RESEARCH ON THE CENTRAL AUDITORY MECHANISMS: SOME RECENT METHODS AND RESULTS[1]

E. A. CULLER,
University of Rochester

Whenever I speak upon the topic of hearing, I am reminded of an incident which occurred some years ago at a meeting of the National Academy of Science. A young man from one of our large universities had just reported a study in audition. As he concluded, Dr. Cattell arose—dean of American psychology and Nestor of American science. His first comment was to this effect: "Whenever you think you've discovered something new about hearing, turn to Helmholtz and you'll find it there." This tribute to the greatest experimental theorist in the history of acoustic research was indeed well deserved; but it was considerably more true when spoken fifteen years ago, than it is today. We now know some things about hearing that even Helmholtz, with his unrivaled insight, did not perceive.

This new knowledge is due, in large part, to new methodology. I need not remind you that the milestones in scientific progress are marked by new methods of research. Emphasis upon methodology is a cardinal distinction between the man in the laboratory and the man on the street. Whenever I speak to laymen about our work, I am often reminded by my hearer that he is not interested in methodology; what he wants are facts. He makes the statement with something of an air, as though he prided himself on being hard-headed and practical. But we all know, if we know anything about science, that the observations we get are a function of the methods we employ; that facts are the fruit of operations. For that reason let us begin with a few methods that are basic in auditory research as a means to understanding some of the facts which I wish to report.

The first method historically was doubtless *clinical.* If everybody had perfect and uniform hearing from birth until death, never suffering any impairment because of accident or disease, it is doubtful that hearing would ever have been a problem. Because some of us hear better than others, because we hear better early in life than later, because hearing may be completely destroyed through some injury, we are forced to think about the mechanisms of hearing—how they operate and what can be done to restore them. In other words, the accidents of Nature prod man to research. In this sense, Nature may be called the first experimenter. One of the great contributions of Darwinian theory is its revelation that the world we inhabit is an experimental instead of a static universe. In the clinical method Nature sets the

[1]Communication No. 37 from the Laboratory of Physiological Psychology (Animal Hearing), which was transferred from the University of Illinois to the University of Rochester in 1938. This laboratory is maintained with aid from the Research Council, American Otological Society.

problem and man tries to solve it. A patient whose hearing disturbs him appears in the consulting room of an otologist; who thereupon, in addition to other tests, plots a complete audiogram of each ear. He thus determines as well as possible the locus and nature of the malady. Ofttimes little can be done beyond prescribing a hearing-aid. The patient is then examined year by year to note what changes occur and finally, if the physician lives long enough and the patient dies soon enough, the ears which have been so often tested are removed and sectioned in order to correlate their anatomical deficiency with the functional hearing-loss. The procedure is sound but has several great defects. 1. It is insufferably slow. The patient may live longer than the physician; so that the answer to a simple question of fact may require several generations of careful work by many investigators. 2. But a still graver difficulty is that Nature, although the first experimenter, is unquestionably one of the poorest. A young man of the laboratory, who could not plan his experiment better than Nature does, would find it hard to win even a bachelor's degree. A clinical lesion usually implicates so many separable factors in the ear that it is quite impossible to say which one is responsilbe for the hearing-loss. At Johns Hopkins Medical School is located one of the world's most extensive collections of sectioned human ears, together with audiograms showing the functional condition of each one. This vast body of material has accumulated over many decades and represents a huge expenditure of time, energy, and money; yet I venture to say that we can learn more by the use of modern experimental techniques in six months from a cageful of guinea pigs about localization of function in the cochlea than we can from this great assemblage of clinical evidence. While the clinical method will never be superseded, its deficiencies are such that little real progress could be made until adequate *experimental* methods were devised.

Of these experimental methods, the first to consider is *conditioning*. This term is familiar to you. It was bestowed by the Russian physiologist Pavlov and is illustrated in one form by the familiar laboratory picture in which a dog stands with one foot resting upon a metal grid which can be charged with a small electric potential. If you sound a tone about two seconds before the paw is stimulated, the animal will soon begin replying to the tone by withdrawing his foot from the grid. We say that he has been "conditioned" and now reacts to the sound as he formerly did to the shock. After conditioning has been established, the tone is made weaker and weaker. The animal continues to react as before until at last he begins to falter, responding sometimes but not always. With continued reduction of intensity, a point is eventually reached where no response occurs at all: this implies that the tone is now completely inaudible. This simple procedure has proved extraordinarily fruitful in studying problems of hearing. The older experimenters, who tried to get away from the limitations of the clinic, were impaled upon one horn of a dilemma. If they worked with human patients, they could test the subjects's hearing but they could not operate surgically on him. After all, we can't drill a hole in our neighbor's ear to see how that would affect his hearing. If, however, they

tried to use animals, they could indeed operate on the subject but they were unable to measure what it *could* and *could not* hear. Until very recent times, effective laboratory research on hearing was blocked by this dilemma. Now, however, by the conditioning procedure we can train a dog or cat or guinea pig to react visibly to every sound it can hear, however faint, and thereupon measure its audiogram. We can then anesthetize the animal and make some well defined lesion in the acoustic tracts. As soon as the animal recovers from anesthesia, it will tell us by its reactions the exact effect of our lesion. By making comparative tests on our trained animals and on ourselves, we have proved that a test-animal is fully as reliable a witness as a good human patient. Almost every problem that arises in the otological clinic with human beings can now be tested with experimental controls in the animal laboratory.

