

AUDITORY-EVOKED FAR FIELDS AVERAGED FROM THE SCALP OF HUMANS

BY

DON L. JEWETT AND JOHN S. WILLISTON

*(From the Departments of Physiology and Neurological Surgery,
University of California, San Francisco, California 94122, U.S.A.)*

INTRODUCTION

AVERAGING, when used to extract extremely small signals from relatively high levels of background noise, allows detection of evoked potentials at surprisingly large distances from the site of neuronal activity. In animals, volume-conducted potentials from brain-stem auditory structures can be recorded throughout the brain (Grinnell, 1963; Bullock *et al.*, 1968; Jewett, 1970) and even from the scalp (Jewett, 1970). In humans, auditory-evoked potentials can be detected at the vertex due to neural activity from subcortical structures (Jewett, Romano and Williston, 1970) as well as from primary cortical areas (Vaughan and Ritter, 1970). Under the conditions of skull and scalp boundaries and intracranial inhomogeneities, recordings from a single electrode position offer little indication as to the location of a wave's neural generator(s), whereas multiple recording sites may be more informative.

We have found it useful to borrow concept and terminology from engineering to distinguish between two parts of the volume-conducted field: the *near field* and the *far field*. Operationally defined, for biological systems, the near field is characterized by significant differences in wave shape (i.e. in amplitude, polarity, or both) at electrode positions a short distance apart. In contrast, far field electrode positions short distances apart show no significant differences in wave shape, assuming that there is no boundary, no other extreme inhomogeneity, no anisotropism, etc.

Differential recording between closely spaced electrodes is useful for locating a neural generator since such a recording configuration can only detect near fields and is uninfluenced by the far fields of distant generators. Far field recordings (which imply that the generator is at a distance) offer advantages in that the position of the electrode is not critical for obtaining satisfactory recordings and in that potentials from widely spaced generators can be detected at a single electrode. Both of these advantages can be seen in the work presented here, where far field potentials evoked by auditory click stimuli are recorded from the scalps of humans. On the basis of some indirect evidence, it is possible to deduce the location of the

generators of some of the waves. It is clear that far fields at least 10 cm. from their brain-stem generators can be recorded from humans and that electrical activity from any brain location within the human skull may be detectable at the scalp, given a satisfactory method of synchronizing the activity with the averager.

MATERIALS AND METHOD

Twelve normal subjects, ranging in age from 18 to 39 years, relaxed on a comfortable "chaise-longue" with the head resting on a pillow (neck muscles relaxed). Subjects often fell asleep during the recording sessions, which lasted from one to three hours. Auditory "clicks" or, on a few occasions, damped tone pips from a tuned filter, were delivered binaurally (unless otherwise noted) via a pair of Clevite Brush ED-300 stereo earphones energized by a Lafayette 224-A stereo amplifier. The input to the amplifier was controlled by a Hewlett Packard dB attenuation box Model 350A which received 0.05 msec square waves from a Tektronix Type 161 waveform generator. The accuracy of the attenuation box was verified by a Bruel and Kjaer Type 2203 sound level meter. Click intensity was measured in dB above the subjective threshold for the stimulus (SL). The intensity was usually 60 to 75 dB SL except as noted. The repetition rate, which was 2 stimuli/sec. unless otherwise noted, was determined by a free running Tektronix Type 162 waveform generator whose rate was carefully adjusted so that any 60 Hz power-line interference would be cancelled on successive summations of the averager (Jewett, 1970). For all runs, 2048 stimuli were averaged.

EEG disc electrodes with unshielded leads (Grass Instrument Co.) were attached to the scalp with Grass EEG electrode paste after the scalp had been cleaned with acetone. Subjects were grounded by an EEG electrode attached to the left ear lobe or to the neck. In one subject, recordings from the ear canal were obtained through a hypodermic needle (insulated except at the tip) inserted beneath the skin of the anaesthetized posterior ventral wall of the external auditory meatus near the tympanic membrane (Yoshie, Ohashi and Suzuki, 1967). Recordings were also taken from the ear canal via a saline-bridge wick electrode placed several millimetres from the ear drum and held in place with a small spring clip. All recordings were taken with the right ear lobe as the reference point.

For each of three recording channels, a pair of Grass P9 amplifiers were cascaded to obtain the necessary gain of approximately 2×10^6 . Each channel was separately monitored on a Tektronix 565 oscilloscope and recorded on an Ampex-300 FM tape recorder.

The frequency response of the preamplifier system was approximately 10 to 10,000 Hz at the 6-dB point and the upper frequency response of the FM tape recorder was 2,500 Hz. No significant differences were found between on-line and tape-recorded averages. In a few instances, a tape recording was averaged when the playback was limited by a high frequency filter with a 100 Hz limit (3-dB point) and a 12 dB/octave roll-off. The fourth channel of the tape recorder recorded a trigger pulse 4 msec before the delivery of the click; this permitted re-runs which could show the flatness of the base line preceding the click stimulus. The single channel all-analogue averager, a 100 capacitor Princeton Applied Research TDH-9 Waveform Eductor, was specially modified at the factory to provide a linear mode of summation, rather than the asymptotic method of operation available on the standard model. This was accomplished through the use of a constant current amplifier so that the amount of charge placed upon a given memory storage capacitor was directly proportional to the input voltage. The averager input was AC coupled (1.6 Hz at 3-dB point) from the preamplifier, or from an operational amplifier used as a buffer on the output of the tape recorder. The prefilter of the averager was used, but the system frequency-response was limited by the preamplifier and tape-recorder limits previously mentioned. The output of the Eductor was photographed on the 565 oscilloscope using a Tektronix C-12 camera with Beattie-Coleman 70 mm. Tranaset back and Dupont Lino-writ photographic paper. In some figures, not all 100 ordinates are reproduced. The triggering of the averager was controlled by a pre-set counter and could also be interrupted by the awake subject by means of micro-switch normally held closed by the weight of his relaxed thumb.

