Initial Discharge Latency and Threshold Considerations for Some Neurons in Cochlear Nuclear Complex of the Cat

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SUMMARY AND CONCLUSIONS

1. Latency behavior of neurons in the cochlear nuclear complex was studied in 45 barbiturate-anesthetized cats. Stimuli were tonal bursts usually 50–500 ms in duration.

2. Latency of the initial discharge is a systematic function of the frequency and intensity of the tone for a large class of neurons which are termed latency precedence cells. Most cells in the anteroventral cochlear nucleus and many neurons in the anterior division of the posteroventral nucleus belong to this class. Unless otherwise stated, all findings pertain to this cell group.

3. There is usually a correspondence between the discharge rate of a given neuron and the latency of the initial discharge, the higher the discharge rate the shorter the latency. Hence, for any intensity level evoking less than saturation discharge rate, initial discharge latency tends to be shortest for best-frequency stimuli and lengthens systematically as the stimulating frequency departs in either direction from best frequency. However, for some cells, intense stimuli above best frequency evoke initial discharges at latencies which are similar to those produced by best-frequency stimuli.

4. An unexpected finding was that the initial discharge at threshold is a low probability event that can be evoked, except for a short initial time period, by any stimulus cycle throughout the tone duration. Hence, tone duration is a parameter in determining the threshold. Within limits, the longer the tone duration the lower the threshold and the longer the mean latency. It is well known from psychoacoustic studies that in man, threshold is dependent on tone duration. The relation is often thought to be caused by integration processes in higher auditory centers. However, our findings demonstrate this relation for cells in the cochlear nuclear complex and suggest that this result reflects the way action potentials are evoked by auditory receptors.

5. As stimulus intensity is increased a central latency value becomes apparent and the mean latency shortens rapidly. The latency reduction is a smooth function for aperiodic cells (not phase-locked discharges) but occurs in steps equal to the stimulus period for periodic cells (phase-locked discharges). Some 20–30 dB above threshold the mean latency starts to approach asymptotic values. Generally, the shorter the latency the smaller the variability around the mean. For moderate and intense stimuli the dispersion about the mean is often strikingly small. While the arousal time is critically dependent on the position of the stimulus within the frequency-intensity domain of a neuron, the time of arousal, in turn, is probably a significant parameter in competitive activation of the synaptic targets of the cell.

6. Some population measurements were made. No systematic relation was found between the latency of the initial discharge and threshold of the neuron when the tonal stimulus was set at a specified number of decibels above threshold; such a relation was apparent, however, when the stimulus
was at a specified SPL. The latter observation implies that lower threshold cells tend to respond at a given SPL with shorter latencies than do neurons with higher thresholds. There is a systematic relation between mean latency and best frequency. This relation was utilized to derive an estimate of the travel time of the mechanical disturbance along the cochlear partition.

7. There are cells in every major division of the cochlear nuclear complex whose latency behavior differs in various ways from that of the latency precedence neurons. A few such cell types are described.

INTRODUCTION

Several studies have described the response latency of auditory neurons as a function of the intensity and frequency of tonal stimuli (1, 2, 7, 10, 12, 13, 16). Aside from one study of the inferior colliculus (13) and one in the nuclei of the lateral lemniscus (2), there is little systematic information about the latency of responses to tone bursts throughout the response area of a neuron and no information about the relation of phase-locking to latency in the cochlear nuclei.

The purpose of this series of experiments was to explore the latency behavior of cells located in the anteroventral cochlear nucleus. It soon became apparent that most anteroventral neurons, as well as many neurons located in the anterior part of the posteroverentral nucleus, belong to a distinct neuronal group for which the latency to the first spike is a systematic and sensitive function of the frequency and intensity of the tonal stimulus. The major goals of this paper are to evaluate the latency behavior of neurons in this class, to define the conditions under which the cell is aroused, and to consider some physiological implications of the findings. However, there are neurons in all major divisions of the cochlear nuclear complex which react differently as regards the latency of the initial discharge. It was therefore thought useful to characterize briefly some of these cells.

