Microelectrode study of superior olivary nuclei

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GALAMBOS, ROBERT, JOHANN SCHWARTZKOPFF AND ALLEN RUPERT. Microelectrode study of superior olivary nuclei. Am. J. Physiol. 197(3): 527-536. 1959.—The superior olivary nucleus of barbiturate anesthetized cats was explored with microelectrodes. Both slow wave and single unit activity was recorded to clicks, tones and noise delivered to the two ears. The several segments of the superior olivary complex (e.g. the n. accessorius and n. trapezoid body, to mention 2 of the 5) are differently innervated from the two ears, and the physiological findings correlated well with the known anatomical data. In response to tones most units displayed a best frequency and a response area here as elsewhere in the auditory system. Intensity increase aroused more activity from most units and brought additional ones into action, but several important exceptions to this rule were studied. Units in n. accessorius proved to be exquisitely sensitive to whether the right ear or the left was stimulated first by paired clicks; the unique physiological and anatomical characteristics of these cells seem relevant to the binaural sound localization problem. Several lines of evidence, finally, suggest the existence of a class of units concerned chiefly with preserving the exact time of arrival of stimuli at the cochlea, this class being different in important ways from those dealing with tone-frequency mediation.

This study deals with the neural responses of the superior olivary nuclei to sounds. Each superior olive is strategically located in the auditory pathway in that it receives, for the first time, the input from the two ears. This part of the brain is therefore probably involved in such phenomena as sound localization where both ears are required and, since it is also a relay nucleus in the neural pathway from cochlea to cortex, events related to the mediation of sound frequency and intensity as well. The electrophysiological study summarized here undertook, therefore, to discover what activities are aroused here when sounds are presented to either ear and to both.

Materials and Methods

The anatomical relationship of the superior olivary complex (SO) to the rest of the auditory system has been recently reviewed (1-5). In the cat, the animal used in the present study, at least five separate nuclear masses are recognized of which the major three are shown in figure 1. Papez's terminology for them will be employed. The characteristic lateral S-shaped segment (S. seg.) receives fibers predominantly if not exclusively from the ipsilateral side. The accessory nucleus (n. access.) receives afferents from both ears; its cells bear two (or more) large dendrites, one pointed medially, the other laterally. It is a remarkable fact that endings upon the medially-oriented dendrite stem almost exclusively from the contralateral side, while those on the lateral dendrite originate predominantly on the ipsilateral side (4). Most of the input to these cells must come from the two cochlear nuclei, but other sources cannot be excluded (e.g. descending fibers, other superior olivary). Dorsal cells in the rostral third give origin to the efferent olivo-cochlear tract and in the most caudal region cells characteristic of both n. access. and n. trap. seem intermingled.

The nucleus of the trapezoid body (n. trap.), the most medial member of the complex, can be subdivided into a dorsal portion where calyces of Held are the characteristic synapse, and a ventral one in which they are not. While the published descriptions are not entirely clear on this point, the n. trap. probably receives afferents from both sides, with the contralateral innervation predominating especially in the dorsal portion.

The chief remaining nuclei, the medial and lateral preolivaries, are located most ventrally and laterally. Their afferent supply is probably bilateral, with ipsilateral predominating. Besides these reasonably well organized cell clusters, other small collections can usually be identified. These include cells surrounding n. access. and S. seg., of which the retro-olivary group dorsal to S. seg. is prominent. Afferents to these are not well understood.

In preparation for the present study an atlas of sections cut in the Horsley-Clarke plane was prepared. Table 1 shows the rostral and caudal limits of the nuclear masses shown in transverse section in figure 1, which is the P-4.5 plane.
Sixty-five cats were used in these experiments. Most were anesthetized with sodium pentobarbital 60 mg/kg and maintained thereafter in a ‘light’ stage of anesthesia. Rectal temperature was maintained between 35° and 39°C by intermittent heating. On occasion ether followed by Flaxedil (Gallamine triethiodide), or Dial in urethane, were employed. The head was routinely fixed in a stereotaxic instrument in the Horsley-Clarke planes; each ear bar was hollow and its free end bore an earphone through which a sound stimulus could be presented (6). The routine operative procedure involved bilateral exposure of the round window upon which a fine silver wire was fixed for continuous monitoring of the cochlear response. If during the course of the experiment this response failed to meet the criteria established for it at the start, the neural activity obtained from the SO was thereafter treated as suspect. The indifferent electrode for all leads was a silver wire buried beneath the skin of the neck.

