and intensity. In experiment IV, the frequency of the first tone burst was held constant while the frequency of the second burst was varied. The intrapair time was held constant at 3 msec, and both bursts were presented at the same SPL (attenuation at each frequency was slightly different in accordance with the calibration curve).

The amount of adaptation produced by the first tone burst was measured by its effect on the response to the second tone burst. The adaptation produced by the first stimulus at different frequencies is shown in Figure 5. In Figure 5, *A*, the frequency of the first stimulus was held constant at 4 kHz, while the frequency of the second stimulus was varied from 2 to 8 kHz. The latency of the response to the second stimulus is shown when: (1) the second stimulus was presented singly; and (2) the second stimulus was preceded by a 4-kHz stimulus. The difference in latency between the two conditions reflects the amount of adaptation produced by the first stimulus. Figure 5, *B*, shows data obtained when the first stimulus was an 8-kHz tone burst and the second stimulus was varied from 4 to 16 kHz.

Figure 5, *A* and *B*, illustrates that latency delay or adaptation is greatest when paired stimuli are the same frequency. This effect was most prominent with wave IV, an unexpected finding in view of previous studies showing similar tuning curves for the different waves (Mitchell and Fowler, 1980; Brown and Abbas, 1987). Adaptation was generally less if the frequency of the second stimulus was either above or below that of the first stimulus.

Experiment V. Adaptation at Different Frequencies, Intensity Effects

The purpose of the fifth experiment was to determine the effects of intensity on adaptation at different frequencies. The intensity of the stimulus pair was raised, and the adaptation produced by the first stimulus was measured by its effect on the response latency to the second stimulus, as in the previous experiment. The first stimulus of the pair was held constant at 16 kHz while the frequency of the second stimulus was varied from 8 to 32 kHz. The intrapair interval was maintained at 3 msec, and both stimuli were presented at the same SPL. Figure 6 shows the latencies of responses to the second stimulus when it was presented singly

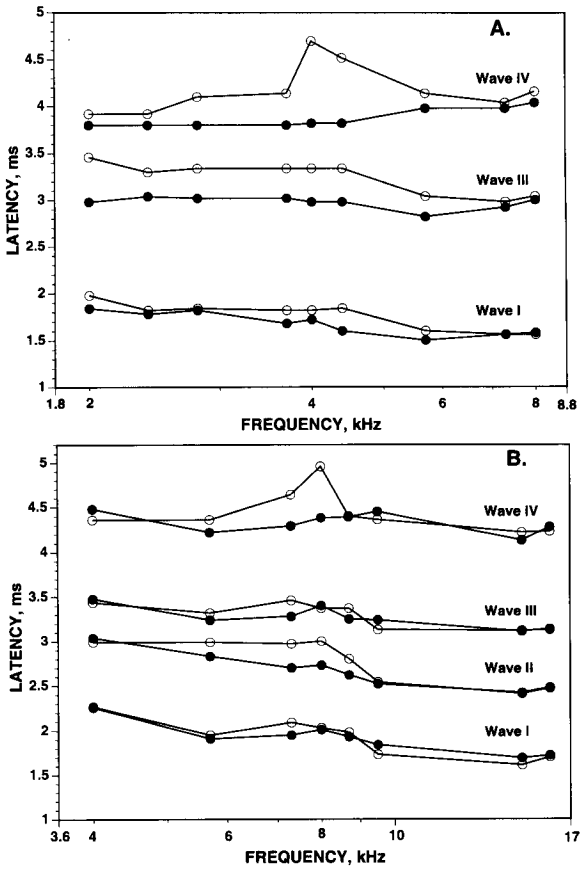

Figure 5 The effects of adaptation when the first stimulus was held at a constant frequency and the frequency of the second stimulus was varied. The intrapair time was constant at 3 msec; both stimuli were presented at the same intensity but may be at different frequencies. The adaptation produced by the first stimulus is shown by the difference in latency between the response to the second stimulus presented alone (line with closed dots) and when it follows the first stimulus (line with open dots). *A*, Adaptation produced by a 4-kHz tone burst at 80 dB SPL. Wave II is not shown, due to overlap in the plot. *B*, Adaptation produced by an 8-kHz tone burst at 50 dB SPL.

