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THE AUDITORY NEURAL NETWORK IN MAN

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INTRODUCTION

This discussion of the auditory system in man first covers - very briefly - the principles of anatomy and physiology necessary for understanding the brain wave recordings made from the scalp of normal people. It then describes the brain waves evoked by sounds and relates certain of their features to the physical aspects of the stimulus, on the one hand, and to the psychological state of the listener on the other. This essay takes the position that such data obtained through probes located outside the head can reveal a surprisingly large amount of detail about what is going on inside the head. It argues that analysis of such records enables one to detect the response of the nervous system to an acoustic message at the moment of its inception at the ear, and to follow the progress of the acoustic message up through the various brain levels as progressively more complex operations are performed upon it. We shall see that even those brain events responsible for the highest level of signal processing - distinguishing between similar signals and making decisions about them - seem to generate characteristic and identifiable electrical waves.

This paper also introduces some theoretical speculation about these electrophysiological data because the organizers of this conference have encouraged us all to do this. Perhaps these speculations will provoke both the physiologists and physicists into an interdisciplinary discussion aimed at generating a more heuristic model of the functioning brain than any of the ones we now possess.

AUDITORY ANATOMY AND PHYSIOLOGY

In vertebrate animals like ourselves a sound striking the ear activates nerve cells in the particular sequence and order diagrammed in the left half of Fig. 1. In this wiring diagram the input, or cochlea, is where the sound signal is converted into nerve impulses, the coin of the realm for all nervous systems. This physiological transducer, the cochlea, closely resembles a microphone in that it converts sound pressure waves having dimensions of frequency, amplitude and duration into energy in another dimension. But here the similarity to a microphone ends, for the new signals are nerve impulses, not electrical signals. Since nerve impulses are physiological membrane depolarizations that propagate themselves from the site of initiation along the entire length of the nerve fiber and into its terminal ramifications, they do in fact generate electrical events which can be recorded at a distance, but these are epiphenomena related to, but not critical for, the signal-analysis in which the brain is engaged.

Each sound initiates discharges in many nerve cells, and the details regarding number and temporal distribution of these discharges is what characterizes one sound from another (1, p. 1487). The neural input to the system, the human auditory nerve, contains some 30,000 separate nerve fibers collected into a cable through which must pass all the auditory information that ever enters the brain. This cable of nerve fibers terminates in the cochlear nucleus, the first relay region of the auditory network (Fig. 1). Here each of the 30,000 separate input fibers distributes its message, through synapses, to postsynaptic nerve cells; a ratio variously estimated as 1 input (or presynaptic) neuron to tens of hundreds of output (or postsynaptic) neurons exists, even though the total number of output neurons is only about twice the number of input neurons (Table I). The input-output relationships just described for the cochlear nucleus can serve as the model for what takes place in each synaptic relay beyond. Every auditory nucleus - for example the medial geniculate nucleus of Fig. 1 - receives an input from below, performs synaptic operations upon it, and delivers an output to the next higher level in the network.

Two additional features of the auditory network that increase its complexity are worth mentioning. First, as shown in Fig. 1, another collection of fibers also conducts impulses from cochlea to cortex, doing this via what is called the reticular formation (shaded portions of the figures). Although this reticular pathway of the network also contains many synapses, there are no identifiable collections of them to which specific names can be given. These reticular synapses, unlike those in the classical pathway, can be completely inactivated, or switched out of the circuit, by certain drugs and anesthetics. The second feature of note pictured on the right in Fig. 1, is the substantial collection of neurons that originate at higher levels and feed backwards into lower synaptic regions where some of them at least seem to exert negative feedback control over the signal. In what follows no further consideration will be given to these two additional details of the auditory wiring diagram.

An important characteristic of the auditory network is that it continuously expands in size. Some idea of the extent of this expansion is conveyed by Table I which summarizes the results of counting the post-synaptic cells in the several specific auditory nuclei of the monkey. It would however, be a mistake to think of the auditory network as ending at the specific cells in the cortex which receive input from the medial geniculate; these cortical cells in turn project upon other cells both within the cortex and outside of it, and these in their turn pass the message along still further. The total number of cells involved in these extensive ramifications of the auditory network beyond the specific auditory cortex cannot be stated accurately, and the number 10^8 given in Table I intends only to indicate that it must be huge.

The anatomical considerations here under discussion have been summarized diagrammatically in Fig. 2 where the artist has put the human auditory pathways and nuclei in their proper places. The figure also pictures the electrical responses that would be evoked in each region after a sound such as a click strikes the ear. These imagined responses have actually been recorded in animals with separate electrodes embedded in each of the nuclei. Three points should be made regarding them. First, the electrical response can be seen to begin progressively later in time as the message progressively invades the auditory network; in physiological terms the delay (latency to onset of the response) progressively increases with distance from the input, with the auditory cortical latency measuring about 15 msec in man. Second, the duration of the response activity produced increases as the effects of the stimulus reach higher and higher levels in the nervous system. Finally, note the similar shape of these responses; all move initially downwards - which is active-electrode positive in the conventions used here - and then in an upward, or negative direction. Physiologists have correlated the positive portion of such an electrical sequence with the arrival of impulses at the nucleus and the negative portion with the synaptic events going on within it. I shall make use of these three facts in the final section of this paper.

