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Authors
Don, M
Allen, AR
Starr, A

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EFFECT OF CLICK RATE ON THE LATENCY OF AUDITORY BRAIN STEM RESPONSES IN HUMANS

MANUEL DON, PHD

AARON R. ALLEN, MD ARNOLD STARR, MD

IRVINE, CALIFORNIA

SUMMARY – Auditory brain stem responses are the far-field reflections of electrical activity originating in the auditory pathway in its course from the cochlea to cortex that can be recorded from scalp electrodes using computer averaging techniques. There are seven components in the initial 10 msec following a click signal which have been shown to have an orderly change in latency as a function of signal intensity. The results of this study show that click repetition rate can also significantly affect the response latency measure. Responses were measured in six normal hearing subjects at click rates of 10, 30, 50, and 100/sec and at four intensity levels (30, 40, 50, and 60 dB sensation level). The mean latency shift of component V was approximately 0.5 msec when the responses at 10 and 100/sec were compared. This is equivalent to a 15-20 dB decrease in signal intensity at the 10/sec click rate. An analysis of the time of occurrence of this shift using brief click trains at 100/sec showed the shift in latency to be complete by the fifth click. The latency shift was similar at the four signal levels tested. The latency shift of component V appeared to be a monaural and therefore a potentially peripheral process. The results are interpreted as an objective measure of adaptation in the human auditory system with implications for the measurement in disorders of hearing.

In 1970, Jewett and his associates described a technique for recording short latency electrical activity in response to auditory stimuli from scalp electrodes in humans.[1] The response consists of a series of seven waves during the first 10 msec following stimulus onset and is presumed to derive from the progressive activation of tracts and nuclei in auditory brain stem pathways. By convention, the positive waves at vertex are labeled from one through seven using Roman numerals (Fig. 1). In the example in Figure 1, an additional wave can be seen between V and VI that is occasionally seen in some subjects. The observation that with increasing stimulus levels the response components decrease in latency and increase in amplitude has been the impetus for studying the contribution of auditory brain stem responses to the clinical evaluation of auditory function.[2-5] In addition, auditory brain stem responses have also been used in the diagnosis of certain types of neurological impairment, and disease.[6]

Particular emphasis has been given to Wave V by various laboratories because of its large amplitude, stability, and its occurrence at or near the threshold of hearing. Jewett and Williston[7] noted that increasing the click rate from 2.5/sec to 50/sec resulted in loss of definition of the early components but that Wave V was little affected. In fact, they reported that the amplitude of Wave V increased at the faster click rates. They did not observe a change in the latency of Wave V as a function of click rate. This study presents results from three experiments investigating the effect of the rate of monaural clicks on the latency of Wave V. The first experiment demonstrates that the latency of Wave V shifts as a function of click rate. This latency shift is considered a form of adaptation. The second experiment delineates the temporal

From the Departments of Neurology and Psychobiology, University of California, Irvine, Irvine, California. Supported by NIH Grant PHS NS 11876-02.