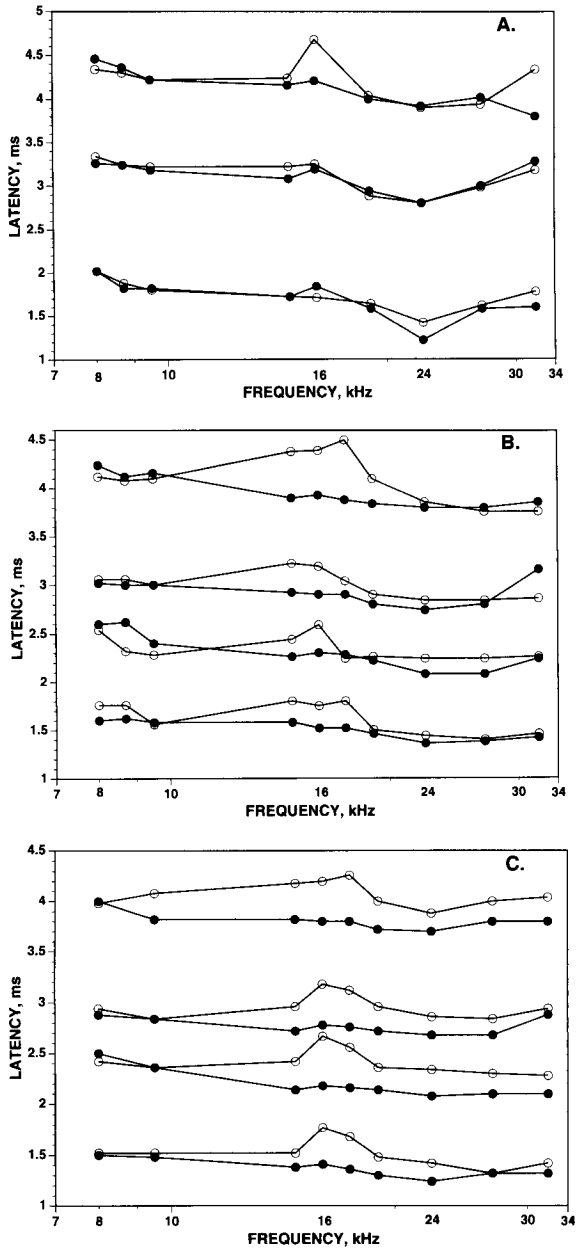

Figure 6 The effect of adaptation when the first stimulus of the pair, a 16-kHz tone burst, was followed by tone bursts of different frequencies (8–32 kHz). The adaptation produced by the first stimulus is shown by the difference in latency between the response to the second stimulus presented alone (line with closed dots) and when it followed the first stimulus (line with open dots). The intrapair interval was 3 msec. Intensities of the tone pairs were: *A*, 50 dB SPL; *B*, 70 dB SPL; *C*, 90 dB SPL.

and when it was preceded by a 16-kHz tone burst. These latency differences are a measure of adaptation produced by the 16-kHz tone burst.

Early waves were delayed less at the lower intensities (Fig. 6, *A* and *B*), but the latency delays among all waves became similar when the intensity of the pair reached 90 dB SPL (Fig. 6, *C*). The latency delay of wave IV was greater than that of wave I at lower intensities. Further, the latency delay of waves I through III increased with intensity. The absolute delay in wave IV, however, did not change systematically with intensity. This resulted in similar latency delays for waves I through IV at the highest intensity.

In each animal, latency delays seen among the different waves were generally the same as shown in Figures 5 and 6 across the frequency and intensity range studied.

DISCUSSION

More efficient methods of cochlear action potential and brainstem response test-

ing will allow more information to be obtained during routine testing sessions. Evoked potential testing, as used clinically, has been limited by the practical length of test sessions, which, in turn, restricts the number of stimuli that can be presented. A means of presenting more stimuli within a session could expand the use of frequency-specific stimuli, as has been the routine in animal testing (Mitchell, Brummett, and Vernon, 1977; Brown, Meikle, and Lee, 1985; Brown and Abbas, 1987). More efficient testing would allow more complete testing of auditory function and aid in the differential diagnosis of hearing impairments. This could also provide opportunities for new tests of auditory function to be developed.