THE HUMAN AUDITORY EVOKED RESPONSE

Fig. 3 schematizes the sound-induced pattern of electrical waves which can be recorded from the human scalp through one electrode placed at the highest point of the skull (vertex) and another located on the mastoid bone immediately behind the ear. Time zero marks the delivery of a click of moderate intensity through earphones or a nearby loudspeaker. The click induced brain wave pattern displays a series of apparently minor events during the first 50 msec, then develops into a sequence labelled P_1-N_1-P_2-N_2. The wave shape shown here is a composite of data from 10 normal listeners in our laboratory.

Fig. 4 replots the electrical events shown in Fig. 3 on logarithmic coordinates. This method of display permits the waves having short latencies and small amplitudes to stand out, and, so to speak, allows the eye to give approximately equal emphasis to each of the waves in the complex. One now clearly sees that the click stimulus triggers off some 15 distinguishable electrical events which follow one another in a particular and immutable temporal sequence. Every wave presumably reflects activity going on in some limited brain area, and the temporal sequence represents the orderly and progressive spread of the effects of stimulation through the pathways depicted in Fig. 1, and then from one cortical region to another.

It will be convenient to divide the time axis of Fig. 4 into three equal parts, an early decade (1-10 msec), a middle decade (10-100 msec) and a late decade (100-1000), and discuss separately the neural events taking place in each.

The early decade (1-10 msec) reflects in its first event (wave I) the activity of the auditory nerve, and in its later one (waves II-VI) the successive activation of the fiber tracts and nuclei up to approximately the medial geniculate level shown in Figs. 1 and 2. Exactly which brainstem structure is responsible for each wave is problemmatic, but one can be sure from all available evidence that the complex of events labelled II through VI displays the successive activation of the brainstem nuclei as the auditory message penetrates progressively deeper into the auditory network.

Both the size of these waves and their latency are sensitive to the strength of the acoustic signal that evokes them. Thus the latency of wave V decreases from a maximum value of about 9 msec for a sound just barely heard to a minimum of around 6 msec for the same sound 60 dB more intense. The curve describing this relationship is remarkably similar in all normal people and it shows latency to change at a rate of about 40 microseconds per dB of stimulus intensity. This tight dependency of latency upon intensity is so highly reliable in fact, that a person who knows the rule can predict with an accuracy of

± a few dB what stimulus strength some other experimenter had used to produce a record that is now being examined for the first time. Whether or not the subject had been listening at the time is irrelevant, as are other and related questions about his state of mind: whether awake, asleep, even unconscious. These waves I-VI provide, in fact, such a remarkably precise index of the stimulus strength that they can be thought of as a high quality physiological sound level meter, a very important detail that has prompted several laboratories to look into their possible use as an objective test of hearing in the clinic (2).

The waves appearing in the middle (10-50 msec) period are sometimes contaiminated by unwanted signals from such generators as the eyeball which is electrically polarized, and when moved, alters the scalp distribution of the steady current flow caused by its front-to-back polarization of several mV. With competent control of such artifactual sources of current, however, the waves in this 10-50 msec epoch seem, like their predecessors, to be strongly stimulus-bound and not state-dependent.

The late decade waves labelled N_1-P_2-N_2, by contrast, do vary in amplitude with change in subjective state. Thus N_2 is much enhanced in sleep, and the N_1-P_2 deflections increase in size when a person deliberately listens to a particular sound. The evidence for these statements has been developed over the past 10 years in many laboratories and is summarized in part in recent reports by my collaborators (3,4,5). To explain this lability in the size of the N_1-P_2 waves one must suppose that "attention" either changes the amount of activity in the generators already at work, or that some new generators are added in parallel, and at the same time. Whichever of these explanations is correct, the essential point is that a study of the responses to an auditory signal permits one to state whether that signal was processed with or without attention. The critical changes first become observable, by the way, only after the activity created by the attended signal has penetrated into the auditory network as far as it manages to get in 70-80 msec.

In certain experiments where listeners attend, the brain develops still another generator that produces a remarkable wave, the P_3 wave, with a latency of 300-500 msec. An experiment in which this happens is simple to perform and goes as follows. The listener receives clicks through earphones. These are regularly spaced at intervals of 1 sec. or so. Occasionally, and at random, a click of somewhat weaker intensity than the standard one is introduced into the train. The listener's task is to count these weaker clicks. When the evoked response to them alone is examined it reveals not only the enhancement of N_1-P_2, but the new P_3 wave as well. If this experiment is done so that the target listened for is a missing click, i.e. no stimulus at all, only the P_3 wave is visible in the response. In this instance P_3 must be a sign of those processes going on within the brain during perception itself (4).

Fig. 5 summarizes these effects of attention upon the waveshape of the evoked response. The hatched area shows the enhancement in the N_1-P_2 waves when an auditory stimulus is attended, as well as the P_3 response which appears with recognition or identification of a stimulus the listener is particularly set to hear. In the missing click experiment just described only the P_3 wave is present (4).