METHODS

The data were gathered in essentially the same experimental material and using the same procedures as described earlier (20). Therefore, only a brief summary of the pertinent methods will be given. The cochlear nuclear complex was visualized by aspirating the overlying cerebral cortex, white matter, and cerebellum. A short plastic cylinder was then cemented to the skull to provide support for a Davies microdrive used to advance indium electrodes into the tissue. The pinna ipsilateral to the cochlear nuclei to be studied was removed and a short, hollow earpiece inserted to a point approximately 2 mm from the tympanic membrane. A calibrated probe-tube condenser microphone was used in conjunction with a General Radio wave analyzer (model 1900) to measure the sound pressure level (SPL) at the tympanic membrane for stimulus frequencies between 20 Hz and 25.6 kHz. The calibration data were stored in a LINC computer and used in conjunction with a computer-controlled oscillator (General Radio 1309 A) and attenuator to generate tonal stimuli transduced by a Telex dynamic earphone. The stimulus envelope was shaped by an electronic switch that produced a linear rise/fall time which was usually set to 6 ms.

After a preliminary determination of the approximate threshold and the frequency range to which a given neuron was sensitive, the response area of the neuron was determined by presenting, under computer control, a matrix of stimulus frequencies and intensities. Sets of tone bursts were presented initially at the lowest intensity and lowest frequency, then at higher intensities at that frequency, and then the intensity series was repeated at each higher frequency until the highest scheduled frequency-intensity set was presented. A set consisted usually of 10, 20, or 50 stimuli; on occasion much larger sets were used. In addition, after every eight stimulus sets, the level of spontaneous activity could be assessed by inserting a set in which no stimuli were presented.

Tonal stimuli were usually 50-500 ms in duration. The repetition rate varied with duration of the tonal burst. The rest period between bursts commonly exceeded 4–5 times the duration of the stimulus. In some experiments the effect of stimulus cadence on the latency of the first discharge was studied extensively.

On-line analysis of the data provided a response area plot of the number of spikes versus frequency at each selected SPL. Since the range of spontaneous activity was known for each neuron, the approximate threshold could be ascertained from the first consistent increase of the rate-intensity function. For neurons which were silent when not stimulated, a precise definition of threshold will be given when presenting the data.

Neural signals and appropriate synchronizing
RESULTS

Latency precedence neurons

LATENCY RESPONSE AREAS. Figure 1A illustrates the spike-count response area for a high best-frequency neuron. Spontaneous activity was less than 0.1/s. For each stimulus set, 10 tone bursts of 200 ms duration were presented at 1 s intervals. On a linear frequency scale the isointensity contours are almost symmetrical about the 11.6-kHz best frequency (as determined in 0.2-kHz steps) and the threshold was about 7 dB SPL. To facilitate comparison of the spike-count area and the latency response area shown in Fig. 1B, increasing latency values are plotted toward the bottom of the ordinate. For clarity of presentation, latency values greater than 15 ms are not shown in Fig. 1B. At 17 dB SPL the latency was at a minimum for best frequency; latencies for the next higher and lower frequencies were longer than 15 ms and are off scale. Figure 1C shows, on a compressed latency scale, the latency values and spike counts for the best frequency stimulus over the entire intensity range tested.

Let us consider first Fig. 1B. Mean latency of the initial discharges increased as stimulus frequency departed from best frequency, although at the higher intensities there was a range of frequencies around best frequency that evoked discharges at very similar latencies. For each stimulus frequency, mean latency decreased as stimulus level increased from 17 to 77 dB in 10-dB steps. The variability of first-spike latencies bears an inverse relation to the mean value. When the standard deviation of the initial-spike latency is plotted against stimulus frequency for several intensities (Fig. 1D) the functions appear to parallel the latency functions. Variance was least around best frequency and increased as stimulus frequency departed from best frequency. For any frequency, variance decreased as intensity increased, and variability of the first-spike latency quickly assumed remarkably small asymptotic values.

