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# A 40-Hz auditory potential recorded from the human scalp

**(hearing tests/auditory evoked potentials/40-Hz brain waves/sensory processing)**

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**ABSTRACT** **Computer techniques readily extract from the brainwaves an orderly sequence of brain potentials locked in time to sound stimuli. The potentials that appear 8 to 80 msec after the stimulus resemble 3 or 4 cycles of a 40-Hz sine wave; we show here that these waves combine to form a single, stable, composite wave when the sounds are repeated at rates around 40 per sec. This phenomenon, the 40-Hz event-related potential (ERP), displays several properties of theoretical and practical interest. First, it reportedly disappears with surgical anesthesia, and it resembles similar phenomena in the visual and olfactory system, facts which suggest that adequate processing of sensory information may require cyclical brain events in the 30- to 50-Hz range. Second, latency and amplitude measurements on the 40-Hz ERP indicate it may contain useful information on the number and basilar membrane location of the auditory nerve fibers a given tone excites. Third, the response is present at sound intensities very close to normal adult thresholds for the audiometric frequencies, a fact that could have application in clinical hearing testing.**

When a person cannot, or will not, tell the interested observer what he hears, it has in the past been difficult to obtain trustworthy measurements of hearing. The recent advent of electrophysiological tests of hearing and comprehension has radically changed this situation (1, 2). In these tests one records the listener's brainwaves while sounds are presented via loudspeaker or earphones; the sounds generate electric responses within the brain that are readily extracted by a computer (Fig. 1A). The resulting sequence of brain potentials, known as event-related potentials (ERPs), begins within a millisecond or two of stimulus delivery and continues thereafter for a half second or more. We deal here with the series of waves that appears 8–80 msec after stimulus delivery, the so-called middle-latency response (MLR). We report a way to extract it from the brainwaves, describe several properties of the response so obtained, and, among other things, show it to predict adult auditory thresholds in a highly reliable manner.

## METHODS

Any group of instruments that competently generates acoustic signals, amplifies brain waves, and averages ERPs (Fig. 1A) can be used to demonstrate the phenomenon to be described here. The response was, in fact, discovered by one of us (P.J.T.), using a stimulator, amplifier, and computer built in the laboratory (3). Since then we have used four different types of signal generators, several types of earphones (including a hearing aid transducer) to produce the monaural clicks or tone bursts (usually 6-msec duration, 2-msec rise and fall) employed in this study, and four different commercial brands of averaging computers. The brain waves, usually recorded between electrodes at forehead and earlobe of the ear stimulated, were amplified at a gain as near to $10^5$ and with bandpass as near to 10–100 Hz as the settings of the particular amplifier in use allowed.

Subjects were 20 adults, including two of the authors (R.G. and S.M.) all of whom (except R.G.) were audiometrically normal. Three subjects, repeatedly studied over a 3-month period, provided most of the data reported here. Recordings were made with subjects seated or lying comfortably, usually awake but sometimes dozing or in light sleep. Ambient sound ranged from that in a sound-proofed chamber to that of an ordinary laboratory room. R.G. made most of his own recordings by himself, wearing earphones while seated facing the apparatus he was operating. We wish to emphasize that successful recording of the phenomenon we report can become routine wherever available instruments and expertise make the recording of human evoked potentials possible.

## RESULTS

### The 40-Hz ERP phenomenon

Our method for displaying the MLR can be described as follows, with the help of Fig. 1. Fig. 1*B* shows typical click-evoked MLRs extracted from the electroencephalogram recorded through electrodes located at forehead and on the ear. The response consists of a series of forehead-negative (N) and positive (P) waves to which subscripts a, b, c, and d have been assigned. The time interval between the successive waves in the series is about 25 msec, and so the sequence resembles a train of three or four sine waves approximately 40 Hz in frequency.

The lower section of Fig. 1*B* shows what might happen if: (*i*) every auditory stimulus were to evoke such a train of 40-Hz sinusoids, (*ii*) these stimuli were to be repeated at a rate of 40 per sec, and (*iii*) a computer triggered by every other stimulus in the train were to extract an average from the ongoing electroencephalogram measurements. The computed average, represented at the bottom of the figure, would show single waves in each 25-msec epoch, all of which would be identical in form because each represents the composite, or algebraic sum, of the waves labeled a, b, and c in the MLR sequence.