The approach to the SO was either from above, in which case the cerebellum may or may not have been previously removed, or from below after removal of the bone between the bullae. The latter approach was used in our best experiments, on 23 cats. In these cases the stereotaxic instrument was rotated 90 degrees with the right ear down to permit easy access for operative procedures and the insertion of the electrode.

The microelectrode carrier was a hypodermic syringe so mounted on the stereotaxic instrument that advancement in the Horsley-Clarke frontal plane was ensured. Medio-lateral angulation was permitted, and most of our punctures proceeded at an angle of about 30 degrees to the sagittal plane. An oil-filled hydraulic system was used to advance the electrode (6).

The microelectrode most often employed was the coated tungsten wire described by Hubel (7). This electrode usually produced very little damage, and records taken during withdrawal often were indistinguishable from those taken during penetration. At various times pipettes with tips ranging from 0.5 to 5 μ and filled with saline or 3 M KCl, as well as the electrode described by Dowben and Rose (8) were used; all types gave essentially the same physiological results.

The sound system consisted of the click, noise and tone generators, with control and attenuating devices already described from this laboratory (6). For recording from the microelectrode a Tasaki cathode follower, Tektronix type 122 amplifier and a four-beam oscilloscope and camera were employed.

Our usual procedure was to advance the electrode in steps of 10-50 μ with observations of responses to the sound stimuli at each step. Units, when encountered, were intensively examined; most of these encounters were of brief duration, but some units were studied for an hour or longer. In all more than 400 u were seen, of which substantial information was obtained on about half this number with pictures taken of the behavior of 60. A given puncture was ordinarily considered complete when we decided the electrode had passed beyond the auditory system. A small current was often passed through the electrode at this point of deepest penetration and the lesion so produced considerably simplified later identification of the track. In many animals more than one puncture was made. At the conclusion of the physiological studies the animal was perfused with 10 % formalin and serial histological sections of the SO region were prepared. The electrode tracks were then reconstructed (in 47 cases in 23 cats) and an estimate of the electrode location at the time of each physiological observation was made. For various reasons a number of animals escaped this histological study; the physiological data from these, when included here, have received the special treatment dictated by ignorance of their anatomical source.

RESULTS

Slow Wave Pattern

The basic plan of these experiments involved advancing a microelectrode through the SO region with frequent pauses en route to record the responses evoked by acoustic stimuli delivered to the ears. Very often at such recording points single units were not seen; the stimuli, however, nearly always evoked ‘slow wave’ re-
TABLE I. Distribution of Medullary Auditory Nuclei

<table>
<thead>
<tr>
<th>Nucleus</th>
<th>Hornsley-Clarke Coordinate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pons (at surface)</td>
<td></td>
</tr>
<tr>
<td>Vent. n. lat. lemniscus</td>
<td>P-1.5</td>
</tr>
<tr>
<td>N. trap.</td>
<td>P-2.0</td>
</tr>
<tr>
<td>N. access.</td>
<td>P-2.75</td>
</tr>
<tr>
<td>S. seg.</td>
<td>P-4.0</td>
</tr>
<tr>
<td>Coch. nuclei</td>
<td>P-4.0</td>
</tr>
</tbody>
</table>

Responses. Certain constant features of these slow waves are worth describing.

Figure 1 shows a section through the medulla of an animal in which the electrode traversed the SO region. The slow wave responses to click stimulation are also shown for various positions along the track. These data, which can be considered typical, demonstrate that both ears evoke responses throughout the SO. Modest activity or none at all is seen when the electrode lies medial or dorsal to the SO, but voltages between 100 and 500 µV are regularly seen within it.