RESULTS

A remarkably distinct series of waves in the first 9 msec. after a click stimulus can be averaged from the human vertex (fig. 1A). With a likelihood approaching inevitability, we chose to label the waves sequentially with roman numerals (fig. 1A). (In

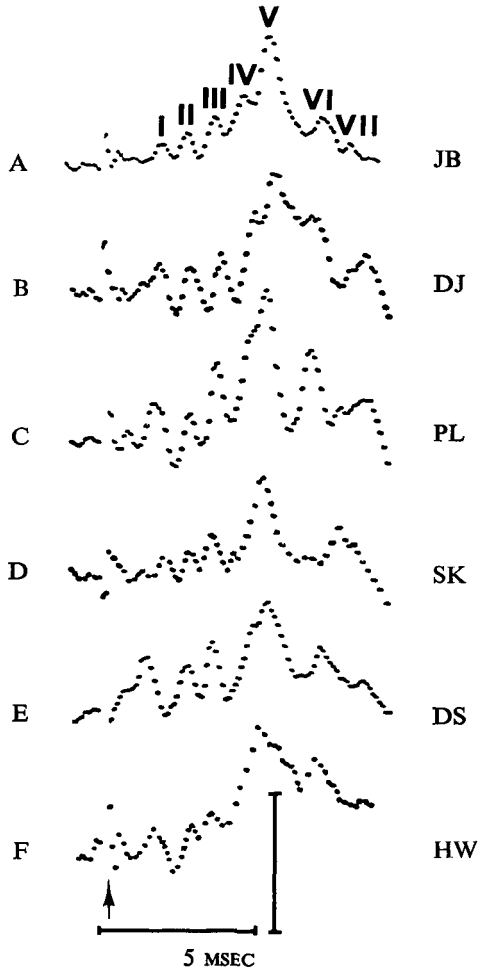


FIG. 1.—Auditory far field potentials recorded at the vertex, reference at right ear lobe, from six subjects. Click stimulus delivered at the arrow. In A, roman numerals label each wave. Repetition rate in A, 2.5 stimuli/sec; in B-F, 2 stimuli/sec. Vertical calibrations: A, 1.0 μ V; B-E, 1.3 μ V; F, 1.2 μ V. To allow across-figure comparisons, in this and all other figures the initials at the right of the figure are those of the subject.

all figures unless otherwise noted, positivity of the scalp relative to the ear is plotted upward; the initials at the right side of a trace identify the individual subject for across-figure comparisons.) That these waves are auditory responses and not electronic artifacts was shown by control recordings made with the ear canals blocked but with all electronics energized (fig. 5D).

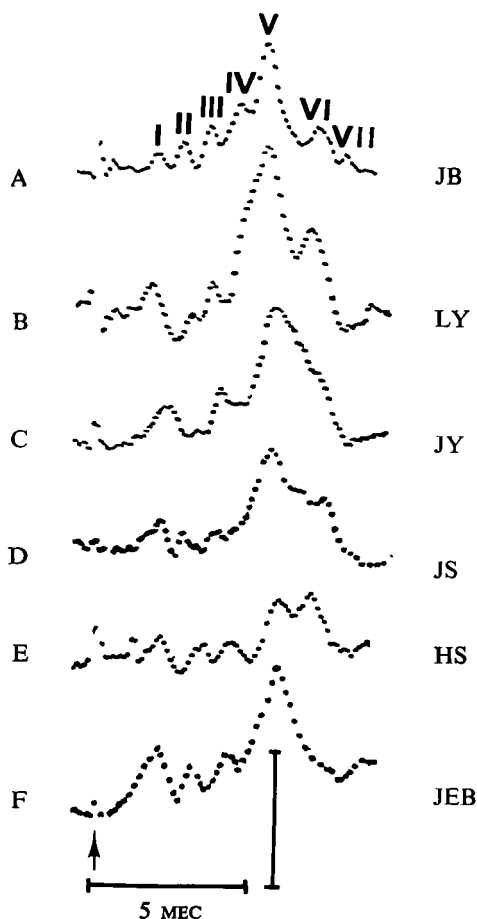


FIG. 2.—Auditory far fields from five additional subjects. Click stimulus delivered at the arrow. For purposes of comparison A is the same as fig. 1A. Repetition rate 2 stimuli/sec except for A (2.5 stimuli/sec) and D (10 stimuli/sec). Vertical calibrations: A-C and F, 1 μ V; D, 1.3 μ V; E, 1.6 μ V.

Figs. 1 and 2 combined show a vertex-ear recording for each of the 11 subjects studied with clicks. While variability is apparent in figs. 1 and 2, there are also considerable similarities in the waveforms. With a few exceptions, the vertex was positive to the ear through wave VI and sometimes beyond. The waves showed a general increase in magnitude from I up to V. The amplitudes of the waves were quite similar across subjects, wave I, for example, ranged from 0.09 to 0.5 μ V, wave V from 0.6 to 1.4 μ V. After careful perusal of the similarities of figs. 1A, 1B, and 1C, we could, with the courage of conviction, find all the waves through VI in all of the traces of figs. 1 and 2. Wave I usually had a clear starting point although it was sometimes obscured by artifact or noise (figs. 1B, 1D). However, the peak of wave I was clearly visible in each case, having a range of latency (measured from the time of arrival of the sound at the eardrum) of 1.4 to 1.8 msec. In figs. 1 and 2, wave I ends with a deflection below baseline in five averages but in the other six it ends at

the baseline; this observation suggests that there are no prolonged potentials from the generator of this wave that extend into the period of wave II (*see Discussion*).