That this diagrammatic formulation must be approximately correct is suggested by the several recordings of Figs. 1, 2, and 3, which show actual computer-extracted responses to sounds repeated at rates near 40 per sec. We wish to name this composite of the MLR the auditory 40-Hz event-related potential or *the 40-Hz ERP*.

### The rate series

Fig. 1C illustrates the synthesis of the 40-Hz ERP by using actual recordings. Each record is displayed on a 100-msec time

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Abbreviations: ERP, event-related potential; MLR, middle-latency response; dB, decibel; dBSL, decibels above threshold.

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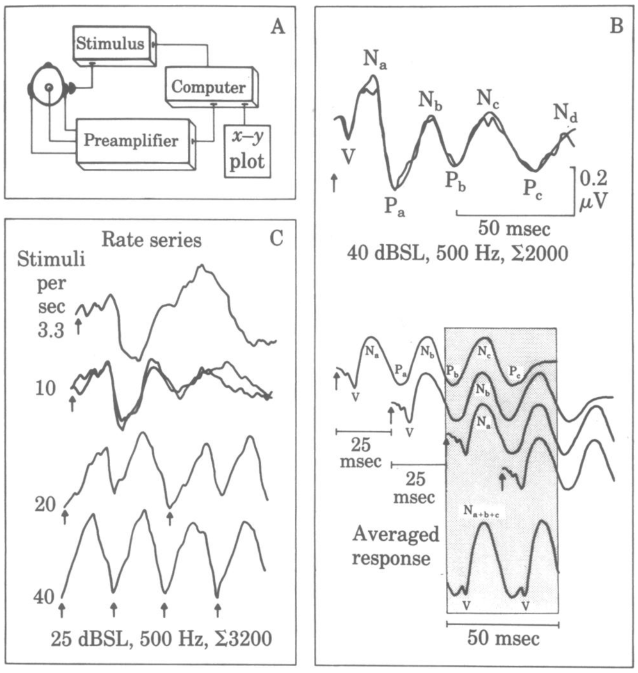


FIG. 1. (*A*) Block diagram of equipment for extracting auditory ERPs. Electrodes pasted to the subject's scalp (left) conduct brainwaves to amplifier and computer. A stimulator simultaneously energizes the earphone and initiates the computer averaging process. After the subject receives several hundred stimuli the computer memory contains only those brain potentials timelocked to the stimuli, the others having algebraically summed toward zero. (*B*) Upper, time-locked brain potentials evoked during the first 100 msec after click stimuli (arrow; 10 per sec) consist of the brainstem wave V (latency about 6 msec) and the MLR, a sequence of negative (N) and positive (P) waves subscripted a, b, c, and d (subject S.M.). Lower, diagram to show how the computer could sum the several MLR waves shown above into a single wave if the stimuli were presented at a rate of 40 per sec. (*C*) Recordings from a subject (R.G.) receiving 500-Hz tone bursts at different rates (including the 40 per sec rate of *B*) to illustrate actual synthesis of the single wave at 40 Hz from the multiple waves at lower stimulus frequencies. dB, Decibel; dBSL, decibels above threshold; Σ indicates the number of responses averaged.

base with the moments of stimulus applications indicated by arrows. At the lowest rate shown the $N_a$–$P_a$ deflection is followed by a large negative wave at about 70 msec whose relationship to the $N_1$ wave seen by those who stimulate at even lower rates (1) is unclear. At the 10 stimuli per sec rate (actually slightly less than this so as to permit every response to enter the computer for averaging) the $N_b$–$P_b$ deflection appears and the wave sequence now resembles that shown for the subject of Fig. 1*B*, despite some differences in detail. At the 20 per sec rate every 50-msec interstimulus interval contains a pair of waves not unlike the two that occupy the first 50 msec of the 10 per sec response. When the stimulus rate rises to 40 per sec, each 25-msec interstimulus interval contains a single wave, the approximate algebraic sum of the two waves seen at corresponding places in the 20 per sec response. Fig. 1*C* thus suggests that the 40-Hz ERP does indeed result from the consolidation, or superimposition, of the successive N–P deflections seen in recordings made at lower rates.