DISCUSSION

The electrical responses in the preceding figures portray the voltage differences developed over time between 2 relatively large conductors applied to the skin of the human head. These voltage differences reflect the algebraic sum of all the currents generated within the brain after they have passed outward through that structure and traversed the overlying bone and skin to reach the electrodes. The total number of such current generators located deep within the brain substance is large but unknown. For some of them (e.g. the auditory nerve), a location can be specified reasonably accurately, but even for these any statement regarding the direction, magnitude and time course of their output current flow contains a large error factor. To the physicist this can be thought of as the problem of a 3-dimensional volume conductor within which numerous dissimilar electrical generators drive currents of varied onset and duration along unknown paths of unknown impedance, and he may therefore consider the effort to make an analysis of the problem hardly worth his time. Many physiologists agree that these scalp recordings of brain activity are unattractive for analysis and they turn instead to the far more precise microelectrode technique. As Dr. Eccles shows elsewhere in this volume, the location of the generator in that case - a single nerve cell - can be accurately specified with microelectrodes, and its input-output relations can also be described with gratifying detail and precision.

As we have seen, however, the analysis in man of these gross surface electrical phenomena generated by auditory signals has led to certain interesting new findings and conclusions. The early group of waves (1-10 msec) reflect several aspects of the stimulus parameters with gratifying accuracy, and this fact may well lead to useful new clinical hearing tests for human patients who cannot be evaluated satisfactorily with conventional methods in the clinic. Furthermore, as we have seen, the later waves in the sequence (100-1000 msec) give us a glimpse of the brain doing its important work, so to speak, and raise the hope that they can be used to decipher ever more useful details about the brain mechanisms underlying such interesting psychological phenomena as attention and perception.

In man, where routine use of microelectrodes is clearly out of the question, scalp recordings like these are just about all there is for an electrophysiologist to study. Human subjects, when intelligent, cooperative and responsive, comprehend and follow complicated instructions to perform complicated tasks. Such people make ideal subjects for the physiologist seeking, as we do, correlations between electrical brain activity and such complex brain states as level of attention, or the ability to distinguish subtle differences between stimuli, or the performance of actions that require retrieval of information stored in memory.

Now for the theoretical speculations. If you reexamine Fig. 4, the human vertex response, you may be impressed, as I have been, by the fact that the peaks of the 15 waves seen there are almost equally spaced on this log plot. Is it possible that this spacing of the peaks reveals some useful rule about how the nervous system performs its increasingly more complex processing of the input signal?

If so, the rule would appear to be a logarithmic one relating the amount of time needed to process the incoming impulses at a given level of the auditory net to the amount of time taken for the nerve impulses to reach that level. In the simple case, which of course, the data only crudely approximate, the rule would be

$$\log(\text{processing time}) = k + \log(\text{latency})$$

where "processing time" is the duration of the input-induced synaptic events within the region in question, and "latency" is the time required to transmit the message to that point from the cochlea, the entry point into the network. This simplifies to the statement that processing time is proportional to latency.

One test of this rule is to see if it fits actual data recorded from the several auditory nuclei shown in Fig. 2. Such a comparison cannot be done for man, but it can be done for the cat auditory nuclei, using the data published by W. O. Wickelgren (6). Replotting his cat responses on the log time base (Fig. 6) suggests that some such log rule may also be being obeyed by the cat brain too, at least roughly, since, with few exceptions, the cat waves can all be said to have much the same form: the positive (or input) deflections measure out to cover almost the same number of millimeters as each of the negative (or synaptic) deflections. The agreement in the case of the medial geniculate response is particularly impressive.

To what extent can known physiological facts account for this log relationship suggested by both cat and human data? An obviously pertinent relationship will occur to the physiologists, namely the relationship between nerve fiber diameter and its conduction velocity.

This rule states that the bigger the fiber the faster it conducts its impulse. Since the numerous fibers connecting one auditory nucleus to the next do indeed vary in diameter, a 10-1 difference in conduction velocity among the fibers delivering impulses into a given nucleus is not unreasonable to postulate. Such a difference in conduction velocity would indeed cause a temporal dispersion of the input message, and it might in fact actually account for the observed increase in duration of the positive or input waves in the cat records at progressively higher structures.

We seem to need another hypothesis however, to account for the progressively increasing processing time (negative wave) noted as the message penetrates ever-deeper into the nerve net. The time taken to complete a single synaptic event does not vary as a function of where it is measured in the nervous system, so far as I know. Hence the temporal dispersion at the output of a given nucleus such as the medial geniculate might be expected to resemble the temporal dispersion at its input; instead the duration of the negative waves also progressively increases, an observation that holds for every one of the nuclei for which hard data exist. Presumably the number of intrinsic neurons available for activation within a given nucleus and/or the complexity of the circuits the nuclei make with each other accounts for this increased processing time. If so, the number and complexity of this local activity seems to grow in an orderly way with distance from the cochlea.

This prompts two questions, First, to the biologists: are there relevant morphological or physiological facts about synaptic regions that similarly show an orderly gradient as one penetrates deeper into the nervous system? If we cannot now cite any, how are we to explain the increased duration of the slow waves shown in Figs. 4 and 6?