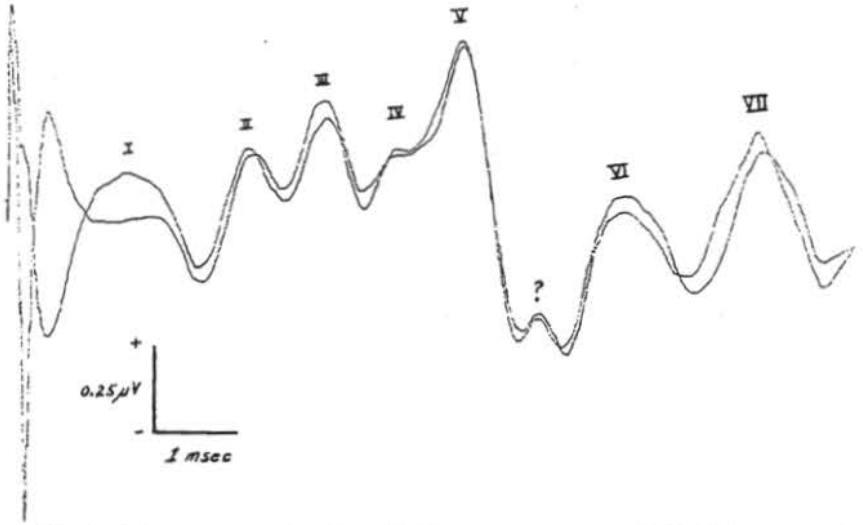

Fig. 1. Two averages of auditory brain stem responses to 8192 clicks presented at 60 dB sensation level showing the seven prominent waves occurring within the first 10 msec after stimulus onset. Positivity at the vertex electrode is in the up direction. The deflections at the very beginning of the tracing represent the stimulus artifact.

course of adaptation and the third experiment shows that this adaptation is confined to the stimulated monaural pathway.

METHODS AND RESULTS

EXPERIMENT 1

Latency of Wave V as a function of click rate and intensity.

Methods. In the first experiment, the latency of Wave V was measured as a function of both intensity and rate of stimulation in six adult subjects with normal hearing (ages 18-34). The acoustic stimuli were clicks produced by a 0.1 msec positive pulse applied to an earphone* with a cushion.** The acoustic wave form measured free field by a 1/2 inch microphone† placed at 1 cm distance is shown in Figure 2. The clicks were presented to the left ear at four rates; 10, 30, 50, and 100/sec and at four intensities; 30, 40, 50, and 60 dB sensation levels (SL).

Auditory brain stem responses were recorded by metal disc electrodes attached to the scalp at vertex (C_z) and left earlobe (A_1). Electrical activity was amplified by a factor of 10^5, filtered with a band pass of 100 Hz to 3 kHz (3 dB down points) and fed to a summing computer. The computer was triggered to sample for 10.24 msec (256 points, 40 μsec per point) from the onset of the click. The response to 2048 clicks was summed and the latency to the peak of Wave V was measured by positioning a cursor on the peak of the wave. The computer provided a digital readout of the cursor's position. The reproducibility of localizing the cursor to the peak of Wave V was within ± 40 μsec.

Results. A plot of the latency of Wave V as a function of click intensity at the four different click rates is shown in Figure 3. For all of the click rates there is a decrease in the latency of Wave V as the intensity of the click is increased. The slopes of these functions are similar to those reported by others[1,3,4,6] with a 0.4 msec decrease in latency for each 10 dB increase in click intensity. Figure 4 contains the same data but now plotted to show the latency of Wave V as a function of click rate for each of the four signal intensity levels. The vertical lines through each point represent the standard deviation. It is obvious that for any of the four intensity levels used, there was an increase in the latency of Wave V as the click rate became more rapid. A two-way analysis of variance indicated that the effects of click rate and intensity on the

* Model TDH 39. Grason-Stadler Co, Bolton, MA.
** Model MX-41 AR. Grason-Stadler Co, Bolton, MA.
† Bruer and Kjaer microphone. B & K Instruments, Inc., Cleveland, OH.

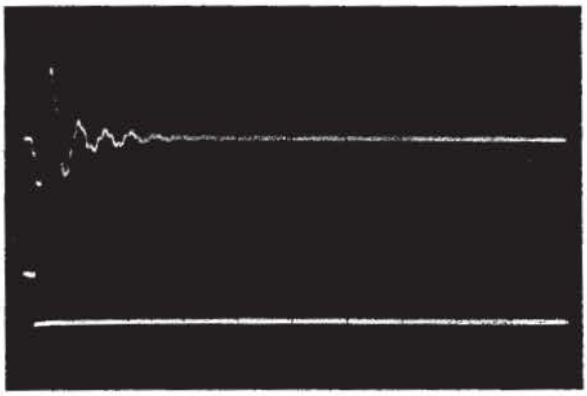

Fig. 2. Acoustic output of the TDH 39 earphone to a 0.1 msec pulse. The lower trace contains the input voltage to the earphone. The upper trace is the acoustic output of the earphone. The sweep duration is 5 msec.

latency of Wave V were significant beyond the .01 level.