Still another way to visualize how the 40-Hz ERP evolves out of the more or less independent 40-Hz sinusoids that make up the MLR is to plot wave amplitudes against stimulus rate, as in Fig. 2*A*. The maximal response amplitude is attained with a 40-Hz stimulus rate, as would be predicted if algebraic summation of separate 40-Hz sinusoids were taking place. Similarly, the minimal amplitudes seen at stimulus rates around 25 and 55 Hz are also predicted by the theory because near these rates the successive 40-Hz waves should appear out of phase and thus cancel in the computer memory during the averaging process.

These rate studies, though so far performed on only a few normal adults, permit several conclusions. First, the MLR, in the frequency domain, resembles one or more cycles of a 40-Hz sinusoid. Next, though individuals vary in the number of such cycles they produce at low stimulus rates, at the 40-Hz rate their responses are similar. Third, the 40-Hz ERP is easy to record from normal subjects; we have not failed in over 20 attempts. Finally, the 40-Hz ERP has with one exception always peaked in the 35 to 45-Hz region at a rate near 40 Hz, but the actual optimal rate probably varies from one person to the next. Validation of these conclusions awaits the outcome of the extensive parametric studies that need to be performed.

### The intensity series

A plot of response amplitude against intensity for 250-Hz tone bursts appears in Fig. 2*B*, along with several of the records used in its construction. The 40-Hz ERP varies with intensity in the following two interesting ways.

First, response amplitude rises with intensity increase, and this amplitude rise is so rapid near threshold that at 10 or 15 dBSL it reaches nearly half the size it will display at 40 or 50 dBSL. This relationship undoubtedly reflects a similar steep amplitude rise known to characterize certain of the MLR waves (4, 5).

This remarkable property can be applied to threshold estimations as in Fig. 2*C*, where 40-Hz ERPs to clicks and tones are shown to approximate, within a few dB, the behavioral threshold (0 dBSL) of two subjects. These estimates were made with no difficulty and within a short period of time (each tracing shown there took about 2 min to obtain). The reliability of the 40-Hz ERP as an estimator of threshold was further tested with seven young adults, who received monaural 500-Hz tones at 5, 10, and 15 dBSL. All developed 40-Hz ERPs to the 15- and 10-dB signals, and all but two did so to the 5-dB signals. These results indicate it should be possible to apply the test routinely to clinical patient populations, and to expect reasonably accurate threshold estimations from them.

The 40-Hz ERP also varies in latency with stimulus intensity. Technically, latency is the time interval between stimulus onset and the response it initiates. In the present context this "response" must be defined arbitrarily as some feature of the 40-Hz ERP that regularly follows the stimulus, and for convenience this feature will be taken to be the peak of the forehead-positive wave that follows the stimulus. In Fig. 3*A* this point is marked by arrows.

The latency of the 40-Hz ERP as defined in this way ranged between 100 and 200 μsec (mean 156) for each dB of intensity change in 11 determinations on two of our subjects (R.G. and P.G.). The signals used included clicks and tones (250, 350, and 500 Hz) presented at intensities between 5 and 50 dBSL. (The variability in the data is probably measurement error, not a systematic relationship to stimulus type or intensity.) The corresponding change in latency for a different ERP threshold measure, the auditory brainstem response, is precisely known: 40 μsec/dB (2). As for the MLR, the values are said to vary from 0 for the $N_a$ wave through 75 for $N_b$ to 175 μsec/dB for $P_c$ (1, 5). Our estimate of about 150 μsec/dB for the 40-Hz ERP agrees reasonably only with the $P_c$ estimate, and so, tentatively, we may suppose that the physiological processes that determine the way $P_c$ latency changes with stimulus intensity also operate for the 40-Hz ERP.