In the current study, adaptation was first measured by progressively shortening the time between paired stimuli (the intrapair interval). Adaptation, as measured by a latency delay, was found in all waves, I through IV, at intrapair intervals less than 10 msec at all frequencies tested (2 to 16 kHz). These findings were used in a parallel study where multiple high-frequency stimuli were used to elicit the auditory brainstem response in humans (Fausti et al, 1994). The results are also in general agreement with previous studies of paired click stimuli in humans (Robinson and Rudge, 1977; Kevanishvili and Lagidze, 1979; Hess and Ludin, 1987), except for one point of disagreement. Two studies (Robinson and Rudge, 1977; Hess and Ludin, 1987) using intraclick intervals of 5 msec or less reported no changes in the latency of wave I elicited by the second click of the pair. One possible explanation for this discrepancy is that the AC cochlear potential (or cochlear microphonic) may have obscured wave I adaptation. The AC cochlear potential, which immediately precedes wave I, does not show adaptation (McGill, 1952; Rosenzweig and Rosenblith, 1953; Peake, Goldstein, and Kiang, 1962; Spoor, 1965). Since wave I is small when recorded from the vertex of the human, and monopolar clicks can produce a cochlear potential with a waveform similar to that of wave I, the cochlear and neural potentials may have been confused. In the current study, to minimize the possibility of such confusion, tone-burst stimuli were presented with a random onset phase in order to cancel the cochlear potential.

The current findings suggest that the threshold level of waves I through IV were unaffected by adaptation, even at intrapair intervals as small as 3 msec. These findings are in agreement with reports in humans where multiple-intensity stimuli (Hamill et al, 1991, 1992) or rapid repetition rates (Sinninger and Don, 1989) have been used in threshold determination. Together these findings indicate that multiple-stimulus methods may be useful for threshold determination even in situations where some adaptation may be present.

Some studies using high-stimulus repetition rates have reported that adaptation varies with intensity (Eggermont and Odenthal, 1974; Thornton and Coleman, 1975; Stockard and Stockard, 1983) while others have not (Don et al, 1977; Weber and Fujikawa, 1977). It is possible that these conflicting findings are due to individual differences and the small number of subjects tested. It is difficult to compare these studies with the current study, because the effects of paired stimuli are quite different from repetition-rate studies. When repetition rates are studied, both rapid and slow adaptation, as well as forward masking effects, are present. When paired tone-burst stimuli of short duration are used, as in the current study, the effects of slow adaptation and forward masking are minimized and only rapid adaptation may be present (Spoor and Eggermont, 1971). This important difference prevents a comparison of the current study, which used paired stimuli, with repetition-rate studies. Other studies using paired stimuli did not determine the effect of intensity. The current study suggests that adaptation is less near threshold and somewhat more at higher intensities.

Increased variability of adapted responses, especially in waves II and III, as compared with unadapted responses, was observed in the current study. Similar increased variability of adapted responses has also been reported in previous studies (Kevanishvili and Lagidze, 1979; Hess and Ludin, 1987). This variability may be related to the multiple sources of waves II and III (Jewett, 1970; Mitchell and Fowler, 1976).

The findings of experiment V suggest that rapid adaptation is not directly related to synchrony of nerve firing. For example, at low intensities, the frequency effect may be present in later waves (e.g., wave IV) without being apparent in the early waves (I and II). Neural synchrony is very important for obtaining the compound action potential (wave I) and relatively less important for later waves (Goldstein and Kiang, 1958). Thus, if adaptation reduced synchrony, one would expect a major effect on wave I with lesser effects on the later waves, the reverse of what was observed. The current find-

ings also suggest that rapid adaptation is a cumulative, trans-synaptic process, perhaps general to the auditory pathway and not specific to the cochlea or auditory nerve.

The data from experiment V also suggest a potential problem with latency measures of adaptation. Absolute delay due to adaptation may be greater at low intensities when only a few nerve fibers are activated than when a larger number of fibers are activated at high intensities. Thus, the sensitivity of latency as a measure of adaptation may vary with intensity. It remains for future studies to determine to what extent latency change is a useful and valid measure of adaptation.

The data in Figures 3 and 4 suggest that adaptation does not change greatly with intensity, while other results (Fig. 6) show adaptation to vary with intensity. In the first case, the stimulus pair consisted of two stimuli that were always the same intensity and frequency. Thus, both stimuli of this pair would be expected to activate the same nerve fibers at each intensity level tested. In the latter case, where adaptation varies with intensity, the two stimuli were at the same intensity but at different frequencies. We would, therefore, expect the nerve fibers activated by the first and second stimuli to be different. The first stimulus activates and adapts a given population of fibers. The second stimulus, at a slightly different frequency, would be expected to activate some of the same fibers as well as other fibers. The relative mixture of nerve fibers activated by the two stimuli would change with intensity, because the area of activation along the basilar membrane changes with intensity. Thus, the number of adapted fibers would change with intensity, yielding a change in adaptation with intensity (Fig. 6). In order to avoid this adaptation at high intensities, the frequency differences between successive stimuli need to be greater than when stimuli are at low levels. From the data in the current study, the frequency difference necessary to avoid adaptation at high intensities approaches 1 octave for the 3-msec intrapair interval.