The results of the study also indicated that the amount of latency shift observed when increasing the click rate from 10/sec to one of the faster rates was independent of signal intensity. Figure 5 is a plot of the change in latency as a function of click rate at the four different signal intensities when compared to the reference click rate of 10/sec. Visual inspection of the data suggests that the amount of latency shift of Wave V that occurs when the click rate was increased from 10/sec to 30, 50, or 100/sec was similar at the four signal intensities. An analysis of variance test supported this observation.

The latency shift observed when the click rate was increased from 10/sec to 100/sec could be as much as a 0.9 msec which is of the same magnitude as if the intensity of the click at a single repetition rate of 10/sec were decreased by 15-20 dB.

In summary, the first experiment reveals that, 1) the latency of Wave V shortens as click intensity is increased as was previously known, and 2) the latency of Wave V lengthens with increasing click rate. The amount of latency shift between click rates of 10/sec and one of the faster rates (30, 50, or 100/sec) is statistically independent of click intensity in the range of 30 to 60 dB sensation level.

Experiment 2

The temporal development of latency shift at a 100/sec click rate.

Methods. The paradigm outlined in Figure 6 was used. Trains of 20 clicks were presented monaurally with a 0.5 sec silent interval between stimulus trains. The repetition rate of the clicks within the train was 100/sec and their intensity was 40 dB sensation level. The computer's memory was divided into four sections. Auditory brain stem responses to the first click in the train was summed in the first quarter of computer memory denoted QM1 in Figure 6. The response to the fifth click was summed in the second quarter of memory (QM2), the response to the tenth click was summed in the third quarter of memory (QM3), and the response to the twentieth or last click in the train was summed in the fourth quarter of memory (QM4). This selective summing operation was repeated for 1024 trials of the 20 click train bursts. After recording the latency of Wave V for the 1st, 5th, 10th, and 20th click in the train, the procedure was repeated and the latency measured for the 2nd, 4th, 6th, and 8th click in the train (Run 2).

Results. A plot of the average latency of Wave V as a function of click number or position in the 20 click train burst for six subjects is shown in Figure 7. This figure also contains the latency values for a continuous sequence of clicks presented at 10/sec (open circle at far left) and 100/sec (open square at far right) derived from Experiment 1. Note that the latency of Wave V for the first click in the train is similar to the latency obtained with click signals at 10/sec. However, for the subsequent clicks in the train, the latency of Wave

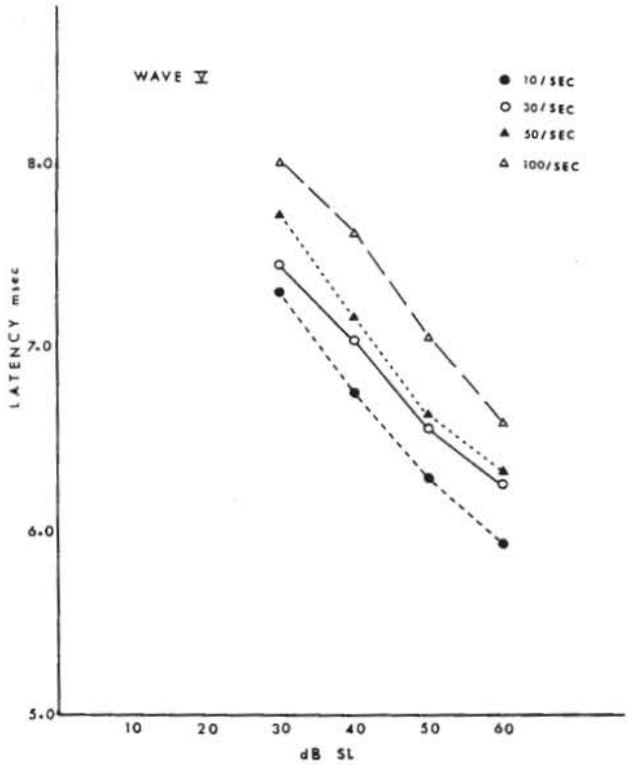

Fig. 3. The mean latency of Wave V as a function of click intensity at four click rates.