Wave II was usually distinct, and usually smaller than wave I. Wave III could be found easily in all records. Wave IV was, in all records, on the ascending limb of wave V, usually being little more than an inflection. Wave V was the largest and most consistent wave in the period under consideration. The peak latency of wave V (measured from the arrival of the sound at the eardrum) was between 4.6 and 5.1 msec. Wave VI was often on the descending limb of V and was sometimes only an inflection (figs. 2C, 2D, 2F). Wave VII was the least constant of the waves; sometimes it was not discernible, even by the authors (figs. 2C, 2D). Between waves V and VI and between waves VI and VII there were sometimes small waves which, should the need arise, might be labelled by letter subscripts.

While the constancy of pattern and amplitude suggests that the early auditory field potentials presented here may have considerable use for empirically based clinical and experimental work, the usefulness of this method will be enhanced if the neural

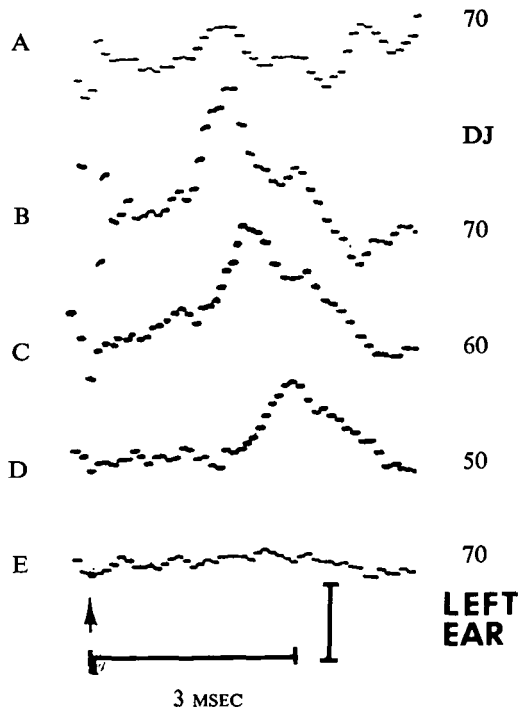


FIG. 3.—Comparison of vertex-recorded far field with recordings from the right ear canal by means of a subcutaneous needle. Reference point on right ear lobe. Click stimulus delivered at the arrow. The numbers at the right indicate the subjective intensity in dB. A, vertex recorded potential, binaural stimulation, recorded simultaneously with B; vertex positivity gives an upward deflection. B-D, ear-canal recordings with binaural stimulation at different intensities; ear-canal negativity gives an upward deflection. E, ear-canal recording as in B, but with monaural stimulation contralateral to electrode. Vertical calibrations: A, 0.5 μ V; B-E, 1.0 μ V. Note that the sweep speed is faster than in the other figures.

generators of the waves can be identified. The extremely short latency of wave I agreed well with the findings of Yoshie (1968) and Coats and Dickey (1970) with regard to the latency of N_1 recorded from the ear canal (*see* Discussion). In the one subject in which a needle electrode was used in the ear canal, recordings showed a short latency negative wave whose height decreased and whose latency increased with decreasing sound intensity (fig. 3), in good agreement with Yoshie (1968). The wave shape was similar to that recorded in cats by Ruben *et al.* (1960, fig. 11) and in humans by Yoshie *et al.* (1967, fig. 3, 60 dB) and Coats and Dickey (1970, fig. 5). The waves shown in fig. 3B were present with ipsilateral but not with contralateral stimulation (fig. 3E). If the sound source was moved away from the ear, while subjective intensity was held constant, the peak latency of the first wave was increased by the time expected for air conduction. There was good agreement between the starting peak latencies of the first wave on the ear canal (fig. 3B) and those of wave I recorded simultaneously at the vertex (fig. 3A).

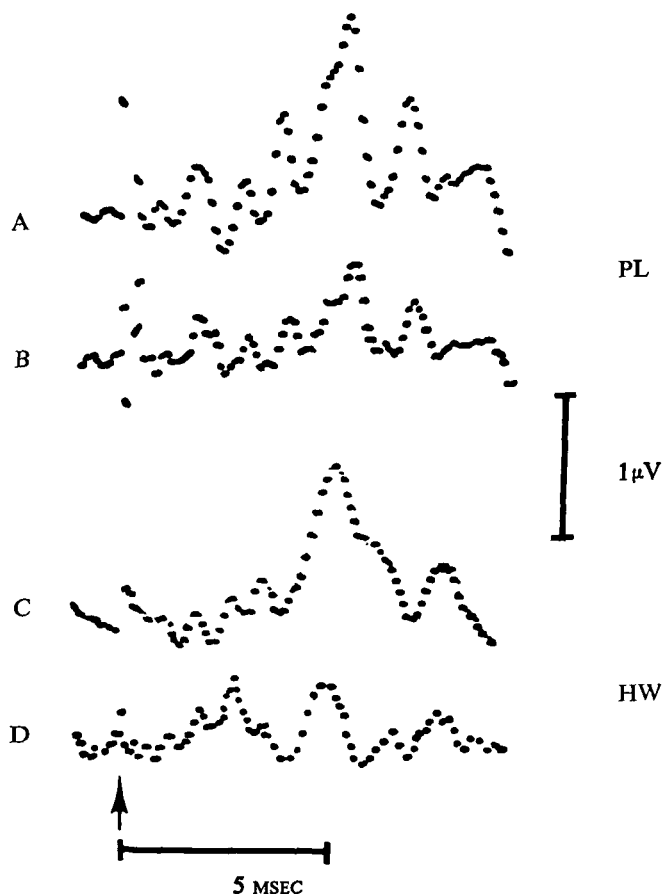


FIG. 4.—Simultaneous recordings from the vertex and either the ear-canal or the mastoid. Click stimulus delivered at the arrow. A and C, vertex recordings; B, right ear canal (wick electrode) simultaneous with A; D, right mastoid recording, simultaneous with C. Positivity relative to right ear lobe plotted upward in all traces. A is the same as fig. 1C.