The second question is for the physicists. We have here (Figs. 4, 6) the physiological demonstration that the longer it takes for an event to arrive at a given level in the auditory pathway, the greater the amount of time required to process, or digest it, if you will, at that level of the nerve net. I have suggested the log rule which, if correct, would have the idealized form shown in Fig. 7. Are there physical systems which similarly oscillate back and forth, doing this approximately logarithmically, as they proceed? If so, they might offer useful models for our own nervous system which approximates this temporal characteristic as it proceeds to process the acoustic signal from an initial purely physical transform into the final psychological transform we call perception, recognition, classification.

SUMMARY

A click delivered through earphones to a normal listener initiates activity in his auditory nerve which then spreads into other areas of his brain along more or less well-known anatomical pathways. This march of activity through the neural net generates electrical events over an interval lasting several hundreds of msec. Some 15 electrical waves of nearly equal amplitude (of the order of 1 microvolt) normally appear with the peaks of the successive waves being approximately equally spaced when plotted upon a logarithmic time base. This suggests that the time required to process the acoustic message increases according to a logarithmic rule as the message spreads from the auditory nerve toward the most distant structures in the network.

The form of the electrical response from the brain can be altered by certain physical changes in the input signal (e.g. its intensity, frequency distribution, rate of application) as well as by the subjective state of the listener (e.g. his level of attention, motivation, accuracy in signal detection). The dependency upon purely stimulus variables is high during the first tens of msec but decreases with time; dependency upon subjective state is the reverse, being absent initially, progressively more important beyond 50 msec post-stimulation, and the exclusive determining factor at 200-300 msec and thereafter. Thus the electrical waves generated in response to an acoustical signal reflect the features of the stimulus itself decreasingly well as the neural net is progressively invaded, whereas they reflect the "significance" of the stimulus to the listener more and more as the brain proceeds with its analysis of the signal.

The human auditory nerve net can, therefore, be described as having the following physical properties 1) it is entered at only one point (the auditory nerve) from which activity spreads into an increasingly larger number of elements; 2) the spread occurs stepwise, not continuously, because of neural barriers such as synapses imposed enroute; 3) the farther from the source such a barrier lies, the greater the time employed there to process the signal, with the rule approximating log (processing time) = K + log (conduction time); 4) human intellectual activities such as attention and the recognition of significant signals alter activities in those portions of the network most distant from the source, which is where the largest total number of elements are active and where their activities take the longest time to run their course.

Is there a non-biological system that displays similar properties and hence could serve as a model for the human auditory system? If so, it will display the following properties: 1) oscillate regularly between 2 states at a rate that slows logarithmically as it proceeds, and 2) perform increasingly more complex operations as time goes on, and 3) culminate in some final terminal state which satisfies a requirement and turns the system off.

ACKNOWLEDGEMENTS

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TABLE I

Nerve cells in the auditory nuclei expressed as multiples of the number of auditory nerve fibers. Monkey; from K-L Chow. J. Comp. Neurol. 95: 159-175, 1951.

Auditory nerve	1 (30,000 in man)
Cochlear nucleus	2
Superior olive	2.5
Inferior Colliculus	13
Medial geniculate	14
Auditory cortex	340
Entire cortex (estimated)	10^8

FIGURE LEGENDS

Fig. 1 Diagram of the auditory pathway in a typical vertebrate like man.

Fig. 2 Schema of the human auditory system in place with records showing the local electrical activity generated at each station in the pathway by a click delivered to the ear.

Fig. 3 The electrical response of the human brain following activation by an auditory stimulus. Scalp electrodes (top of head, behind the ear); gain $X10^5$; computer average of 1-200 clicks delivered at time zero.

Fig. 4 Same as Figure 3 but redrawn on log-log coordinates.

Fig. 5 Effects of attention on the brain response to clicks. Solid line: response to inattended clicks;

Fig. 6 Click-evoked electrical activity recorded via electrodes permanently implanted in the auditory nuclei of a cat; replotted from the original on log time base. CN: cochlear nucleus; SO: superior olive; IC: inferior colliculus; MG: medial geniculate; CTX: auditory cortex.

Fig. 7 Idealized representation of Figures 4 and 6 and a plot of equation given in the text.