V increased, reaching an asymptotic value by the 4th or 5th click, equivalent to the latency measured for the continuous click rate of 100/sec. As a control experiment, the procedure was repeated using a 20 click train burst in which the repetition rate within the train was 10/sec instead of 100/sec. No latency shift was observed between the first and twentieth clicks.

Experiment 3

Restriction of the latency shift to the monaural pathway.

Methods. It is likely that Wave V represents activity originating in the midbrain.[8,9] The observed latency shift could be attributed to changes occurring centrally at this site or a reflection of changes taking place more peripherally in the auditory pathway. The paradigm shown in Figure 8 was used to explore this question. A train of 20 clicks was presented at a rate of 100/sec and at a sensation level of 40 dB. The first click in the train, which served as the control signal, was presented to the right ear and the response summed in the first quarter of memory (QM1). The second through nineteenth clicks were presented to the left ear to serve as the adapting stimuli. The last or 20th click in the train, which served as a probe or test click, was again presented to the right ear and the response summed in the fourth quarter of memory (QM4). This procedure was repeated for 1024 trials of click train bursts. If the adaptation to rapid click rates were a binaural and therefore a central process, the train of 18 clicks presented to the left ear would produce a shift in latency of Wave V in response to the twentieth click (the probe stimulus) relative to the first or control click.

Results. Figure 9 shows that the latency of Wave V for the probe click (denoted as "20th") is essentially identical to the latency of the control click (denoted as "1st") and both are similar to the latency of a continuous train of clicks presented at 10/sec. Had the latency shift induced by rapid click rates been initiated centrally in the auditory pathway the latency value for the probe click would have been similar to the delayed values obtained with a

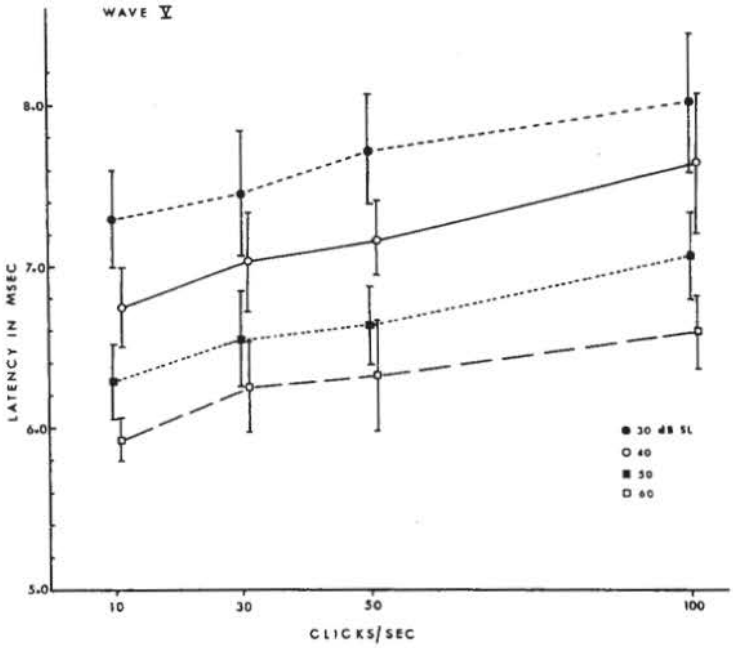

Fig. 4. The mean latency and standard deviation (vertical bars) of Wave V as a function of click rate at four signal intensities.

continuous train of clicks presented at 100/sec. Thus, the shift in latency of Wave V that occurs with rapid click rates is restricted to inputs arising from the stimulated ear and does not affect the latency of Wave V arising from stimulation of the contralateral ear.