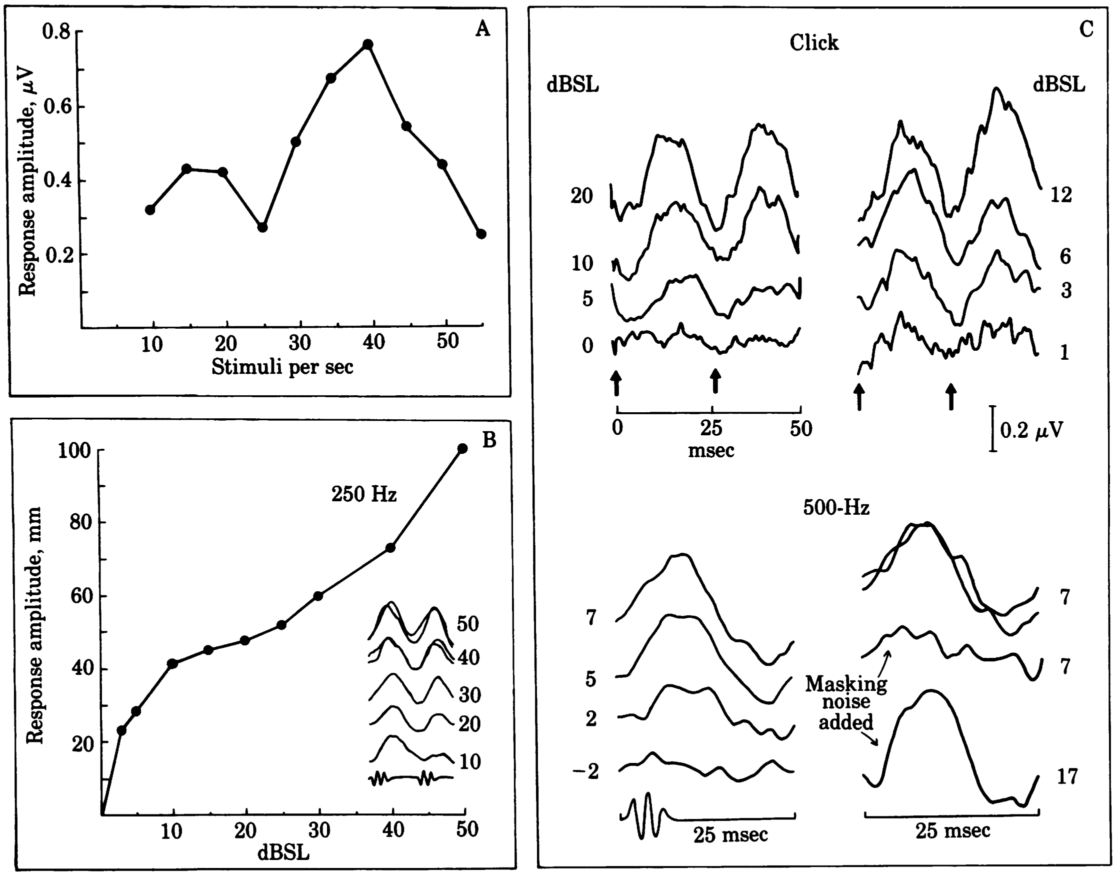


FIG. 2. (*A*) Response amplitudes at different stimulus rates for one subject (P.G.), showing a peak at about 40 stimuli per sec and minima at about 25 and 55 stimuli per sec. (*B*) Response amplitudes at different intensities of a 250-Hz stimulus. *Inset* shows some of the data and the stimulus sequence employed, on a 50-msec time base (subject P.G.). Response is given in terms of peak heights at constant $x$–$y$ plotter settings. (*C*) Threshold estimates obtained with click stimuli from a male adult (S.M.; upper left recordings) and with click and tone stimuli from a female adult (P.G.; other three sets of recordings). In each case 0 dBSL refers to the monaural threshold intensity established immediately prior to obtaining the records shown. Recordings at lower right illustrate in addition the masked threshold approximation; the 40-Hz response to the 7-dBSL tone disappeared when wide-band noise just sufficient to abolish the sensation was added, but reemerged when, after the tone intensity was raised to 17 dBSL, the tone was heard once more.