These slow waves generally have an early sharp and a later slow component when the electrode is located within or near a nuclear mass; the obvious interpretation of these components in terms of arriving impulses followed by postsynaptic discharge within the nearest collection of cells seems reasonable. The polarity of these slow waves, however, presents an interesting problem. As can be seen from figure 1, when the electrode approaches n. access. from medially and below (our usual approach), contralateral click stimulation regularly produces a response that is negative in sign, while ipsilateral clicks evoke a mainly positive slow wave complex. Within the n. access. the contralateral response turns positive, and in this location both responses may be astonishingly similar in shape. Just beyond n. access. and onward into S. seg. the ipsilateral response turns negative, the contralateral remains positive and the two responses are again nearly precise mirror images. In such cases presenting the clicks simultaneously in time results in almost complete abolition of the response under the microelectrode.

The SO location where the slow waves reverse polarity has repeatedly been demonstrated to be in the n. access. This statement holds true for the major part of this nucleus, for the phenomenon has been observed in one cat or another to occur throughout most of its dorsoventral and rostro-caudal extent. In favorable cases electrode excursions of a few hundred microns carry the tip through the critical region. Lesions made in such cases define a roughly dorsoventral line running through the center of the nucleus as the locus of the polarity reversal.

This finding may be related to the anatomical peculiarity of n. access. discussed above. As has been stated, its cells have one dendrite directed toward the left and another toward the right; terminals from axons originating on the left side of the head predominate on the left dendrite while those from the right side of the animal usurp the right dendrite. An attractive explanation of the physiological findings can be derived from this anatomical fact. An electrode located medial to n. access. will be close to or upon the dendrites innervated by the contralateral ear; a partial depolarization of this dendrite would lead to the observed mainly negative slow wave that follows contralateral stimulation. Depolarization of the opposite dendrite would result from ipsilateral stimulation, and this would create in the region of the electrode a source rather than a sink of current, thus accounting for the observed positive sign of the slow waves. If the electrode is located at the center of n. access. it is in the vicinity of the cell bodies and thus symmetrically oriented with respect to the left and right dendrites; with partial depolarization of either of these the soma should therefore act as a source of current, and since this should be equally true for each dendrite, the symmetrical positive slow waves shown in figure 1 would be expected. Should the electrode now be moved lateral to the n. access., the argument outlined for the polarities seen at the medial location would account both for the sign of the slow waves and for the fact that they had reversed. We recognize some difficulties in the above formulation but suspect that it, or something closely like it, will eventually prove acceptable.

Response to Tones

The sensitivity to tones was determined for as many as possible of the units isolated by our microelectrode. To do this the ears were separately stimulated with tones, and the best frequency and the response area (g) were established for each unit. As is shown in figure 2,
SO units respond to a limited region of the auditory spectrum, and their response areas show with rare exceptions the triangular shape and steep drop-off at the high frequency border seen at the cochlear nucleus (g-r1). Response areas determined for units located in one SO segment could not readily be distinguished from the others, or indeed, from response areas determined at other auditory nuclei. Furthermore, their best frequencies (i.e. the tone or band of tones at which the energy required to excite a given unit is minimal) cover the entire auditory spectrum, except for very low frequencies.

Figure 3 shows the best frequency of 31 units selected from our collection of some 230 tone-responders on the basis that a) the anatomical location of each is precisely established, and b) the physiological data are complete or very nearly so; and c) the threshold of each round window response was 'normal' for click (i.e. between 80 and 120 dB) at the time of the determinations. Most SO units respond only to ipsi or contra tonal stimulation and not to both, and this was true of all the units of figure 3. There is one S. seg. unit in figure 3 and it was driven only by ipsilateral stimulation; no S. seg. unit was ever found to be driven by contrastimulation. Contrastimulation, on the other hand, activated about 80% of the units in n. trap., and about 30% in n. access.