The current study has extended information obtained from previous studies of adaptation (Rosenzweig and Rosenblith, 1953; Sorensen, 1959; Peake et al, 1962; Spoor, 1965; Teas, 1966; Eggermont and Odenthal, 1974; Robinson and Rudge, 1977; Kevanishvili and Lagidze, 1979; Hess and Ludin, 1987; Abbas and Brown, 1991). Multiple-stimulus methods for evoked-potential testing could increase the efficiency of data collection by a factor of 4 to 10 (Hoke et al, 1991; Mitchell, 1991; Fausti et al, 1992; Hamill et al, 1992), and perhaps more. Understanding the temporal, frequency, and intensity boundaries of adaptation is a prerequisite to the development of efficient and useful multiple-stimulus techniques. Further investigations comparing single and multiple stimuli, such as described in the companion study (Fausti et al, 1994), are clearly needed.

Acknowledgment. Funding for this research was provided by Grant #G10860006 from the U.S. Department of Education, Rehabilitation Services Administration.

REFERENCES

Abbas PJ, Brown CJ. (1991). Electrically evoked auditory brainstem response: refractory properties and strength-duration functions. *Hear Res* 51:139–148.

Brown CJ, Abbas PJ. (1987). A comparison of AP and ABR tuning curves in the guinea pig. *Hear Res* 25:193–204.

Brown JJ, Meikle MB, Lee CA. (1985). Reduction of acoustically induced auditory impairment by inhalation of carbogen gas. I. Temporary pure-tone induced depression of cochlear action potentials. *Acta Otolaryngol (Stockh)* 100:218–228.

Burkard R, Shi Y, Hecox KE. (1990). Brain-stem auditory-evoked responses elicited by maximum length sequences: effect of simultaneous masking noise. *J Acoust Soc Am* 87(4):1665–1666.

Coats AC, Dickey JR. (1972). Postmasking recovery of human click action potentials and click loudness. *J Acoust Soc Am* 52(No. 6, part 2):1607–1612.

Don M, Allen AR, Starr A. (1977). Effect of click rate on the latency of auditory brain stem responses in humans. *Ann Otol* 86:186–195.

Eggermont JJ, Odenthal DW. (1974). Electrophysiological investigation of the human cochlea. *Audiology* 13:1–22.

Fausti SA, Mitchell CR, Frey RH, Henry JA, O'Connor JL. (1994). Multiple-stimulus method for rapid collection of auditory brainstem responses using high-frequency (≥ 8 kHz) tone bursts. *J Am Acad Audiol* 5:119–126.

Fausti SA, Mitchell CR, Frey RH, Schaffer HI. (1992). *A Multiple Stimulus ABR Technique.* Presented at the American Speech and Hearing Association Meeting, San Antonio, TX, November, 1992.

Fowler CG, Swanson MR. (1988). Validation of addition and subtraction of ABR waveforms. *Scand Audiol* 17: 195–199.

Goldstein MH Jr., Kiang NYS. (1958). Synchrony of neural activity in electric responses evoked by transient acoustic stimuli. *J Acoust Soc Am* 30(2):107–114.

Hamill TA, Hussung RA, Sammeth CA. (1991). Rapid threshold estimation using the "chained-stimuli" technique for auditory brainstem response measurement. *Ear Hear* 12(4):229–234.

Hamill TA, Yanez I, Collier CE, Lionbarger JA. (1992). Threshold estimation using the "chained stimuli" audi-

tory brain stem response technique. *Ear Hear* 13(3):165–172.

Hess CW, Ludin HP. (1987). Auditory brain-stem potentials studied with paired stimuli in normals. *J Neurol* 234: 298–302.

Hoke M, Panter C, Ansa L, Lutkanhoner B, Herrmann E. (1991). A time saving BERA technique for frequency specific assessment of the auditory threshold through tone pulse series stimulation (TOPSTIM) with simultaneous gliding high-pass noise masking (GHINOMA). *Acta Otolaryngol Suppl (Stockh)* 482:45–46.