DISCUSSION

Far field auditory brain stem responses are currently being used to define the integrity of the auditory system in humans.[1,3,6,10] The response, when evoked by brief acoustic signals can be detected close to hearing threshold and the latencies of the response components decrease in a monotonic fashion as signal intensity is raised.[3,6,7,11] While the slopes of the latency-intensity functions for the most prominent component of the response, the vertex positive wave occurring in the 5 msec range (Wave V), are quite similar among the various studies, the absolute latency values reported vary by as much as 0.5 msec.

The principal finding of the present study is that click repetition rate can also significantly affect the latency of auditory brain stem responses. Wave V was shifted by as much as 0.9 msec when click repetition rate was increased from 10/sec to 100/sec. The extent of the latency shift was independent of signal intensity over the range of 30 to 60 dB SL. A change of latency of 0.9 msec of Wave is not trivial as it is equivalent to the latency shift that would occur if click intensity were changed 20 dB at a single repetition rate. Previous studies of click repetition rate on auditory brain stem responses noted the amplitude decrement of the initial components as stimulus rate was increased but did not observe any latency effects.[7,11] However, a recent report by Thornton and Coleman[12] confirms the observation that stimulus rate has significant effects on both amplitude and latency of auditory brain stem response components.

In the present study the slope of the function relating the latency of Wave V with click repetition rate was fairly linear between 10 and 100/sec. Eggermont and Odenthal[13] recording the VIII

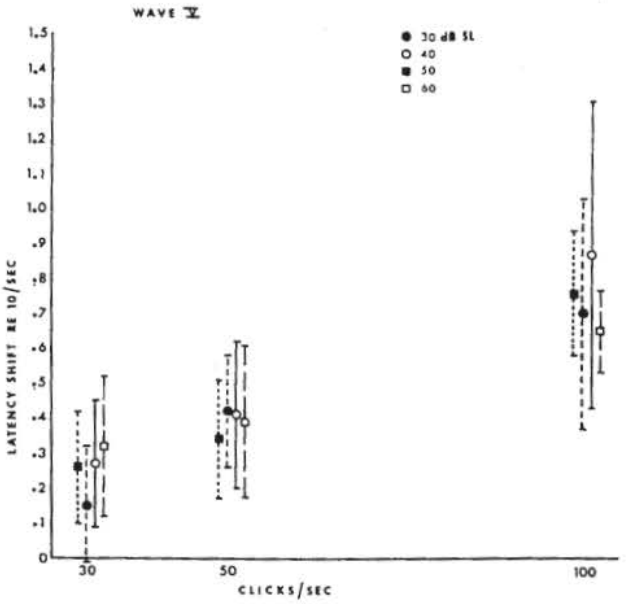

Fig. 5. The difference in latency of Wave V between a 10/sec stimulation rate and each of the three faster click rates (30, 50, and 100/sec) at four signal intensities. The vertical bars represent the standard deviations.

nerve action potential in humans by electrocochleography observed VIII nerve response to also increase in latency over approximately the same range of repetition rates. However, the slope of the function relating the latency of N_1 with click repetition rate appeared logarithmic. These findings suggest that peripheral and central portions of the auditory pathway differ in their responsiveness to repetitive acoustic stimulation. It was unfortunate that the latencies of Waves I, II, and III of the brain stem response could not be precisely defined at repetition rates greater than 50/sec, preventing the identification of the specific site along the central pathway of which a linear response function is first encountered.

Sensory systems require a finite period of time following an adequate stimulus to fully recover their responsiveness. If subsequent stimuli occur before recovery is complete. the system's response will be altered (attenuated or prolonged in latency). We consider the shift of latency of the brain stem response components with rapid stimulation rates as a manifest of incomplete recovery. The major determinants of recovery time are, 1) refractory periods of neural elements, 2) changes in synaptic transmission, and 3) receptor adaptation or fatigue. It is unlikely that the neural refractory period can account for the latency shift seen with increasing click rates because the time course of this phenomenon is rapid (1-2 msec) compared to the long time interval between the click signals even at the fastest repetition rate (10 msec at 100/sec). The possibility that alterations in central synaptic transmission could account for the latency shift was not substantiated by the results of the third experiment of this study in which a probe click delivered contralateral to the ear receiving the rapid stimulus train evoked a response at the same latency as when the rapid click train was not present. This experiment does not exclude the possibility that the postulated central synaptic change is restricted to the monaural pathway.[14] It is most likely that a change in receptor function known as adaptation or fatigue is the cause for the latency shift induced by rapid stimulation. Fatigue