The fact that 'best frequencies' exist in a given auditory structure demonstrates that tones produce focal excitation at particular points there. A regular and orderly distribution of such points seems to characterize the cochlea and the auditory cortex, and so we were interested to discover whether an orderly arrangement occurs in SO also. The data of figure 3 are clearly insufficient to settle this point. If however we relax our criteria somewhat and include units whose anatomical location is imperfectly known, for which the response area was incompletely worked out, or from cats in which the round window response was not entirely normal, a sample of 86 units in 21 cats becomes available. When we plot the anatomical location of each of these tone-responders against the rostro-caudal dimension of its nuclear mass, no clear ordering of frequency appears. Figure 4 is such a plot in the rostro-caudal axis for n. trap., and it demonstrates that at each level in the Horsley-Clarke plane almost any tone can be expected to excite. Such results have also been reported by others (10). The plots made for n. access. and S. seg., on the other hand, suggest that at least a limited frequency segregation may exist in SO, for it turns out that nearly all units responding to tones below 1000 cps were located in n. access. and S. seg., while the units responding to high frequencies were located mainly in n. trap. However the segregation of frequencies is not complete, sharp or particularly orderly even in these data. It is therefore our feeling that the question of whether tonotopic organization exists in SO has not yet been entirely settled.

Another much-debated question is whether the frequency of tonal stimulation is preserved within the auditory brain as a frequency of discharge in nerve impulses. Figure 5 summarizes a detailed study of this question on a unit with a best frequency of 600 cps. It was activated by 50-msec tone bursts ('bleeps') presented every 2 seconds to the contralateral ear at levels adequate for evoking consistent responses. The frequency of the bleep is shown on the records in figure 5; where responses appear side by side there the left member was selected because it shows the weakest response and the right member because it shows the largest response to the stimulus. It is evident that identical stimuli did not invariably evoke the same response from this auditory unit. The unit sometimes followed the frequency of stimulation precisely, for there was exact synchrony at 700 cps and, for a time, even at 900 cps. At other times, however, responses were dropped (at frequencies as low as 500 cps) or the unit discharged not to both, and this was true of all the units of figure 3.
no exception to the rule that auditory units display both the ability and the frequent unwillingness to discharge in synchrony with the tonal stimulus (1, 11, 12).

Threshold Considerations

Turning now to the matter of the threshold of SO units, figure 3 shows a considerable range to occur in our most reliable data for tones. The question of whether such a range of thresholds occurs in a single animal is answered by table 2 where threshold values for tone, click and noise are separately tabulated for a typical cat. Fourteen units from a single puncture are identified by number, of which ten were reasonably well studied with tones. The tone thresholds range from 1 25 db (unit II) to 80 db, with the majority between 90 and 100 db. Since our sound system drops off above 10 kc at a rate of about 20 db/octave, it is not easy to compare threshold values for frequencies that are widely separated. For units like 5 and 25, however, which respond to nearly the same frequency, a comparison is perhaps permissible; here the difference in threshold is nearly 20 db. In other cats similar comparisons confirm the idea that different units responding to the same frequency may be far apart in their thresholds, and threshold differences of 50 db or more have been observed in some instances.