Another experimental method which has proved of the greatest value in recent years is *electrical.* It has long been known that the activity of living cells is often attended by electric phenomena. So well was this understood even fifty years ago that these electric potentials were designated "signs of life." One could, for example, distinguish a living seed from a dead one by means of the minute electric currents generated by the former. There are, of course, other signs of life. A living cell will give off CO_2 at all times; an active cell will emit more CO_2 than a cell which is resting. This has been well demonstrated by an instrument known as the biometer or "life meter," which reveals that an active nerve fiber gives off fully twice as much carbon dioxide as the same fiber when at rest. Likewise living cells when active emit heat; even the minute nerve-cells generate small quantities of heat when they are conducting impulses. The peculiar advantage of electrical procedure is, however, that living cells can be studied *in situ* more readily than by any other means. Electric techniques are so highly developed that we can put an electrode against the inner ear or the auditory nerve, pick up the minute potentials therein generated, lead them through an amplifier into an oscillograph, and study their properties. The contribution of this method to understanding the function of the ear and its associated tracts is hard to overstate. What we may call the modern period of auditory investigation begins with the application of electric methods to the study of the cochlea and the cochlear nerve.

In many cases the two experimental methods, electric and conditioning, are applicable to the same problem. When used in combination, they constitute an extremely powerful tool for the study of acoustic mechanisms.

In recent years research by use of these methods has been principally of two kinds. 1. Some investigators have continued to study the activity of the cochlea in different animal-forms and to seek an adequate description of the peripheral structures and operations by which a sound-wave is converted into discrete nerve-impulses. 2. Others have examined the structural characteristics and functional problems of the neural conduction-system in its course from cochlea to cortex; the purpose of these studies being to describe and evaluate the neural events which unite the functional levels of the acoustic system.

It may be well to remind you that both the cochlea of the inner ear and the neural components of the acoustic system emit electric potentials when sound vibrations are impressed upon the ear. These two types of potential, however, differ in certain important respects. 1. Synchronized cochlear potentials can be detected as high as 6000 cycles or more whereas synchronized neural potentials seldom are reported beyond 2500 or 3000 cycles. 2. The cochlear potential usually resembles (apart from aural distortion) the wave form of the impressed sound, whereas the neural potentials look like similar potentials in other sensory nerves, being essentially monophasic and negative. 3. The cochlear voltages are many times as large as the neural, with the result that they spread by ordinary electric transmission to points several centimeters away from their origin. The neural potentials being much feebler can usually be detected only in close proximity to the nerve-cell which generates them. 4. Cochlear electrophonics, which thus spread in all directions by ordinary transmission, travel at considerably higher velocity than do neural impulses which propagate at the usual speed of nerve-impulses (e. g., 30 meters per second). 5. Cochlear potentials effectively resist narcosis whereas neural potentials are appreciably reduced by most anesthetics. 6. Cochlear potentials may persist for minutes or even hours after demise of the animal, though with reduced intensity, whereas the neural potentials commonly disappear at or just prior to death.

In accord with the original plan of this symposium, I shall confine myself principally to reporting some studies bearing upon the phenomena that occur in the neural acoustic system central to the cochlea; that is, studies which belong to the second group of investigations just mentioned.

1. I shall first notice a study now in progress by W. D. Neff of our laboratory on the effects upon hearing in the cat of partial section of the eighth nerve. Changes in sensitivity occasioned by local damage to the eighth nerve, which connects the cochlea to the brain stem, are observed by the conditioned-response technique. The cat is first conditioned until it responds clearly to any audible sound. The audiogram of the animal is then measured at the various octave frequencies from 125 cycles to 8000 cycles and, in some cases, for two additional octaves (62 cycles and 15000 cycles). When the animal's normal hearing is thus determined, the cochlea of one ear is destroyed so that all auditory impulses must pass to the brain via the nerve that is later to be partially sectioned. Destruction of the single cochlea results in surprisingly small loss of total sensitivity, usually about two or three decibels. (A decibel is the standard unit in acoustic measurements and is, very roughly, that difference in physical intensity of two tones which can just be perceived by a normal ear). As soon as the animal's thresholds for the several frequencies have been determined for the one remaining ear, the second and critical operation ensues. Under complete narcosis the eighth nerve of the intact ear is carefully exposed. The nerve tissue being quite soft can be removed in any desired amount by a suction-pipette so that part of the nerve is left intact but the remaining fibers are effectively interrupted. After the animal is sufficiently recovered

for testing, the postoperative limens are secured. Comparison of these limens with those which preceded the operation will, obviously, reveal the losses due to partial section of the nerve. Results to date reveal that a very small lesion brings no significant loss at any frequency, whereas with larger lesions, marked losses appear at several of the higher frequencies. Since the experiment is not yet complete and histological evidence is not yet available, interpretation must be tentative; but several conclusions are already obvious. First, not all fibers of the eighth nerve need be severed to render an animal deaf to certain frequencies. Secondly, the remaining intact fibers give at other frequencies the same sensitivity (limen) as did the whole nerve.