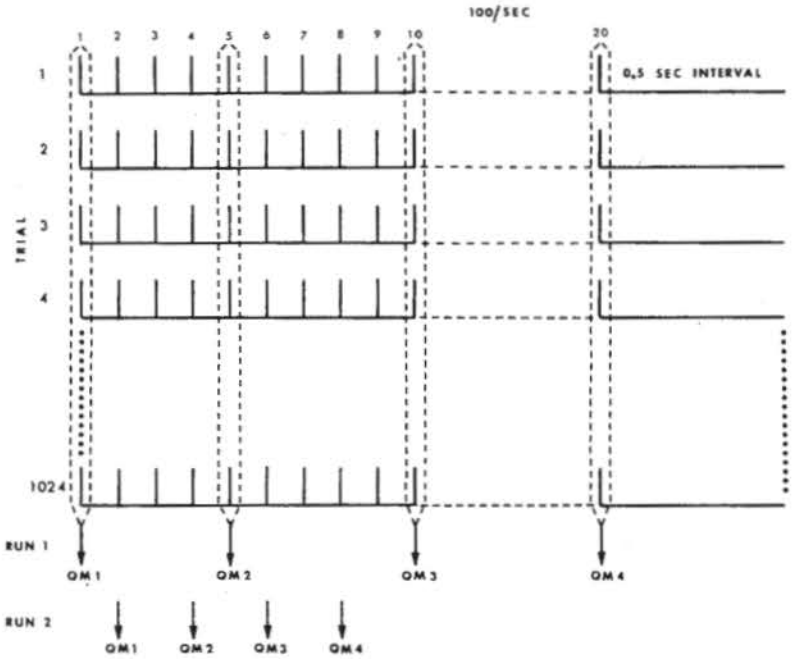

Fig. 6. The paradigm used in Experiment 2 to determine the latency of Wave V as a function of the click number or position in a 20 click train burst presented at 100/sec. See text for further detail.

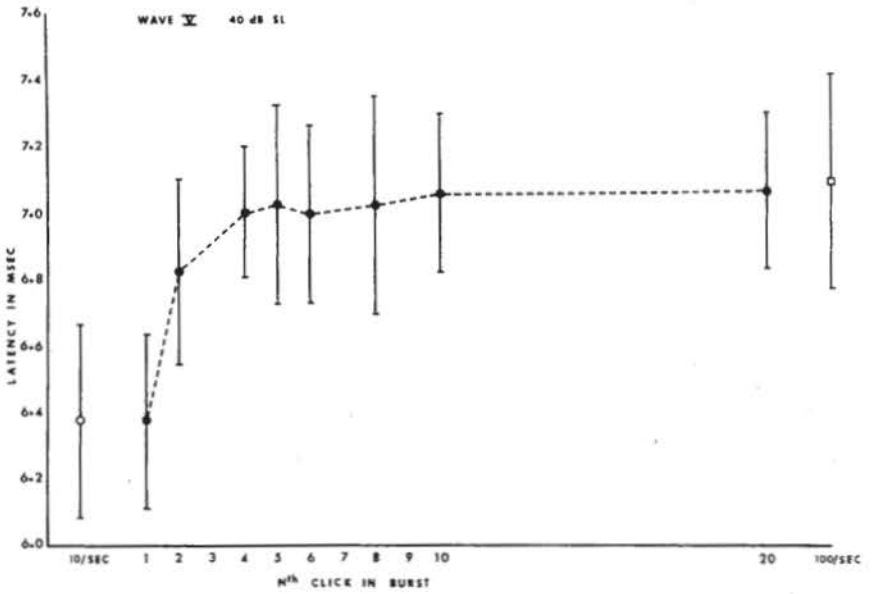

Fig. 7. The mean latency and standard deviation (vertical bars) of Wave V as a function of the click number or position in a 20 click train burst presented at 100/sec at 40 dB sensation level. The open symbols at the sides of the figure represent the mean latency of Wave V to a continuous click train at 10/sec (circle) and 100/sec (square).