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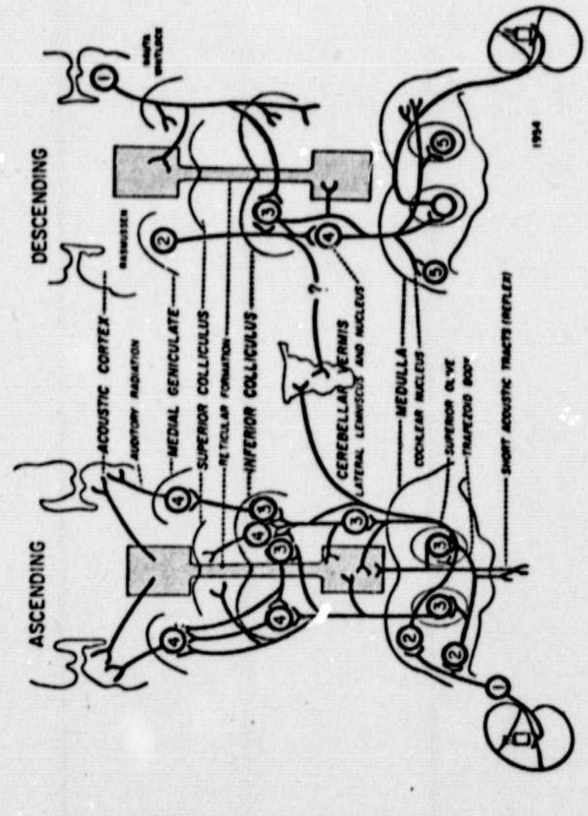