Recordings obtained within the ear canal by means of wick electrodes showed positive waves of smaller amplitude (fig. 4B) but of the same general shape as the vertex waves (fig. 4A). Even recordings from the mastoid (fig. 4D) showed waves I through IV that corresponded with the same vertex waves (fig. 4C).

If the vertex-recorded waves reported here are to meet the criteria of far field responses, recordings made short distances apart should be similar. Fig. 5 shows similar waveforms obtained simultaneously from three electrode positions: at the vertex, 7 cm. anterior to the vertex, and 7 cm. lateral to the vertex. We have not attempted a detailed mapping of these responses on the scalp.

The responses from the same individual were remarkably consistent as can be seen by comparing recordings from the same subject (figs. 1A, 6A and 6B; 1C and 5A;

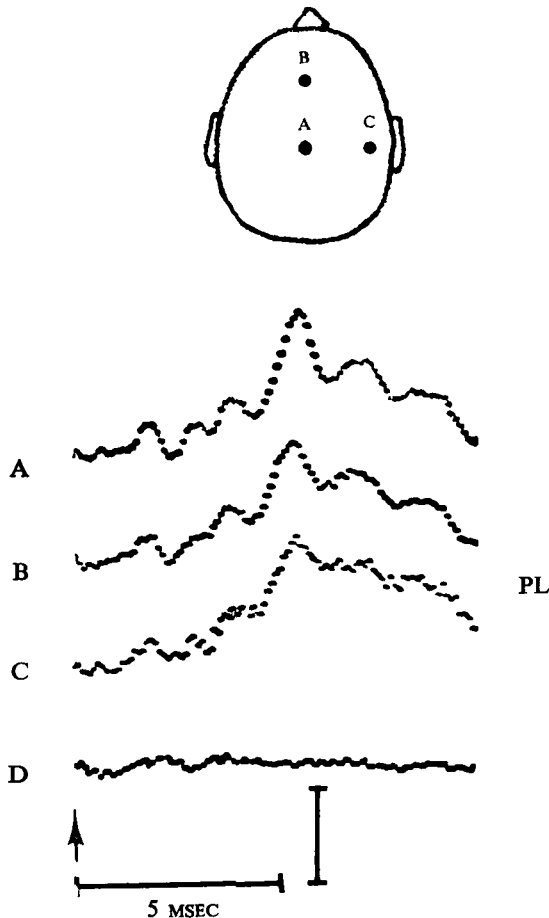


FIG. 5.—Simultaneous recordings from the vertex and from two locations, each 7 cm. from the vertex. Click stimulus delivered at the arrow. A-C, simultaneous recordings from the scalp positions indicated, relative to the right ear lobe. D, control recording, same as A except with both ear canals occluded and ear plugs and earphones still energized. Vertical calibrations: A and D, $0.9 \mu\text{V}$; B, $0.6 \mu\text{V}$; C, $1.0 \mu\text{V}$. Note that calibrations differ because of different pre-amplifier gains; the low frequency cut-off was 1.6 Hz.

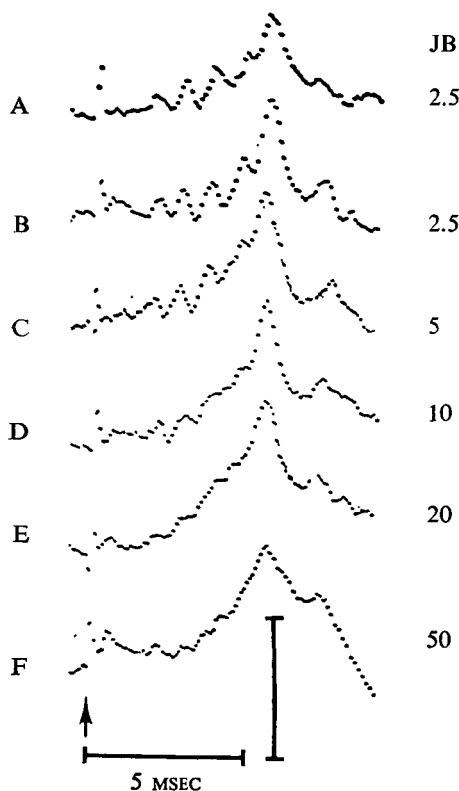


FIG. 6.—Effect of repetition rate on the auditory far field recorded at the vertex. Numbers at right indicate the repetition rate in stimuli/sec. Click stimulus delivered at the arrow. A, recording at 2.5 stimuli/sec recorded six months before B. B–F, recordings from the same recording session, at different stimulus repetition rates. Vertical calibration: A, 0.7 μ V; B–F, 1.0 μ V. Note the loss of definition of the wave components as stimulus rate increases. The height of wave I decreases with increasing rate while wave V increases in amplitude (comparing B and E).

1F and 4C). This consistency was also present when recordings were made six months apart (figs. 6A and 6B). It was our impression that recordings with the most distinct waves were obtained when the subjects were relaxed and well adapted to the experimental procedure. Sometimes such recordings were not obtained until the second recording session. The most relaxed subjects (fig. 1A–E for the most part) often fell asleep during the recording session; no differences between awake and asleep records were noted, but this was not systematically investigated. The provision of a micro-switch, which allowed the subject to turn off the averager (but not the click) prior to voluntary movements, was important in obtaining sufficient relaxation of the subject.