### The frequency series

Just as stimulus rate and intensity control the 40-Hz ERP amplitudes and latencies, so too does stimulus frequency. An example is illustrated for a single subject in Fig. 3*A*, where responses to four different tones have been redrawn and superimposed on the same 25-msec time base. Two effects of stimulus frequency on the 40-Hz ERP stand out: response amplitude drops as frequency rises, and the response latency (as defined in the previous section) shortens. These two effects have been observed in all subjects so far tested, and to approximately the same degree in each of them. Specifically, the ratio of the response amplitudes yielded by 250-Hz tones and 5000-Hz tones, which in Fig. 3*A* approximates 3, has been found to be 3 and 2, respectively, in two other subjects. Similarly, when the latency of the 5000-Hz response is subtracted from that of the 250-Hz response, which in Fig. 3*A* yields about 12 msec, this latency difference was found to be 10.5 and 6 msec, respectively, in the two other subjects. The subject yielding the smallest numbers in each case (R.G.) is the only one with a high-frequency hearing loss.

Several explanations for these dramatic influences of stimulus frequency upon the 40-Hz ERP are possible. First, the stimulus envelope is partly responsible, because it rises to maximal amplitude over a 2-msec interval during which 12 complete cycles of a 6-kHz tone, each progressively greater in amplitude, move the eardrum, whereas for the 500-Hz tone only one such cycle appears. It can be computed from this that, except at threshold, the 6-kHz tone will almost always activate a given auditory nerve fiber somewhat earlier than the 500-Hz tone that can also activate it. A second possible factor is related to the intensity effects discussed in the previous section. The measurements of Fig. 3*A* were nominally made at 40 dB above threshold (40 dBSL), but an error of 1 dB in this estimate would introduce a latency error of about 150 μsec. If this error were to be 10 dB, which is highly unlikely, the latency error would, however, be only 1.5 msec.

There appears, finally, to be only one viable explanation for the coupled facts that amplitude rises and latency increases with a drop in stimulus frequency. With such a drop the length of basilar membrane put into motion increases, the position of the peak of the basilar membrane excursion moves away from the stapes, and more time is needed for the mechanical wave to reach this peak region. In other words, as Bekesy showed, the mechanical wave activates increasingly larger amounts of the basilar membrane and takes a longer time to do this as stimulus frequency drops. Correspondingly, increasingly larger numbers of neurons become excited, and more time is needed to initiate and complete their excitation. The extent to which these changes taking place at the cochlear level are actually reflected in the 40-Hz ERP amplitude and latency changes shown in Fig.