Table 2 also shows the variation in threshold for click

<table>
<thead>
<tr>
<th>Unit</th>
<th>Locus</th>
<th>Ear</th>
<th>Tone</th>
<th>Click</th>
<th>Noise</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>Trapezoid body</td>
<td>Ipsi (L)</td>
<td>30</td>
<td>80</td>
<td>0</td>
</tr>
<tr>
<td>10a</td>
<td>Trapezoid body</td>
<td>Ipsi</td>
<td>15</td>
<td>105</td>
<td>0</td>
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<td>11</td>
<td>Trapezoid body</td>
<td>Ipsi</td>
<td>6</td>
<td>125</td>
<td>120</td>
</tr>
<tr>
<td>16</td>
<td>Trapezoid body</td>
<td>Ipsi</td>
<td></td>
<td>30</td>
<td>80</td>
</tr>
<tr>
<td>17</td>
<td>Trapezoid body</td>
<td>Ipsi</td>
<td></td>
<td>40</td>
<td>90</td>
</tr>
<tr>
<td>19</td>
<td>N. Trapezoid</td>
<td>Ipsi</td>
<td>9.5</td>
<td>95</td>
<td>80</td>
</tr>
<tr>
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<td>N. Trapezoid</td>
<td>Ipsi</td>
<td>16.5</td>
<td>95</td>
<td>80</td>
</tr>
<tr>
<td>21</td>
<td>N. Trapezoid</td>
<td>Contra</td>
<td></td>
<td>100</td>
<td>110</td>
</tr>
<tr>
<td>22</td>
<td>N. Trapezoid</td>
<td>Ipsi</td>
<td></td>
<td>110</td>
<td>110</td>
</tr>
<tr>
<td>23</td>
<td>N. Trapezoid</td>
<td>Ipsi</td>
<td>12</td>
<td>95</td>
<td>40</td>
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<tr>
<td>24</td>
<td>N. Trapezoid</td>
<td>Ipsi only</td>
<td>21</td>
<td>90</td>
<td>85</td>
</tr>
<tr>
<td>25</td>
<td>N. Trapezoid</td>
<td>Contra</td>
<td></td>
<td>110</td>
<td>110</td>
</tr>
<tr>
<td>26</td>
<td>N. Trapezoid</td>
<td>Contra only</td>
<td></td>
<td>0</td>
<td>90</td>
</tr>
</tbody>
</table>

FIG. 5. Responses of a particular unit in n. access to different frequencies. Contralateral stimulation at frequency indicated. Traces only each record show, top to bottom, microelectrode response, round window response, and electrical signal delivered to earphone. Spontaneous and driven activity of unit also shown on left edge of each record.

that is commonly encountered. Units 5 and 23a did not respond to clicks of any intensity to either ear. Unit 11, by contrast, responded to the very weak 120-db click. Furthermore, units 22 and 23, separated nominally by about 50 μ, show a 70-db difference in their click thresholds. Since units 5 through 17, which are presumably axons presynaptic for the SO also show this wide range of click threshold, the observed SO threshold differences may merely reflect activity passed on to it by the cochlea and cochlear nucleus. If so, the absence of any tendency for the threshold values to fall into distinct modes, and especially their failure to fall into two modes, casts doubt upon the importance of the argument that primary neurons connected to internal and external hair cells in the cochlea are excited at distinctively different threshold values. If this should actually occur in the cochlea (15), the distinction appears essentially to have disappeared at the level of SO.

Further examination of table 2 reveals another common finding, namely units showing exquisite sensitivity to some sounds and absolute indifference to others. Unit 23a, for example, could not be aroused by clicks to either ear at any intensity, yet it displayed excellent responses to both tone and noise. Unit 26, on the other hand, responded only to clicks; tone and noise completely failed to arouse activity.

A systematic presentation of the tone-click threshold discrepancies under discussion is to be found in figure 6, where the data from all cats are plotted. First of all, there were 6 units that responded to clicks but not tones, and 11 that responded only to tones. This latter group had best frequencies between 5 and 30 kc, the majority
that of medial geniculate (6, 14) and auditory cortex (15) units, relatively large numbers of which (called auditory units because they respond to clicks or noise or both) prove to be insensitive to tones. The SO observations point out further both that the dichotomy between click and tone responsiveness need not be absolute, and that a segregation of units into click-responders and tone-responders occurs very early in the auditory pathway. It seems highly probable from these facts that the auditory system performs an analysis upon sounds that is different in principle from the simple Fourier analysis of the physical input.

Response to Clicks

As has been stated before, our routine procedure was to advance the microelectrode slowly while clicks were being presented to the two ears. When a unit was encountered it would usually first be seen in the response to one of the clicks, and much of our best information comes from the study of their behavior to the click stimuli.