2. A second study was performed by Ades and his collaborators at the level of the medial geniculate bodies in the cat. These two nuclei, right and left, being the final way-station from cochlea to cortex, provide an ideal site for determining in what manner cochlear impulses are transmitted to the brain. The general procedure was as follows: The intact cat is first conditioned and its normal audiogram obtained for an adequate sample of the audible range (octave frequencies from 125 to 8000 cycles). Localized electrolytic lesions are then effected at corresponding points of the two medial geniculates. The cat is then retested to determine what losses, if any, have occurred in its hearing. Finally, the animal is dispatched and the brain prepared and examined by histologic methods.

Inspection of the audiograms shows that localized lesions in symmetrical areas of the two geniculates result in some attenuation of auditory sensitivity for all frequencies tested, but that the degree of impairment differs widely. The variation is not haphazard but in every case conforms to a definite pattern, the loss being greatest at one or two frequencies, graduating down to a minimum at those most distant from the focal frequencies. Cats with lesions in corresponding areas display a similar distribution of hearing losses. Loci for the several frequencies seem to be as follows: 8000 cycles, dorsal region; 4000, anterior; 2000, lateral; 1000, posterior; 500, medial. The lower frequencies, 250 and 125 cycles, were in no case attenuated to maximal degree, but apparently traverse the ventral side. The several loci thus appear to follow a linear course, beginning with higher frequencies in the dorsal section and circling downward to the ventral region where the lower frequencies appear.

3. The medial geniculate nucleus in the cat has also been explored by Coakley, using an entirely different method. If there is a spatial distribution of fibers within the nucleus, it should be possible to determine their position by recording the electric potentials generated in any given case by the active units. Accordingly, the distribution of potentials in the nucleus has been studied for five frequencies of stimulation arranged in octave steps from 125 to 2000 cycles. Since the potentials above 3000 cycles became so feeble as to be practically imperceptible, our data are limited to frequencies below that point. The potentials generated by an impressed tone were measured at about 120 points arranged uniformly throughout the nucleus and just beyond its margins. Of course only a small number of points could be studied in any one

animal but each point was examined in about six cats. Summarizing the results for all animals, we find that for each frequency applied to the ear, the potentials are maximal for amplitude in one region and become smaller as the needle is moved in *any* direction from this area. If these maxima are arranged in order of frequency, they constitute a figure similar to a conical helix. Further analysis of the data reveals the approximate course followed by each group of fibers. In addition exact synchronization between impressed frequency and neural pulses in the nucleus was observed up to 2500 cycles. This implies that, whatever number of negative (or positive) pulses is generated in the cochlea, the same number will still be found (up to 2500 cycles) in the neural action-currents of the medial geniculate.

4. E. A. Lipman has accumulated some material on cortical function in hearing. The procedure is similar to some already mentioned. The normal audiogram of a trained dog is first measured at the usual representative frequencies (125 to 8000 cycles). The entire temporal (acoustic) area of one side of the cortex is then removed and the animal's audiogram again tested. Even though only one side of the brain is now intact, hearing-losses are quite negligible, being in no case more than three or four decibels. The second and critical operation then follows in which a small localized part of the remaining intact side is removed with the suction-pipette. Postoperative tests again reveal what losses, if any, occur at each frequency.

In general the losses at a specific frequency are not large, about 10 decibels, but the results to date indicate that hearing losses are confined to the area comprised by the medial and posterior ectosylvian gyrus and the adjacent medial and posterior sylvian gyrus. Removal of cortex beyond this area seems to have no effect upon hearing. Thus far lesions in the ectosylvian gyrus are followed by losses at 500 cycles and below, whereas lesions in the adjacent sylvian area seem to bring losses at higher frequencies from 1000 cycles up. These results indicate that focalization of responses is not so sharp as elsewhere but still present. The exact locus for each of the several frequencies awaits further tests.

From these and other observations we may infer that different tonal frequencies, when impressed on the ear, actuate different areas or patterns of receptive cells within the cochlea and that the impulses thus generated traverse differential pathways to the auditory projection center of the cortex; but that the number of pulses per second passing to the cortex rises in step with the impressed tone, and thus provides a second clue by which the organism can perceive pitch. The *relative* contribution of these two factors (spatial and temporal) must await further analysis.