The distinctness and replicability of the earliest waves were markedly affected by the click repetition rate. At rates more than 5 stimuli/sec the wave shapes were less distinct (figs. 6D–F). Wave I was decreased in height while waves IV and V increased (e.g. figs. 6B and 6E). At times, satisfactory recordings were obtained at rates as high

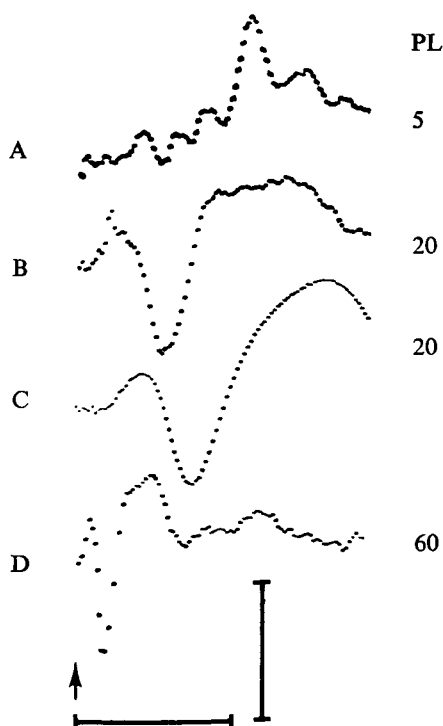


FIG. 7.—Tape re-runs, at different sweep speeds and filter settings, of the same vertex-recorded activity. Stimulus delivered at the arrow. Numbers at the right indicate the horizontal calibration in msec. A (same as fig. 5A), averaged at bandpass of 1.6 to 2,500 Hz. B, same as A except at slower sweep speed (longer duration). C, same as B except on playback from tape, high frequency limit at 100 Hz. D, same as B except at still slower sweep speed. Vertical calibrations: A, $1.3 \mu\text{V}$; B and D, $5.0 \mu\text{V}$; C, $5.7 \mu\text{V}$. Note that in B, the detail of A is barely seen in the first 5 msec., and that a large negativity follows the waves seen in A. In C, the wave shape is smoothed, the waves of A cannot be seen, and a significant phase lag distorts the latencies and hence the apparent polarity at about 10 msec from the stimulus.

as 17 stimuli/sec, but this was not consistent, and the best rate found for a variety of subjects was the lowest tested (2 stimuli/sec). Stimulation rates lower than 2 stimuli/sec made the run of 2,048 repetitions excessively long and made it difficult to cancel the Hz power-line interference by our method of using a free running oscillator (Jewett, 1970).

We frequently found that at click rates higher than about 10 stimuli/sec the baseline preceding the click artifact was not as flat as at slower rates. Fig. 7 shows the re-run from the tape recorder of averages of increasing lengths after the stimulus (band-pass of the system for this run was 1.6 to 2,500 Hz). Coherent waves greater than $0.2 \mu\text{V}$ are apparent as far as 100 msec after the click (fig. 7D). We have not systematically examined greater time intervals because the run-to-run variability at repetition rates of 2 stimuli/sec (500 msec between stimuli) is sufficiently small for our purposes. Study of greater time intervals will require repeated re-runs with

increasing delays from the stimulus rather than increased sweep duration times because, at a sweep duration of 500 msec, the entire 10-msec sweep of fig. 7A occupies only two ordinates—too few to detect the variability seen at the faster sweep speed.

When the tape that gave the average of fig. 7B at a bandpass of 1.6 to 2,500 Hz was re-averaged with a bandpass of 1.6 to 100 Hz, the waves shapes showed less detail and an apparent increase in latency (fig. 7C). Thus we confirmed the suggestion of Mendel and Goldstein (1969) that the apparent latency of the early waves is markedly influenced by the high frequency cut-off filter. Since the first five waves occur in about 5 msec, the high frequency response should be greater than 1,000 Hz, at the very minimum.

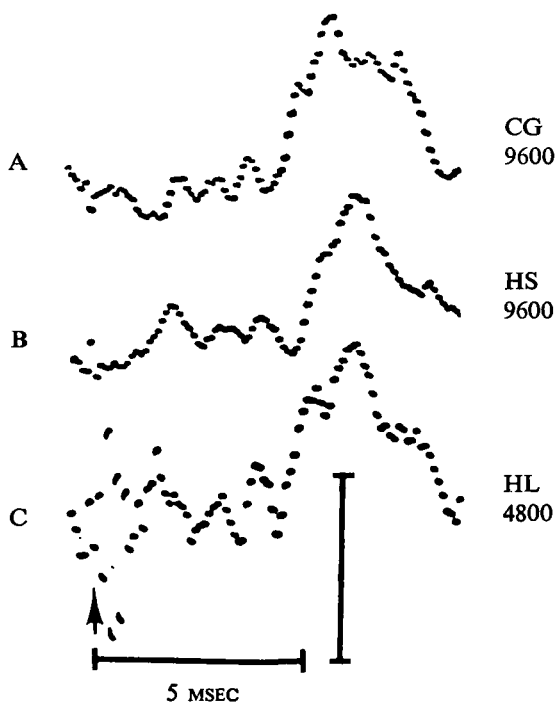


FIG. 8.—Vertex-recorded responses to binaural tone pips. Start of the tone pip delivered at the arrow. The numbers below the initials indicate the basic frequency in the pip. Repetition rates: A, 10 stimuli/sec; B and C, 2 stimuli/sec. Vertical calibrations: A, 1.0 μ v; B and C, 1.2 μ v.