As is clear from table 2, some units are either absolutely or relatively insensitive to clicks, while others react to clicks only. In general the responders do so promptly, some with single discharges, others with multiple spikes. Certain changes in the click stimulus induce changes in the response; three such stimulus-response relationships will be described here.

Absolute latency. Absolute latencies varying between 2.5 and nearly 10 msec. have been established for SO units (figs. 7–10). The shorter latencies tend to occur in n. access., but equally short ones have been measured in other segments also. The data are too few to settle the question of whether long latencies are segregated in one segment or another. Ipsilateral clicks do not invariably arouse response earlier than contralateral ones in a given segment, despite the apparently shorter conduction distance involved. These facts make it evident that any concept according to which the SO is a simple homogeneous relay nucleus one synapse removed from the cochlea is untenable. Postsynaptic activity appears in the SO over a period of many msec., a variability presumably due either to a multisynaptic arrival pathway or to some other delaying mechanism.

Latency change with intensity. The general proposition that auditory units ordinarily respond toward intensity increase of a click stimulus by decreasing their latency (e.g. 9, 14, 15) has been repeatedly confirmed for SO units also, as is shown for typical examples in figures 7 and 8. However, an occasional unit may show a progressively increasing latency and it may even prove, as did the one illustrated in figure 8, to be completely unresponsive to clicks above a certain intensity.

Besides these, the SO contains units that seem to have a fixed latency regardless of stimulus strength. We have studied four such, all located in n. access., and responding repetitively to clicks of which the three of figures 8 and 9 are typical. A remarkable feature of these units is
FIG. 8. Latency shift with click intensity. Top: unit showing much variability in latency at each intensity; latency increases with increased intensity (40–50 db) and unit does not respond to strong (40 db) stimulus. Bottom: unit like that of fig. 7 and with minimum latency of 3 msec.

FIG. 9. Latency shift with click intensity. Repetitively discharging units that show step-wise latency shift and fixed temporal delay between stimulus and response.

the way their latencies cluster about certain fixed values regardless of stimulus strength and response train length. At any given intensity the spike latencies are always distributed through very narrow bands, and often only one value (±0.1 msec.) can be assigned to all examples in a band. If now the click intensity is increased, the spike train may become longer and an even more unusual property emerges: the latencies encountered with the stronger stimuli invariably include those observed with the weaker ones. Now distributions of latencies may appear—some earlier, some later—but these are always a discrete step away from the ones already defined by the weaker stimuli.

Figure 10 shows sample records from one of these units. In A and C, although the click intensity differs by 50 db, the corresponding members of each three-spike train have essentially identical latencies. A and B, on the other hand, are responses to the same click intensity (as will be seen by comparing the round window records); latency comparisons here suggest the simple conclusion that the middle spike of A has dropped out in B. Further, the six-spike train of D contains each latency present elsewhere in the figure, and, in fact, the six latencies of D represent, to within ±0.2 msec., the only ones measured in several hundred responses of this unit to clicks varying over an 80-db range.

From such data one must conclude that certain SO units reflect the instant of stimulation with remarkable precision by responding at precisely fixed time intervals thereafter, a capacity that undoubtedly has significance for auditory phenomena.

Click phase and latency. The extraordinary precision with which SO units can preserve temporal relations existing at the end organ is further shown in studies designed to measure the effect upon latency of reversing the phase of the click.

The click employed throughout these studies was generated by passing a square wave of 0.075 msec. duration through a PDR 10 earphone. The earphone diaphragm is set into movement abruptly by such a pulse and it continues to vibrate in a complex manner for up to 2 msec. thereafter. In our system we can vary the ‘phase’ of the click, i.e. produce an initial outward diaphragm movement (and thus compression in the ear canal) or an initial inward movement (which causes ear canal rarefaction). Thus whether the eardrum and oval window move initially inward or initially outward could readily be controlled for either ear. It is generally accepted that auditory nerve excitation occurs with outward movement of the stapes.