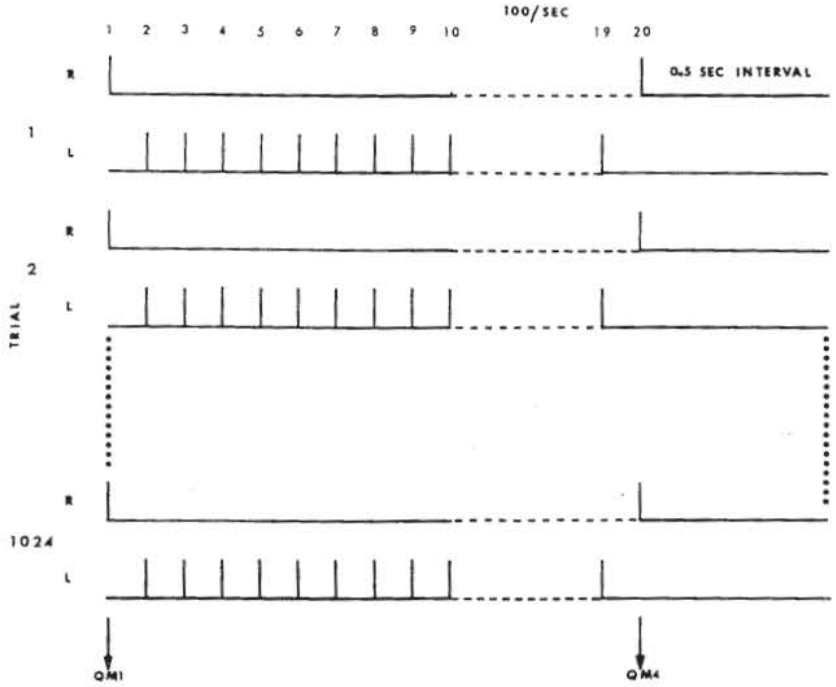

Fig. 8. The paradigm used in Experiment 3 to determine whether the latency shift of Wave V observed with fast click rates is also a binaural phenomenon. See text for further detail.

and adaptation differ in their time course but both are presumed to be due to metabolic alterations of receptor elements consequent on their activation.

Most studies on fatigue or adaptation have employed relatively long stimulus exposure times and/or high levels of stimulation.[15] Any mechanism postulated to explain the adaptation seen with the click rates employed in this study would have to account for both the rapid time course of the changes and the fact that they were elicited at moderate levels of stimulation (30-60 dB SL). Recall that the latency shift of Wave V reached an asymptotic value by the 4th click in a stimulus train presented at 100/sec and at a sensation level of 40 dB. Perhaps a short acting fatigue process in the cochlea similar to that described by Legouix and Pierson,[16] could account for the rapid development of the latency shifts observed in the present experiments.

An entirely different category of mechanisms that might be responsible for the observed latency changes involves efferent feedback systems, *i.e.*, middle ear muscle or olivo-cochlear bundle. Sorensen[17] ruled out middle ear muscle activity as a contributing mechanism for amplitude adaption of evoked responses in experimental animals by utilizing anesthesia to abolish middle ear muscle responses. Since the present experiments employed awake subjects, the middle ear muscle reflexes were presumed to be active. It is well known that the middle ear muscles respond *bilaterally* following an acoustic input[18] and the finding of a latency shift restricted to inputs arising ipsilateral to the side of rapid stimulation (Experiment 3) is strong evidence against their participation in producing the latency shift. This same argument would also exclude the contribution of other efferent neural systems that are activated bilaterally in response to monaural stimulation.