The usual stimulus used was a click, which had high frequency components and which was adjusted to minimize “ringing” as much as possible. We have also found that tone “pips” based on a high frequency (e.g. 9,600 Hz) gave satisfactory responses (figs. 8A, B), comparable to the click responses of the same subject (fig. 8B compared with 2E). Tone pips at a lower frequency (e.g. 4,800 Hz) gave a less distinct wave shape (fig. 8C compared with fig. 8D). The effect of tone-pip frequency has not been systematically studied.

DISCUSSION

Auditory-evoked far field potentials with latencies less than 5 msec, recorded from the vertex of humans, were first reported by Jewett *et al.* in 1970. Our present use of a linearized analogue averager and a slow repetition rate has considerably improved the waveforms obtained. The 300 Hz low-frequency cut-off filter used previously had distorted the low frequency components of the waveform, making interpretation of the waves difficult, as in the case of Sohmer and Feinmesser (1970) who recorded vertex-ear lobe potentials with low-frequency cut-off at 500 Hz. With our present technique, the waveforms obtained are surprisingly similar to those seen in the cat (Jewett, 1970), bat (Grinnell, 1963), and porpoise (Bullock *et al.*, 1968). In these anaesthetized animals, the largest wave is the fourth wave, compared with the unanaesthetized human where wave V is largest. The discrepancy may be due to species differences or to the effect of anaesthesia. In the cat, the origin of the first wave, recorded throughout the brain and on the scalp, is clearly the same as that of N_1 recorded at the round window (Jewett, 1970), and thus can be considered to be a volume-conducted eighth nerve potential. In humans, responses similar to N_1 can be recorded from beneath the skin near the ear drum (Yoshie *et al.*, 1967; Yoshie, 1968; Coats and Dickey, 1970) and from within the middle ear (Ruben, Bordley and Lieberman, 1961; Portmann, Aran and Le Bert, 1968). The peak latency of N_1 responses (click intensity at 65–70 dB) of 1.8 msec (Yoshie, 1968) agrees well with the peak latency of wave I, which averaged 1.7 msec from the time of arrival of the sound at the ear drum. Sohmer and Feinmesser (1970) have found that the wave shape they obtained from ear canal-vertex recordings is similar to those they recorded from the ear lobe-vertex. In the one subject in whom we attempted recording in the ear canal with a needle electrode, N_1 showed the same starting and peak latencies as wave I simultaneously recorded from the vertex. Thus, the evidence that wave I is volume-conducted from the eighth nerve seems good. Furthermore, the latency of wave I is so short that there is insufficient time for any reflex activity to be generated; e.g. insufficient time for action potentials to leave the skull and energize any muscular component (Bickford, Jacobson and Cody, 1964; Borsanyi, 1964; Cody *et al.*, 1964; Davis *et al.*, 1964; Yoshie and Okudaira, 1969). A muscular origin of the waves reported here is unlikely also because of the absence of the response on the neck (Jewett *et al.*, 1970), the absence of neck tension in the recumbent (sometimes sleeping) subject, and the small amount of myogenic component which is detected at the vertex (Yoshie and Okudaira, 1969; Vaughan and Ritter, 1970). The middle-ear muscles show potentials with a latency greater than any of the waves presented here (Fisch and Schulthess, 1963). Since wave I can be obtained at different repetition frequencies, a long latency response from a previous stimulation is ruled out as a possible source of this potential; wave I is time-locked to the auditory stimulus by the averaging process. The identification of the eighth nerve as the source of wave I reinforces our previous conclusion (Jewett *et al.*, 1970) that since intracerebral potentials can be detected on the scalp at such a distance from the generator, distance *per se* should not be a limiting factor in recording from deep

neural structures, given a satisfactory method of synchronizing the averager to periodic activity.

If wave I is generated by the eighth nerve action potentials, then wave II most likely arises from the cochlear nuclei, as in the cat (Jewett, 1970). Double firings from the eighth nerve (Tasaki, 1954) might contribute to wave II, and it seems otherwise likely that wave II is a composite from several generators, at least the dorsal and ventral cochlear nuclei and their efferent axons, both crossed and uncrossed. Later waves are undoubtedly composites from multiple generators, both ascending and descending (Jewett, 1970) in algebraic summation. It is interesting to note that wave I terminates at the baseline in over half of the subjects. This implies that there are no significant slow waves of wave I which extend into the next wave. This feature should make it possible to quantify, by the area under the curve, the relative number of axons firing in wave I when, with the same subject, experimental conditions are varied. A similar comment applies to those cases where wave II also ended at the baseline; in contrast, there is indirect evidence that the second wave in the cat has slow-wave components (Jewett, 1970).

The positivity of waves I through VI is consistent with the hypothesis that these potentials are recorded in a part of the far field toward which the action potentials of the auditory system are moving (*see* Jewett, 1970). Given a field in a three-dimensional volume-conductor, it should be possible at some locations to find negative potentials that arise from the same neuronal aggregates which generate the positive waves recorded at the vertex. Thus, since the polarity of a response is peculiar to the recording location, rather than to the generator, we have, in our labelling of the waves, avoided mention of polarity; we hope this will facilitate comparisons of wave shapes recorded from different locations. Far-field-response wave shapes can probably be compared with each other directly as measured from the stimulus, without concern for phase shifts, since distributive capacitance effects are small; in cats, the latency in the development of an electric field from a 2,000 Hz dipole stimulus occurs in 16 to 21 microseconds over 6 mm. distance (L. Nelson and B. Rutkin, personal communication). No data on skull and scalp effects are available.