We are not aware of any reported experiment in which human subjects were able to tell a difference between clicks that move the eardrum initially inward as opposed to outward. In listening to such clicks ourselves we have been unable to distinguish the one from the other. At the SO level, however, the brain of the cat may indeed do so, as is shown in figure 11. Throughout this figure an initial downward movement of the round window microphonic response signifies an initial outward movement of the eardrum. If the slow wave in A is compared with that in D, its shape is clearly modified by changing the phase of the click. Comparing B with E reveals two other interesting facts: the latency of the late large unit shown there is entirely uninfluenced by phase reversal of the click, but the latency of the smaller earlier one shifts by approximately 0.3 msec. If C is
compared with \( F \), a similar latency shift of 0.3 msec. is seen for the small unit pictured there, while neither the slow wave recorded by the microelectrode nor \( N \), recorded at the round window appear to be appreciably affected.

A few words of explanation are needed for the unit pictured in \( C \) and \( F \) of figure 11. It has a duration of about 0.3 msec. and therefore is much briefer than the 1.0-msec. units customarily recorded with microelectrodes. We have seen about 10 such short-duration units, some of which were studied for long times. It is possible that these 0.3-msec. spikes represent axon (rather than soma) discharges, or that they are somehow specifically related to the use of the tungsten wire electrodes; we have not been able to settle any questions related to them except that they behave in all ways examined like the conventional units isolated in the nucleus. The 0.3-msec. spikes have proved especially valuable when small latency shifts must be measured; for example, it is the extremely brief duration of the unit itself that permits the accurate estimate of the 200–300-μsec. latency shift for \( C \) and \( F \) in figure 11.

The above evidence that the central representation exists for the small difference between initial outward and initial inward movement of the eardrum has been seen several times. The phenomenon is most likely to be observed when the electrode lies in n. access.

Fig. 10. Latency shift with click intensity. Unit like those of fig. 9 showing fixed temporal delay between stimulus and response. In each record top line shows unit response, bottom line round window response. Identical stimuli do not produce same repetitive discharge pattern, but firing always occurs at fixed times after stimulus.

Fig. 11. Effect of click phase change on SO responses. Top row eardrum moved initially inward by click, bottom row initially outward, as indicated by initial upward and downward deflections respectively, of round window responses shown. Note change in pattern of slow wave response (A, D) and in latency of unit discharge (indicated by arrows). Estimated location of electrode shown by white dot in sections; all were in n. access.

**Binaural Interaction**

Nearly simultaneous click stimulation of both ears has revealed certain further interesting properties of SO units. In these experiments the interaural time difference was varied in a systematic way while the effect of this upon the responsiveness of the unit was observed. Whenever a time difference between the clicks to right and left ear influenced responsiveness (and it did not always do so) it a) produced discharge from the unit where monaural stimulation did not, b) produced a marked latency shift or c) suppressed the discharge. We will discuss only the last of these phenomena, namely, suppression of neural activity at certain interaural times, as shown in figure 12. Over a wide intensity range the unit shown there always responded to clicks presented monaurally to the right ear and never to monaural left ear clicks. When the stimuli were applied together the responsiveness of the unit was not influenced unless the right click preceded the left by a small amount, there being complete suppression of the expected response when right preceded left by between 0.5 and 1.1 msec., and some degree of suppression between 0.1 and 1.4 msec. In other words, an inhibitory interaction pursued
its full course of growing to a maximum and then declining during an interaural time interval of only 1.5 msec.

We have examined a total of four units which showed the change in responsiveness illustrated in figure 12. In one the time interval over which the interaction occurred was five times longer than that shown in figure 12. Also, in a single well-studied case, there were two separate time intervals at which the unit could be suppressed, one being at left leading by 0.5-1.1 msec, the unit never responded; slow waves, however, persisted.