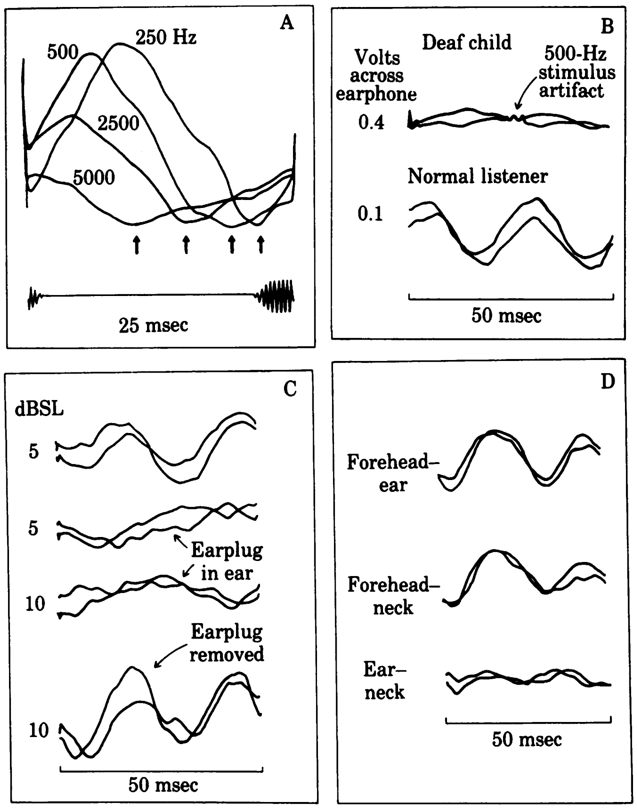


FIG. 3. (*A*) The 40-Hz ERPs evoked at the same sensation level (40 dB) but by tones of different frequency. The same stimulus envelope was used for all stimuli; the bottom trace shows the 2500-Hz tone burst. Arrows locate the points where forehead-positive deflections peak for the different frequencies. Note that as frequency drops the peaks move to the right and the response amplitude increases. (*B*) Recordings taken within minutes of each other, showing that a 500-Hz tone burst that produces the 40-Hz ERP from a normal ear does not do so when presented to a deaf ear despite a 12-dB increase in intensity. (*C*) The 40-Hz ERP produced by a near-threshold 500-Hz signal (top trace) disappeared when an earplug was inserted into the ear (second trace); a 5-dB increase in signal intensity did not make the tone audible nor did it produce a 40-Hz ERP (third trace) until the earplug was removed (bottom). Subject: P.G. (*D*) The 40-Hz ERP recorded between electrodes at forehead and earlobe (top trace) closely resembles that recorded between forehead and neck, which shows that 40-Hz ERP generators are located near the forehead, the ear and neck regions, or both. The nearly flat recording with the ear–neck combination demonstrates that the 40-Hz ERP at both sites is nearly the same, presumably nearly zero because it is implausible that potentials of either muscle or brain origin would be both large and equal at these two sites. Neck electrode is on spinous process of the seventh cervical vertebra. Stimuli: clicks, about 40 dBSL. Subject: R.G.

3*A* is of course an open question. One can, however, estimate that perhaps 5 msec of the latency increase could be explained in this manner, and virtually all of the amplitude change. Arguments supporting these assertions will be presented elsewhere.

### Controls

The measurements summarized in Fig. 3 *B*, *C*, and *D* seem to exclude the possibility that the 40-Hz ERP is an uninteresting artifact of either electrical or physiological origin. They all argue against the idea that the electrical signal energizing the earphone enters the recording apparatus through the recording electrodes and creates a "response" through amplifer overload. Fig. 3 *B* and *C* make the further point that the 40-Hz ERP has been invariably related to whether a sensation is experienced, not to whether or how much electrical energy has been delivered to the earphone. Fig. 3*C* is an especially convincing example of this rule: the earplug abolished both auditory sensation and the 40-Hz ERP at signal intensities (5 and 10 dBSL) that, in the absence of the plug, produced them both. The masking example of Fig. 2*C* similarly stresses that without the sensation of a sound repeated 40 times per second there is no 40-Hz ERP.

Reflex muscle contractions initiated by the sound stimulus represent physiological artifacts that potentially contaminate all MLRs. The muscles of principal concern here lie near the earlobe electrode, where they vary in size, responsivity, and threshold sensitivity from one subject to the next. It is improbable that our recordings represent or even contain muscle artifact because the weak stimulus levels used generally fail to produce reflex responses. Fig. 3*D* specifically argues that the forehead electrode is the major source of the 40-Hz ERP response in the forehead–ear combination of this study. The earlobe electrode, though close to the periauricular muscles of concern, is evidently not near an important 40-Hz ERP generator because little deflection appears in the earlobe-to-neck electrode combination. All records employing an electrode on the forehead, by contrast, show large 40-Hz waves of approximately the same amplitude and phase. The data of Fig. 3*D*, incidentally, are part of a mapping study we do not report here except to state that the forehead electrode site usually yields larger responses than does Pz (as defined in the 10–20 international system for electrode placement on the scalp) and slightly smaller ones than Cz and Fz.

## DISCUSSION

The auditory brainstem response, currently the most widely used method of estimating hearing threshold by electric response audiometry (see ref. 1 for a review), has revolutionized the hearing assessment of infants and children. It provides secure estimates of hearing threshold, even in the premature infant, but unfortunately not at those tone frequencies upon which perception of speech sounds critically depends. To fill this gap both Suzuki *et al.* (6) and Davis and Hirsh (7) offer an ERP that appears about 10 msec after presentation of tones in the speech range (500–2000 Hz) as an alternative or adjunct.