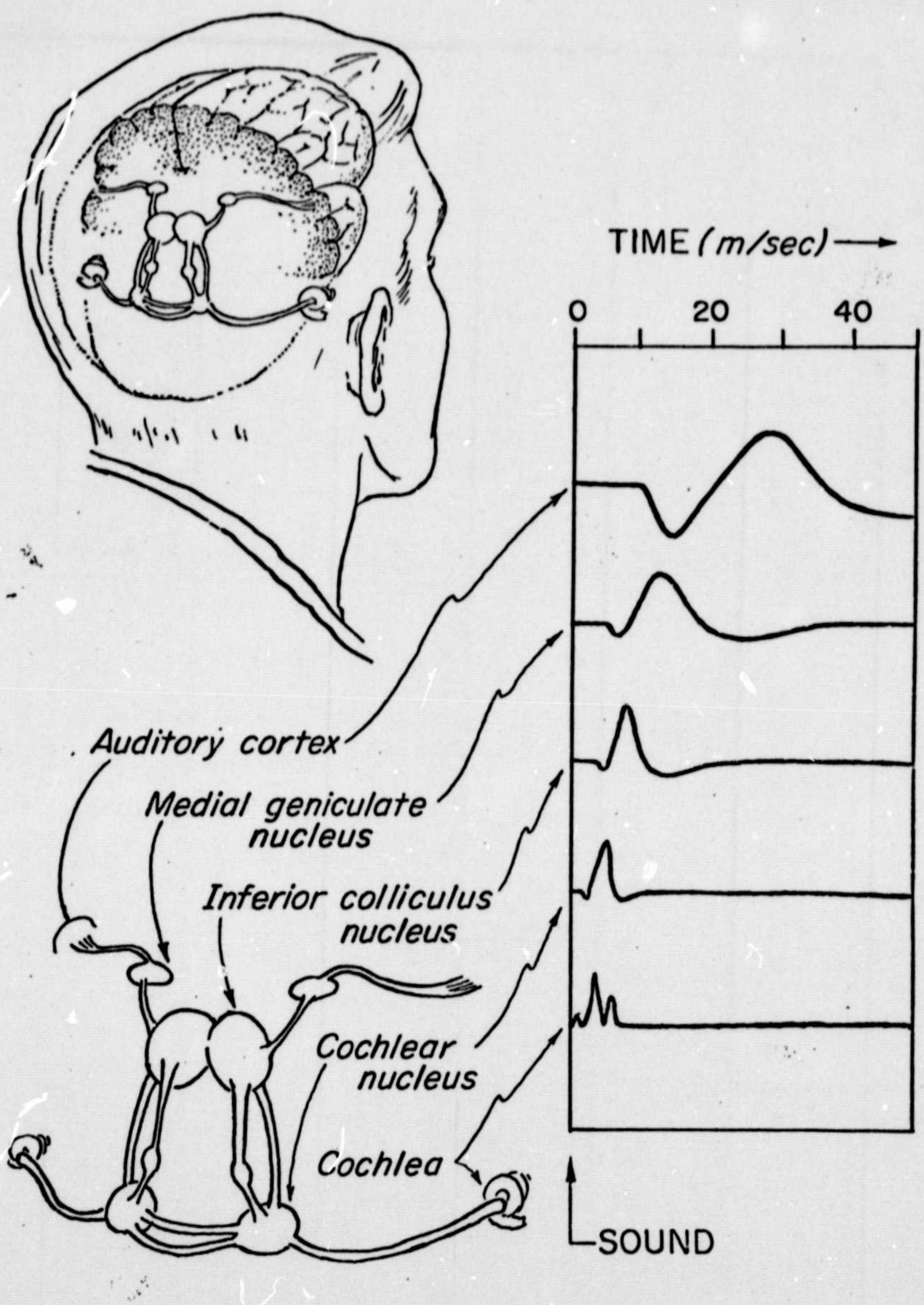
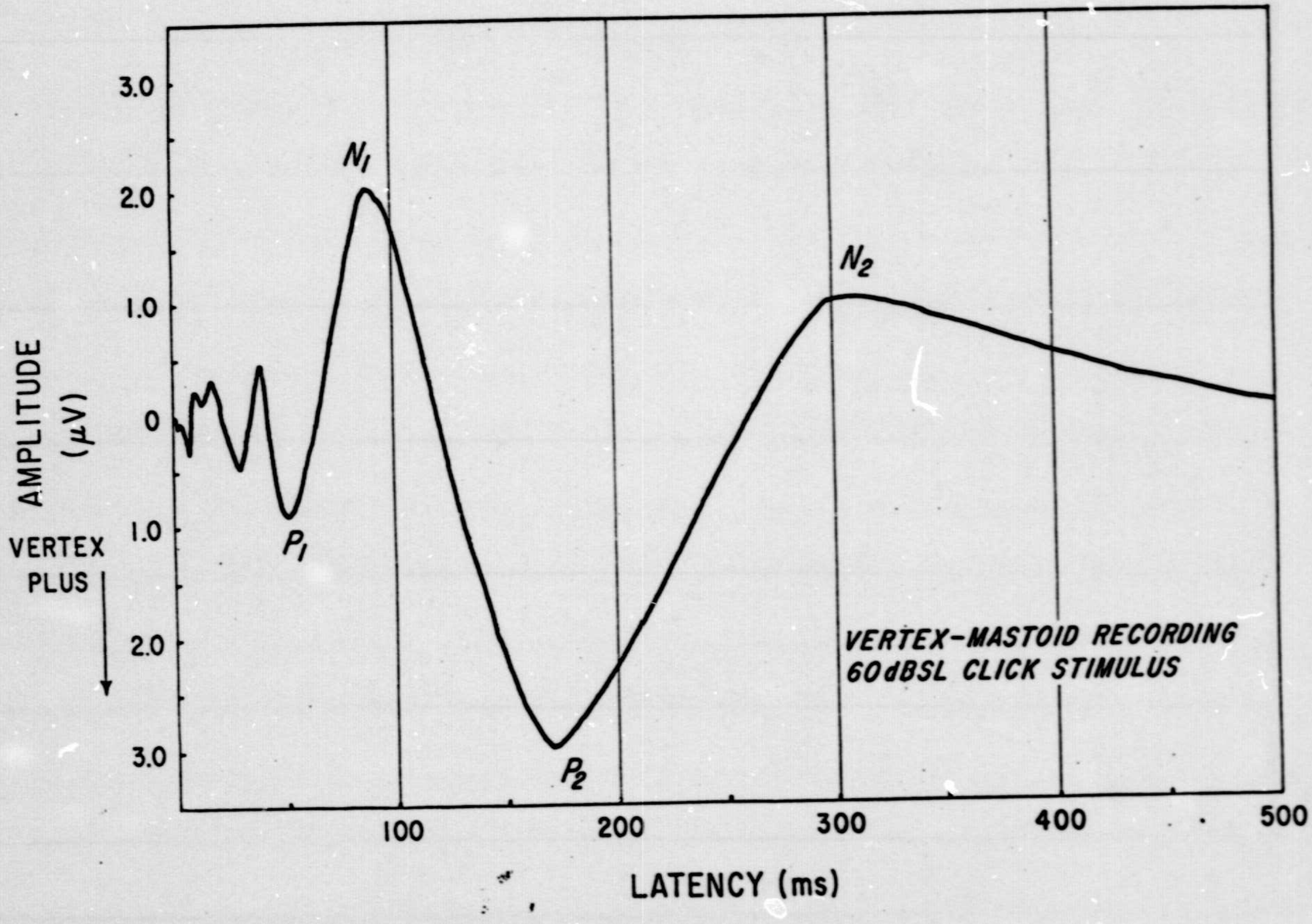
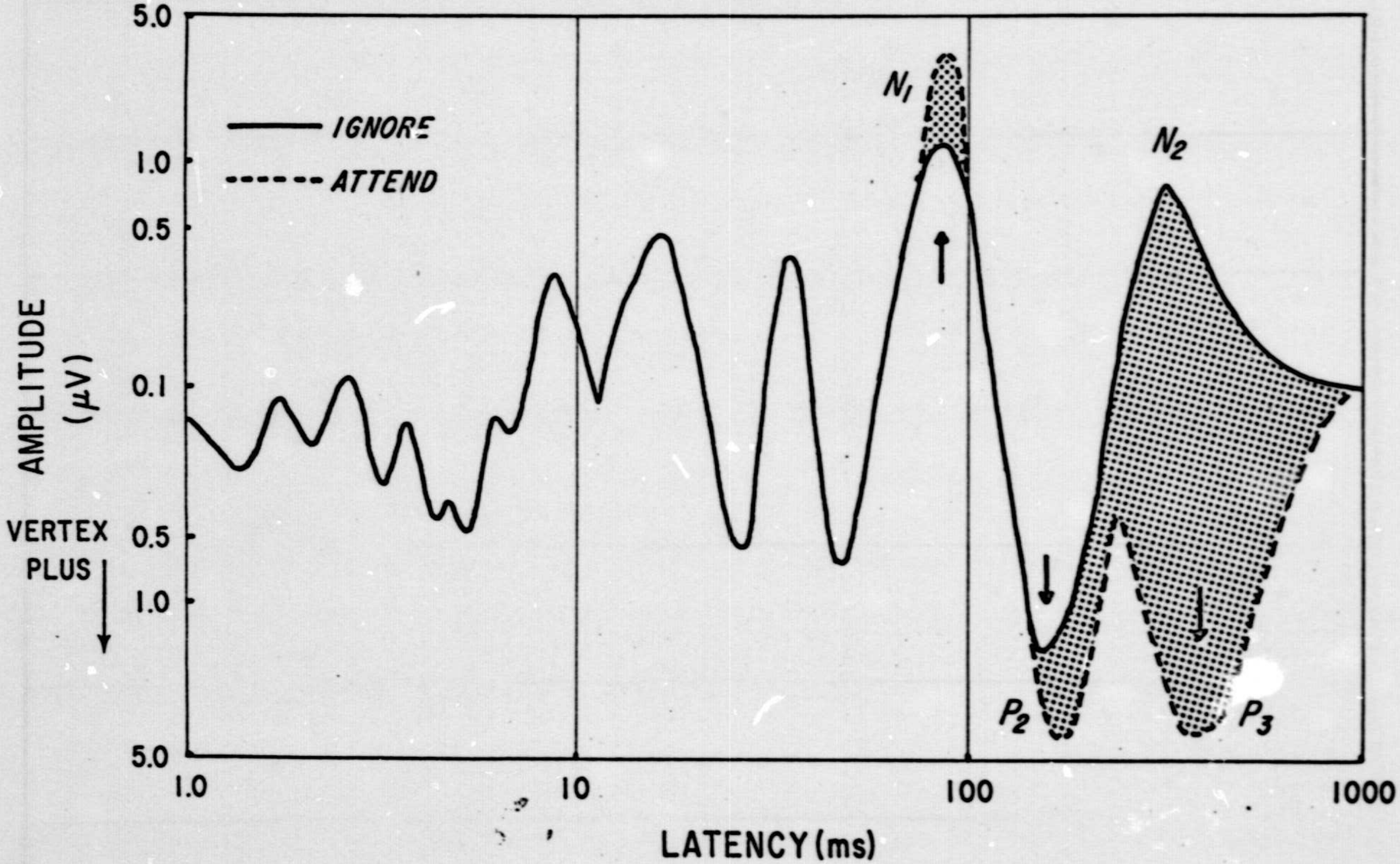