**DISCUSSION**

**Anatomical Correlations**

Certain predictions from anatomical facts regarding SO activity are confirmed in whole or in part by this study. For example, it could be predicted that except for S. seg. both ears should activate the SO region, since n. access. and n. trap. receive afferents from both ears while S. seg. is innervated by the ear on the same side only. Besides this, n. access., with its remarkable dendrites, could be expected to be a place where interaction between impulses from the two ears would be emphasized. On these two points at least, as we have seen, a gratifying harmony exists between the anatomical predictions and the physiological findings (figs. 2, 3, 4, 6). On the other hand, this microelectrode study has failed to reveal any particular difference between the dorsal part of n. trap., where end bulbs of Held are the major synapse, and its ventral part where they are not, nor has it yielded compelling evidence for or against tonotopic organization at the SO.

The physiological exploration seems, finally, to have uncovered relationships within the SO that cannot be explained on the basis of the anatomical connections known to exist. For instance, an occasional S. seg. unit, activated as expected by ipsi stimulation, will be suppressed by a sound delivered simultaneously to the contralateral ear. This finding could easily be explained by supposing fibers to pass, say, from n. trap. to S. seg. of the same side; but such connections have not actually been described.

SO responses and hearing: pitch. Microelectrode studies on the auditory nuclei thus far examined (e.g. 1, 10, 11) reveal a number of neural events to be correlated with the frequency of sound stimulation. A responding unit, for instance, is characterized by a response area with a more or less clearly defined best frequency, facts which indicate that a point on the basilar membrane is related functionally to one or more places within each nucleus. The frequency of the unit discharge, furthermore, appears to be imperfectly related to the frequency of stimulation, although for tones below perhaps 1000 cps units may clearly fire in synchrony with the stimulus frequency or at some submultiple of it. Figures 2-5 show SO units behaving in accordance with these principles. As for the third neural event that commonly accompanies tonal stimulation, namely activation of some neurons with simultaneous inhibition of others, we have on occasion seen inhibition of unit activity by tones in the SO, but our experience in this regard has been so limited that we have not presented the material here.

Loudness. An auditory neuron usually responds to increase in intensity by decreasing its latency and firing more often; besides this, an intense stimulus arouses more units to activity than does a weaker one (1). Figures 2 and 7-9 demonstrate that many SO units follow these rules. Furthermore, units having different thresholds to the same stimulus coexist within the nucleus, and intensity increase influences them both by changing the number of active ones, and by raising the activity of those already responding.

There are, however, exceptions to these rules in the SO and elsewhere. As figure 8 demonstrates, an occasional unit will respond earliest near threshold, later for more intense stimuli, and not at all for strong ones. Medial geniculate units behaving similarly have been described (16, figs. 6, 8), but a meticulous search of the thalamic tactile nucleus has failed to uncover such behavior there (17). What part such curious exceptional elements play in mediating loudness is an open question. It is conceivable that their inactivation with intensity in-
crease is at least as important for loudness detection as is the fact that their neighbors respond more briskly.

Localization. The neural basis for binaural sound localization has been much discussed (18–22). Experimental evidence shows that man localizes a sound to, say, the right side if the stimulus strikes the right ear shortly before arriving at the left ear; this condition was simulated in the experiments summarized in figure 12. If cat resembles man in its ability to localize, which seems reasonable, figure 12 suggests that n. access. plays an important role in the process. This nucleus, which has approximately the same size in man and cat, displays just those unique anatomical and physiological characteristics that would peculiarly fit it for such a function. The symmetrical and equal innervation of its cells by the two ears has already been discussed. A distinction among auditory neurons as all belonging to the same functional group, with the frequency-band to which each responds being the principal difference between them. Exact preservation of temporal relations as just discussed suggests, however, that in addition to the well-known system of auditory neurons concerned with the analysis of tones we must recognize a new system concerned chiefly with preserving the exact time of arrival of stimuli at the cochlea. A similar and probably related dichotomy among auditory neurons is indicated in table 2 and figure 6 where ever units are segregated there into click-responders and tone-responders. For several years it has been pointed out that the ear does not behave like a series of simple resonators, nor can the auditory brain explain sound localization on the basis of difference in amplitude on anatomical matters provided by Drs. William Mehler and Grant Rasmussen.

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