Historically, MLRs have been repeatedly advocated for this purpose (see ref. 8 for a review) because they offer "perhaps the best means of evaluating thresholds at a variety of frequencies" (1). The 40-Hz ERP described here, a composite of the several waves making up this MLR, may prove to be a practical way to establish the reliable frequency-specific threshold estimates so badly needed in electric response audiometry. No other known method, in any event, reveals so promptly the sensitivity to stimulus frequency and intensity shown in the recordings of Figs. 1–3. It remains to be seen, however, whether similarly reliable data can be obtained from those patients who most need this evaluation—the infants and difficult-to-test children who are candidates for hearing aids.

The dramatic changes in amplitude and latency shown in Fig. 3*A* to accompany stimulus frequency change are properties shared by the 40-Hz ERP with its progenitor, the MLR (4). If these changes accurately reflect mechanical events going on at the basilar membrane level, as we suggest here, both responses contain useful and perhaps even detailed information about the population of auditory neurons being excited within the cochlea. If further research supports this hypothesis, the 40-Hz ERP could offer a practical way to examine, through large electrodes placed on the human scalp, the distant basilar membrane events now visualized mainly through microelectrodes inserted into animal brains.

Few data exist concerning the anatomical structures and physiological processes that give rise to either the MLR or the 40-Hz ERP. Furthermore, the literature is largely silent on the extent to which sleep, drugs, anesthesia, post-traumtic coma, and still other altered states of consciousness influence the MLR except to state that sleep and light sedation have little effect, whereas surgical anesthesia abolishes them (8, 9). It is commonly held that the MLR reflects activity in the classical auditory pathway (8), although its sensitivity to anesthetics (9) makes the additional involvement of an extralemniscal, or reticular formation, path seem at least probable. An exclusively "cortical" origin for either the MLR or the 40-Hz ERP seems doubtful for still another reason; Fig. 2*A* demonstrates its amplitudes to be largest at rates around 40 Hz, whereas in both animals (10) and man (1) cortical responses diminish in amplitude when sounds are repeated as slowly as once each second, and they approach zero at rates of 20 per sec. Further experiments aimed at identifying the brain structures and processes that generate both the 40-Hz ERP and the MLR are clearly in order.

The existence of the auditory 40-Hz ERP has led us to look for comparable phenomena in vision and the other sensory modalities. In his classical description of the human ERP to light flash (11), Ciganek showed a pair of deflections in the 30- to 90-msec poststimulus interval (his "primary response") that could be considered analogues of the auditory MLR. In describing the ERPs associated with modulations of light intensity, Regan (12) said they "reach a maximum amplitude in the high frequency range between 45 and 55 c/sec." Regan's optimal rate is approximately double the frequency of Ciganek's primary response, and so his ERPs are not readily related to Ciganek's components in the way the auditory 40-Hz ERP is related to the MLR. However, Regan's discovery that flickering lights produce large ERPs when the flicker rate is around 50 Hz clearly defines a visual "50-Hz" ERP that is at least conceptually like the auditory 40-Hz ERP described here. Whether, for a given subject, the visual and auditory rate series (as in Fig. 2*A*) are similar would be interesting to know.

Namerow *et al.* (13) studied somesthetic ERPs elicited by shocks to the median nerve at the wrist. Their graph of response amplitude vs. increasing stimulus rate (comparable to our Fig. 2*A*) drops nearly linearly except for a small peak at 60 Hz. It should, however, be pointed out that if a somesthetic response comparable to the auditory 40-Hz ERP did exist Namerow *et al.* might have missed it because they used large (20-Hz) jumps in stimulus rate and presented their data as the average over 17 subjects.

In the olfactory bulb the appearance of a burst of 40-Hz brain waves when animals sniff, an act that presumably stimulates smell receptors in the nose, has been known for many years (14). A similar 40-Hz rhythm regularly appears in other mammalian (man, monkey, dog, and cat) and avian brain regions (see ref. 15 for a summary), where it can be significantly increased in amount if the animals (cats) are given milk reward when they produce the waves (16) and if the people perform arithmetic and other cognitive tasks (17). Whether these widespread, labile, ongoing 40-Hz rhythms, which have been interpreted as indexing "a focused state of cortical arousal" (17) are related in any way to the auditory 40-Hz ERP reported here is a matter for future experiments to settle.

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