Hunter KP, Willott JF. (1987). Aging and the auditory brainstem response in mice with severe or minimal presbycusis. *Hear Res* 30:207–218.

Jerger J, Oliver T, Stach B. (1985). Auditory brainstem response testing strategies. In: Jacobson JT, ed. *The Auditory Brainstem Response.* San Diego: College-Hill Press, 371–386.

Jewett DL. (1970). Volume-conducted potentials in response to auditory stimuli as detected by averaging in the cat. *Electroenceph Clin Neurophysiol* 28:609–618.

Kevanishvili Z, Lagidze Z. (1979). Recovery function of the human brain stem auditory-evoked potential. *Audiology* 18:472–484.

McGill WC. (1952). *A Statistical Description of Neural Responses to Clicks Recorded at the Round Window of the Cat.* Harvard University, unpublished doctoral thesis.

Mitchell CR. (1991). *Improved Method for the Rapid Recording of Electrocochleographic and Auditory Brainstem Responses.* Presented at the 14th Association for Research Otolaryngology Midwinter Meeting, St. Petersburg, FL.

Mitchell CR, Brummett RE, Vernon JA. (1977). Frequency effects of temporary N_1 depression following acoustic overload. *Arch Otolaryngol* 103:117–123.

Mitchell CR, Clemis JD. (1977). Audiograms derived from the brain stem response. *Laryngoscope* 87:2016–2022.

Mitchell CR, Fowler CG. (1976). Comparison of gross neural wave forms recorded from various electrode sites in the guinea pig. *J Acoust Soc Am* 60:516.

Mitchell CR, Fowler CG. (1980). Tuning curves of cochlear and brain stem responses in the guinea pig. *J Acoust Soc Am* 68:896–900.

Mouney DF, Cullen JK Jr., Gondra MI, Berlin CI. (1976). Tone burst electrocochleography in humans. *Trans Am Acad Ophthal Otolaryngol* 82(3):348–355.

Peake WT, Goldstein MH, Kiang NYS. (1962). Responses of the auditory nerve to repetitive acoustic stimuli. *J Acoust Soc Am* 34(5):562–570.

Robinson K, Rudge P. (1977). The early components of the auditory evoked potential in multiple sclerosis. *Prog Clin Neurophysiol* 2:58–67.

Rosenzweig MR, Rosenblith WA. (1953). Responses to auditory stimuli at the cochlea and at the auditory cortex. *Psychol Monogr Suppl* 67(13):1–26.

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

Smith RL, Brachman ML, Goodman DA. (1983). Adaptation in the auditory periphery. *NY Acad Sci* 405:79–93.

Sorensen H. (1959). Auditory adaptation in nerve action potentials recorded from the cochlea in guinea pigs. *Acta Otolaryngol (Stockh)* 50:438–450.

Spoor A. (1965). Adaptation of action potentials in the cochlea. *Audiology* 4:154–159.

Spoor A. (1974). Apparatus for electrocochleography. *Acta Otolaryngol Suppl (Stockh)* 316:25–36.

Spoor A, Eggermont JJ. (1971). Action potentials in the cochlea: masking, adaptation and recruitment. *Audiology* 10:340–352.

Stockard JE, Stockard JJ. (1983). Recording and analyzing. In: Moore EJ, ed. *Bases of Auditory Brain-Stem Evoked Responses.* New York: Grune & Stratton, 255–270.

Teas DC. (1966). Interactions between synchronous neural responses to paired acoustical signals. *J Acoust Soc Am* 39(6):1077–1085.

Thornton ARD, Coleman MJ. (1975). The adaptation of cochlear and brainstem auditory evoked potentials in humans. *Electroenceph Clin Neurophysiol* 39:399–406.

Vernon JA, Katz B, Meikle MB. (1976). Sound measurement and calibration of instruments. In: Vernon JA, Smith CA, eds. *Handbook of Auditory Research Methods.* Springfield, IL: Charles C. Thomas, 306–356.

Weber BA, Fujikawa SM. (1977). Brainstem evoked response (BER) audiometry at various stimulus presentation rates. *J Acoust Soc Am* 3(2):59–62.

Westerman LA, Smith RL. (1984). Rapid and short-term adaptation in auditory nerve responses. *Hear Res* 15: 249–260.

Yates GK, Robertson D, Johnstone BM. (1985). Very rapid adaptation in the guinea pig auditory nerve. *Hear Res* 17:1–12.