ASCENDING
DESCENDING
ACOUSTIC CORTEX
AUDITORY RADIATION
MEDIAL GENICULATE
SUPERIOR COLLICULUS
RETICULAR FORMATION
INFERIOR COLLICULUS
CEREBELLAR VERMIS
LATERAL LEMNISCUS AND NUCLEUS
MEDULLA
COCHLEAR NUCLEUS
SUPERIOR OLIVE
TRAPEZOID BODY
SHORT ACOUSTIC TRACTS (REFLEX)
RASMUSSEN
1954

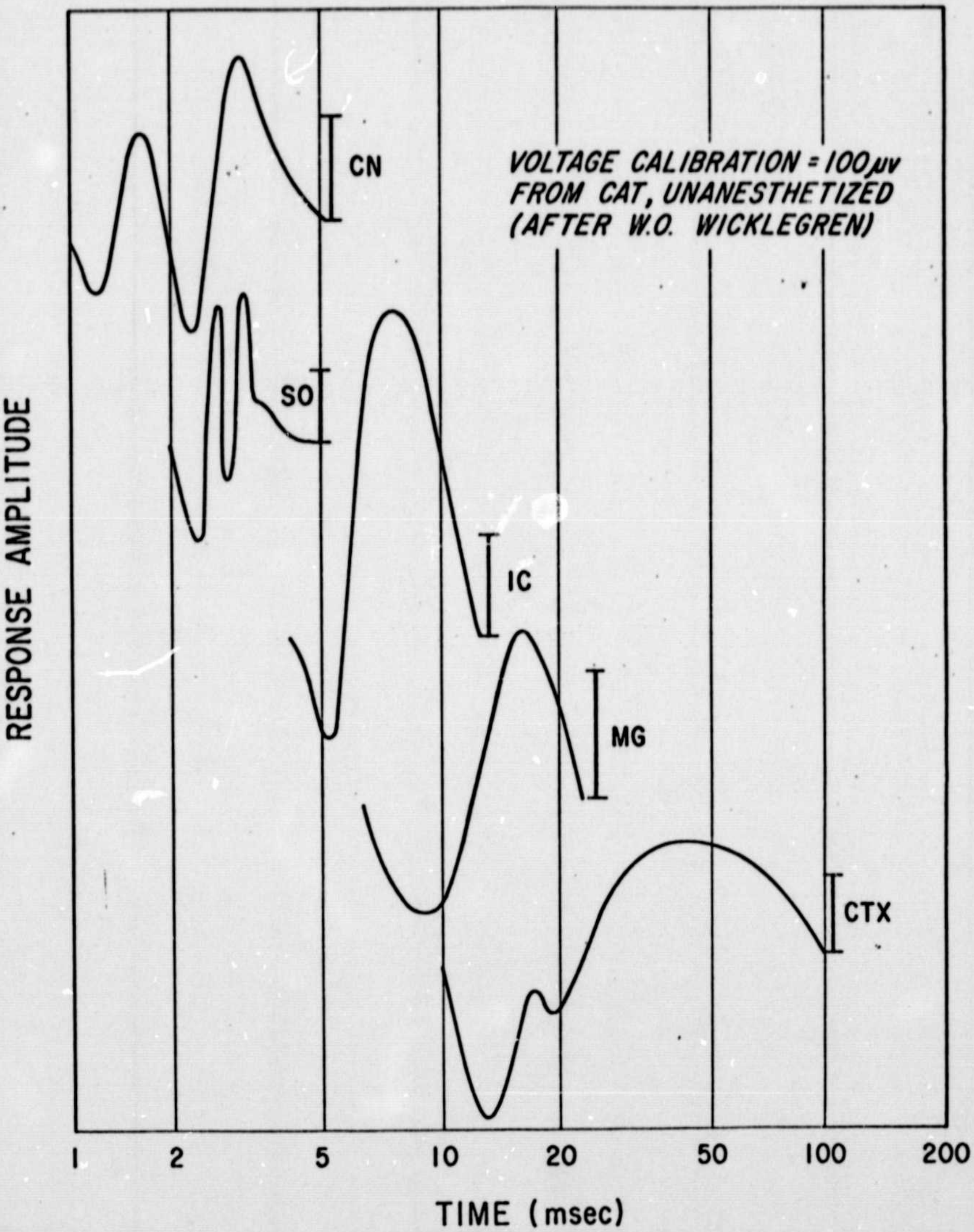

TIME (m/sec) →
0
20
40
Auditory cortex
Medial geniculate nucleus