Wave V represents a far-field summation of neural activity of many ele-

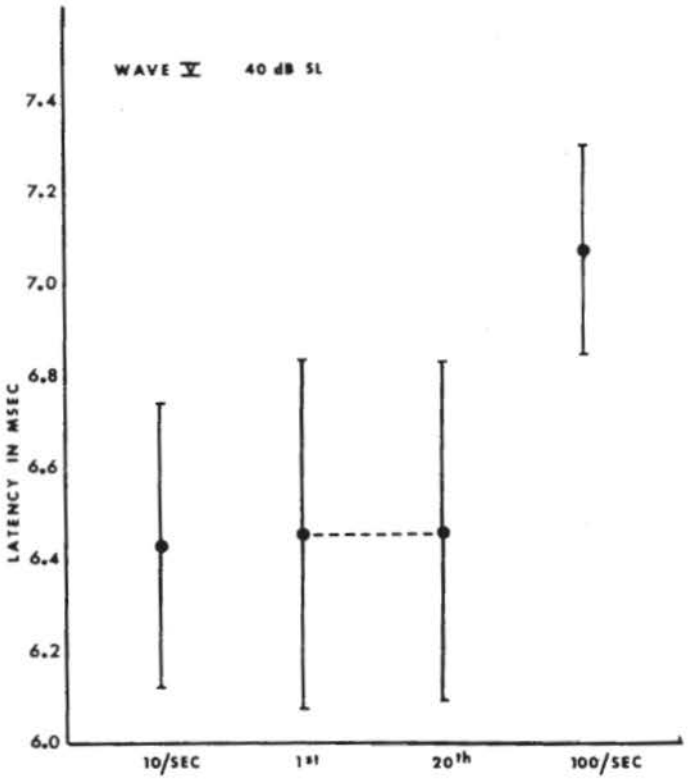

Fig. 9. Mean latency and standard deviation (bars) of Wave V for the 1st and 20th clicks in a train of 20 presented at 100/sec at 40 dB sensation level. The 1st and 20th clicks are presented to the ipsilateral ear and the 2nd through 19th clicks are presented to the contralateral ear. The measures of Wave V to a continuous click train at 10/sec and 100/sec are also included in the figure.

ments.[19,11] The latency of its peak represents either the modal value of the elements comprising the response or the value of the strongest component or some combination of these two. A shift in latency of the peak accompanying rapid stimulation rates could be explained by a change in the synchrony of firing due to: 1) a shift in the modal latency of the neural elements, and 2) an amplitude diminution of the dominant component due to desynchronization such that the latency of longer latency components become prominent. Thus, a shift in latency need not require a reduction in the number of responding elements but could be attributed to varying degrees of synchronization of the components giving rise to Wave V. It is also possible that both a reduction in neural activity and a change in synchronization of the components may be responsible for the latency shifts. The multiplicity of contrived but reasonable explanations for the latency shift of Wave V emphasizes the need for defining in more detail the *precise* generators of the various components comprising the far-field auditory brain stem response.

The shift of latency of the brain stem response with rapid stimulation rates may have use in clinical situations as a measure of the dynamic properties of the human auditory system. Rapid adaptation is a characteristic finding in lesions of the VIII nerve. It may be that the extent of the latency change accompanying rapid stimulus rates could provide an objective definition of adaptation in patients being evaluated for an acoustic neuroma.

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REPRINTS—Manuel Don, PhD, Ear Research Institute, 156 South Lake Street, Los Angeles, CA 90057.

THIRD DANIEL C. BAKER JR. LECTURESHIP

The American Laryngological Association is pleased to announce that the Third Daniel C. Baker, Jr. Lectureship in Laryngology will be presented by Dr. Lewis Thomas, President of the Sloan Kettering Institute, New York City. The lecture will be given at the time of the annual meeting of the American Laryngological Association on May 8, 1977 at the Sheraton Boston Hotel, Boston, Mass.

The subject of the address will be "The Marks of Self: Immunologic and Olfactory Origins."