The scalp-recorded waves we have obtained conform to our definition of far field potentials, namely, the position of the vertex electrode over a distance of a few centimetres is not critical in determining wave shape. This is in marked contrast to the longer latency auditory evoked potentials mapped by Vaughan and Ritter (1970). They concluded on the basis of the differences in wave shape from different scalp locations that the generators of potentials arising 200 msec after the start of a tone burst were in the cortex. Thus, the distribution of the scalp potentials that we recorded is consistent with the interpretation that these potentials (including waves V, VI and VII) arise from even more distant (and deeper) generator locations. The ear canal was the only location examined in which small changes in electrode position significantly affected the waves. Comparison of the needle electrode and wick electrode recordings from the ear canal leads us to suspect that mapping along the canal will show significant changes in wave shape within a short distance. The

extreme ear-canal placements resorted to by some investigators to record N_1 (Yoshie *et al.*, 1967; Yoshie, 1968; Portmann *et al.*, 1968; Coats and Dickey, 1970) suggest that responses further out in the canal do not have the appearance of the published wave forms. Since the wick electrode showed positive waves and the subcutaneous needle showed negative waves, there must be some zero-potential line in the ear canal, possibly beneath the skin surface. Sohmer and Feinmesser (1970) have considered that the potentials they have obtained were due to the ear lobe, relative to an "indifferent" vertex, although they obtained similar waves from the ear canal relative to the vertex. With respect to later waves (about wave III on) Jewett *et al.* (1970) found that the neck as a reference point was similar to the ear lobe and that the wrist and neck were isopotential. Thus, we have tended to refer to these as vertex potentials, although it is unlikely that any point will be on a zero-potential line for all of the multiple generators of these waves. If there are significant potentials at the ear lobe, then the use of the ear lobe as a grounding point could, under some circumstances, influence the wave shapes obtained. Jewett *et al.* (1970) frequently used the wrist as a ground and found no difference between grounding the wrist or the ear lobe, with respect to later waves.

That waves I through IV became increasingly indistinct as the repetition rate increased is of interest. The effect of one stimulus may have overlapped into the period of the following stimulus, as in the case of the N_1 response (Yoshie *et al.*, 1967) and late auditory responses (Davis *et al.*, 1966). Diminution in action-potential height with repetitive firing would lead to decreased wave height, as was observed with wave I; the observed decrease of about 20 per cent in changing from 2.5 stimuli/sec to 20 stimuli/sec is similar to the findings of Yoshie (1968) with respect to N_1 in man. Since post-synaptic potentials may make up part of the observed far-field response (Jewett, 1970), it may be that at higher rates there is a prolongation of these potentials into the time between waves; this could explain the increase in height of waves IV and V. An increasing temporal variability with increasing frequency would make the waves less distinct but would be expected to lower the peaks while keeping the area constant; this is not observed. Finally, descending pathways such as the olivocochlear bundle may have reduced the response. The action of the middle-ear muscles might be expected to have reduced the apparent intensity and hence to have increased the latency of wave I, but there were no observable latency changes (fig. 6F). It should be noted that the waves were particularly indistinct when the repetition rate had been increased until the stimuli were sensed as a low "raspy tone."

These responses are sufficiently reliable that we have presented recordings from all subjects thus far stimulated with clicks. The auditory far field of one additional subject (recorded with a bandpass of 10 Hz to 2 Hz) was published previously (Jewett *et al.*, 1970, fig. 2B); new recordings from the other two subjects first reported in Jewett *et al.* (1970) were made at a similar band-pass and are presented here. The high degree of run-to-run consistency that we have reported (Jewett *et al.*, 1970) was also found by the present recording method which is more consistent than the earliest components found in other laboratories (e.g. Mendel and Goldstein,

1969, fig. 2; Sohmer and Feinmesser, 1970). We thus conclude that waves I through VI have sufficient reliability to be worthy of establishing clinical and experimental norms. Wave V will probably be the best basis of comparison across individuals and between different laboratories because its amplitude makes it the easiest to record and it can be recorded in only 100 seconds at repetition rates of 20 stimuli/sec. Certainly this response might be considered when objective audiometry based upon latency of response to one or a few fixed intensities is developed.

Besides offering a means of recording eighth nerve responses that obviate some of the disadvantages of ear-canal needle electrodes, averaging from the vertex makes possible panoptical recording of electrical events in the auditory system, beginning near the periphery and extending up to and past the auditory cortex (assuming that recordings of longer duration are also obtained). The similarity of human and animal forms (*see* previous discussion) suggests that some waves are generated by synaptically activated neurons in the brain-stem. Thus, these waves may provide a measure of subcortical function in humans under a variety of situations and conditions.

From personal experience, we attest to the almost uncontrollable urge to view the shape of an average evoked potential as being the wave shape of the typical neural response. With such an erroneous view, it is easy to ascribe differences between averages, when no experimental variables are changed, to Gaussian variability of the signal just as one might when viewing single sweep recordings that have a signal-to-noise ratio of 20:1; but the averaging process reduces variability from *all* Gaussian noise sources, including biological noise, while the ratio of the Gaussian variability of the signal to the Gaussian variability of the noise remains unchanged. When dealing, as in our work, with signal-to-noise ratios of 1:500, the ratio of range of signal variability to the ratio of range of noise variability may be on the order of 1:2,000. Under these circumstances, Gaussian signal variability is not detectable and, considering the accuracy with which the averages are recorded, run-to-run differences are best ascribed to variability from uncontrolled systematic variations in the response, from other non-Gaussian variations in the signal, or from noise. Note that the source of the largest amplitude noise, the EEG, has, even at its higher frequencies, periods that exceed the time between waves I and V; variability from this source can easily modify the average of several waves.

SUMMARY

Averaged potentials recorded from the vertex of relaxed humans in response to auditory "clicks" showed a series of waves (labelled I through VII) with latencies as short as 1.4 msec to the peak of the first wave. The waveform was quite consistent from run-to-run in the same subject, even over a period of months. The first six waves were detectable in all subjects, although the wave shapes differed in some details. Wave V, with a latency range of 4.6 to 5.1 msec and a magnitude range of 0.6 to 1.4 μV was the most easily identified across all subjects, and may serve as a basis for clinical norms. Distinctiveness of the waves decreased as the repetition rate was increased; the best averages were obtained at 2 stimuli/sec.