Inferior colliculus nucleus
Cochlear nucleus
Cochlea
SOUND

HUMAN AUDITORY EVOKED POTENTIALS

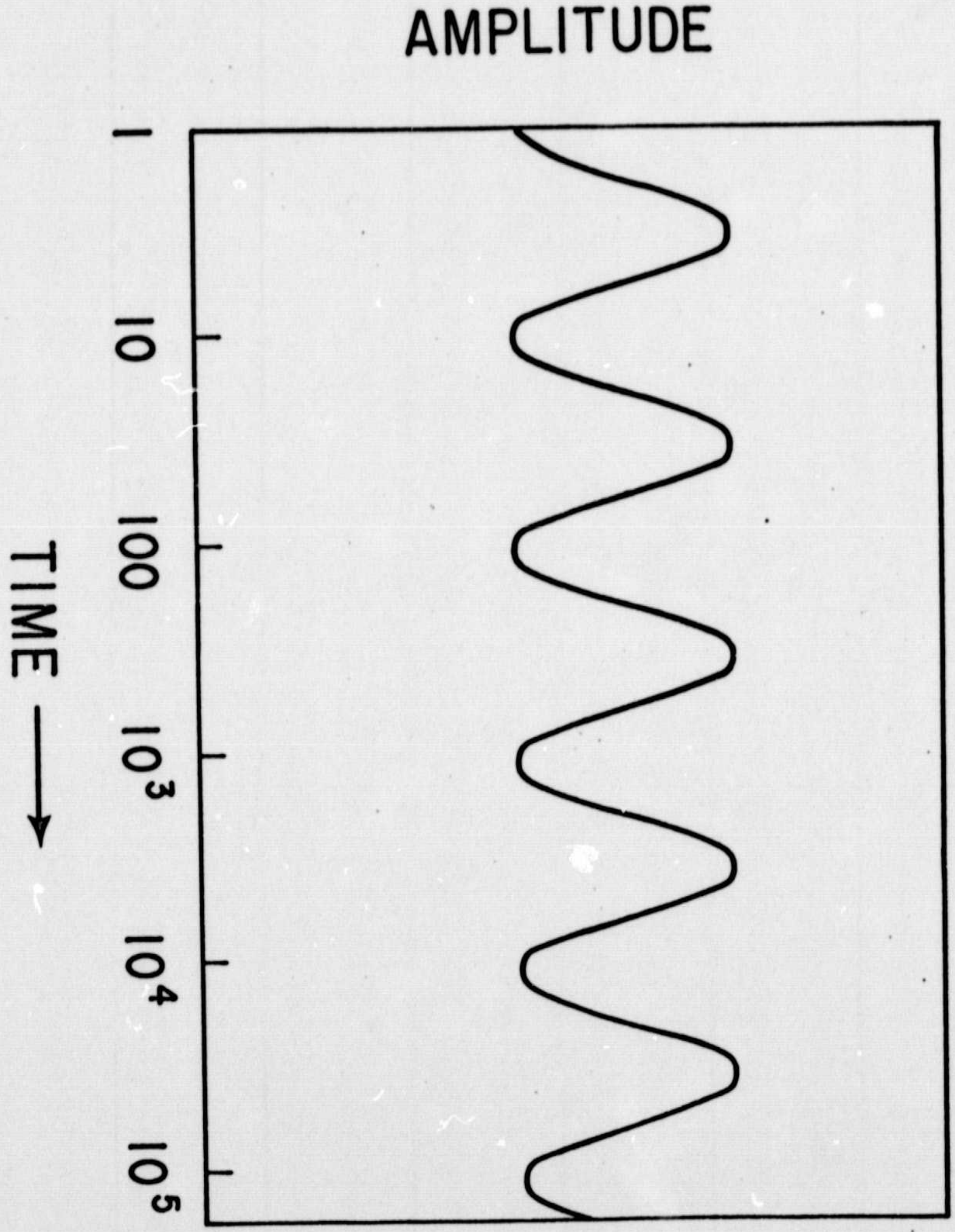


EFFECT OF ATTENTION ON HUMAN AUDITORY EVOKED POTENTIALS





VOLTAGE CALIBRATION = 100 μv
FROM CAT, UNANESTHETIZED
(AFTER W.O. WICKLEGREN)
CN
SO
IC
MG
CTX
RESPONSE AMPLITUDE
1
2
5
10
20
50
100
200
TIME (msec)



AMPLITUDE
1
10
100
10^3
10^4
10^5
TIME →