Wave I showed the same starting and peak latencies as N_1 recorded simultaneously from the ear-canal. This, together with other evidence, suggests strongly that wave I is generated by the action potentials of the eighth nerve. By analogy with similar recordings from animals, waves II through IV are probably from the brain-stem auditory system and can be used to determine subcortical function of the auditory system in clinical conditions. The waves meet the criteria we have set forth for "far field" recordings because there were no significant differences in wave shape in simultaneous recordings from scalp positions 7 cm apart.

If the high frequency cut-off of the recording system was as low as 100 Hz, the waves were not detected and an artifactual increase in latency of following waves occurred. Tone pips of high frequency also gave responses similar to those of the clicks.

ACKNOWLEDGMENTS

We thank B. Rutkin, M.S.E.E., for suggesting the term "far field," H. Dedo, M.D., for placing the ear canal electrode, and J. MacMillan for editorial assistance. Supported in part by United States Public Health Service Training Grant MH-7082 and the University of California, San Francisco, School of Medicine Committee on Research Evaluation and Allocation.

REFERENCES

- BICKFORD, R. G., JACOBSON, J. L., and CODY, D. T. R. (1964) Nature of average evoked potentials to sound and other stimuli in man. *Ann. N.Y. Acad. Sci.*, **112**, 204-218.
- BORSANYI, S. J. (1964) Some aspects of auditory evoked potentials in man. *Ann. Otol. Rhinol. Lar.*, **73**, 61-71.
- BULLOCK, T. H., GRINNELL, A. D., IKEZONO, E., KAMEDA, K., KATSUKI, Y., NOMOTO, M., SATO, O., SUGA, N., and YANAGISAWA, K. (1968) Electrophysiological studies of central auditory mechanisms in cetaceans. *Z. vergl. Physiol.*, **59**, 117-156.
- COATS, A. C., and DICKEY, J. R. (1970) Nonsurgical recording of human auditory nerve action potentials and cochlear microphonics. *Ann. Otol. Rhinol. Lar.*, **79**, 844-852.
- CODY, D. T. R., JACOBSON, J. L., WALKER, J. C., and BICKFORD, R. G. (1964) Averaged evoked myogenic and cortical potentials to sound in man. *Ann. Otol. Rhinol. Lar.*, **73**, 763-777.
- DAVIS, H., ENGBRETSON, M., LOWELL, E. L., MAST, T., SATTERFIELD, J., and YOSHIE, N. (1964) Evoked responses to clicks recorded from the human scalp. *Ann. N.Y. Acad. Sci.*, **112**, 224-225.
- , MAST, T., YOSHIE, N., and ZERLIN, S. (1966) The slow response of the human cortex to auditory stimuli: recovery process. *Electroenceph. clin. Neurophysiol.*, **21**, 105-113.
- FISCH, U., and SCHULTHESS, G. v. (1963) Electromyographic studies on the human stapedial muscle. *Acta oto-lar.*, **56**, 287-297.
- GRINNELL, A. D. (1963) The neurophysiology of audition in bats: intensity and frequency parameters. *J. Physiol., Lond.*, **167**, 38-66.
- JEWETT, D. L. (1970) Volume-conducted potentials in response to auditory stimuli as detected by averaging in the cat. *Electroenceph. clin. Neurophysiol.*, **28**, 609-618.
- , ROMANO, M. N., and WILLISTON, J. S. (1970) Human auditory evoked potentials: possible brain stem components detected on the scalp. *Science, N.Y.*, **167**, 1517-1518.
- MENDEL, M. I., and GOLDSTEIN, R. (1969) The effect of test conditions on the early components of the averaged electroencephalic response. *J. Speech Hear. Res.*, **12**, 344-350.

- PORTMANN, M., ARAN, J. M., and LE BERT, G. (1968) Électro-cochléogramme humain en dehors de toute intervention chirurgicale. *Acta oto-lar.*, **65**, 105-113.
- RUBEN, R. J., BORDLEY, J. E., and LIEBERMAN, A. T. (1961) Cochlear potentials in man. *Laryngoscope, St. Louis*, **71**, 1141-1164.
- , SEKULA, J., BORDLEY, J. E., KNICKERBOCKER, G. G., NAGER, G. T., and FISCH, U. (1960) Human cochlea responses to sound stimuli. *Ann. Otol. Rhinol. Lar.*, **69**, 459-479.
- SOHMER, H., and FEINMESSER, M. (1970) Cochlear and cortical audiometry conveniently recorded in the same subject. *Israel J. med. Sci.*, **6**, 219-223.
- TASAKI, I. (1954) Nerve impulses in individual auditory nerve fibers of guinea pig. *J. Neurophysiol.*, **17**, 97-122.
- VAUGHAN, H. G., Jr., and RITTER, W. (1970) The sources of auditory evoked responses recorded from the human scalp. *Electroenceph. clin. Neurophysiol.*, **28**, 360-367.
- YOSHIE, N. (1968) Auditory nerve action potential responses to clicks in man. *Laryngoscope, St. Louis*, **78**, 198-215.
- , OHASHI, T., and SUZUKI, T. (1967) Non-surgical recording of auditory nerve action potentials in man. *Laryngoscope, St. Louis*, **77**, 76-85.
- , and OKUDAIRA, T. (1969) Myogenic evoked potential responses to clicks in man. *Acta oto-lar. Suppl.*, **252**, 89-103.

(Received 17 March 1971)