The latency behavior shown in Fig. 1B is representative of one of two patterns encountered in our material. Figure 2 shows data concerning the other pattern which occurred frequently. On a linear frequency scale the spike-count response area (Fig. 2A) is much smaller than that of the latency response area (Fig. 2B).
FIG. 1. Data for neuron 70-199-2. A: discharge rate as a function of stimulus frequency and intensity. Numbers indicate sound pressure levels re 0.0002 dyn/cm². B: latency response area. Mean response latency at indicated frequencies and intensities. Latencies longer than 15 ms not shown; longer latencies toward abscissa. C: discharge rate and mean latency as a function of SPL at 11.6 kHz. Mean latency curve based on 50-ms sampling time. Standard error, if larger than 0.5 ms, indicated by a bar. D: standard deviations of response latency. Stimulus: tone burst 200 ms in duration. Each data point based on 10 stimuli presented 1/s. Cell located in PVCN.

2B) was strongly asymmetric since the rate functions declined rapidly above best frequency while extending broadly to low frequencies. The latency-response area (Fig. 2C) generally conforms in shape to the discharge-rate area. It shows most features in common with the latency area shown in Fig. 1B except that the latency values did not significantly increase for the 50- to 80-dB stimuli above best frequency, although the spike counts were severely reduced. For these intensities, the shortest latencies actually occurred in response to 2.8- and 2.9-kHz stimuli and increased only slightly for the 3.0-kHz stimulus which elicited a discharge rate approximately one-sixth the
maximal rate. Dot patterns (Fig. 2A) at 70 dB SPL indicate that the reduction of the discharge rate above best frequency was due to the absence of sustained discharges while the initial discharge was present and its latency was short and relatively invariant.

We shall comment later on the occurrence of the two patterns of the latency area. Now, we wish to stress that the latency behavior shown in Figs. 1 and 2 is typical for a large class of neurons in our sample. We shall refer to such neurons as latency precedence cells. The feature which defines them as a class is that the latency of the first discharge is a sensitive and systematic function of the frequency and intensity of the stimulus; moreover, the timing of the discharge is often fixed within strikingly narrow limits. Thus, in a sample of 75 neurons, the standard deviation of the mean latency, measured at best frequency at moderate or intense levels and usually based on no more than 10 or 20 trials, was <0.1 ms for nearly 25% of the sample, <0.25 ms for more than 50%, <0.5 ms for about 75%, and <1 ms for about 90% of all neurons.

LATENCY AT THRESHOLD. Figure 1C implies that near threshold the latency was long but that it shortened sharply with small increments in stimulus strength. However, the standard deviations and the standard errors were large, indicating that small samples (here 10) were inadequate for determination of the mean latency near threshold. Thus, for example, the standard deviation was 10.42 ms and the standard error nearly 4 ms for the 7-dB SPL condition which was clearly about threshold on the basis of spike counts. The initial latency values ranged between 11.29 and 41.02 ms in different trials during the observation period (sampling time) of 50 ms after stimulus onset. Obviously, the initial discharge can occur at widely different times during presentation of near-threshold stimuli.

Figure 3A shows spike counts and latency curves based on more adequate samples. The best frequency of the neuron was 1.8 kHz but the discharges were not phase-locked. Spontaneous activity sampled during the study of this cell was minimal (<0.01 spike/s). Stimulus sets consisted of 50 trials and the tone duration was 50 ms. Threshold was 30 dB SPL on the basis of rate and only 27 of 50 trials were successful in evoking responses at this SPL. The value of the mean at threshold is more reliable than in Fig. 1C since the standard error is 1.8 ms. However, the standard deviation was again large (9.35 ms) and the individual values ranged approximately between 17 and 47 ms during the 50-ms sampling time.

The latency behavior near threshold, as shown in Figs. 1C and 3A is, we believe, typical for all latency precedence cells whose discharges were not phase-locked. For the sake of brevity we shall refer to
such neurons as aperiodic cells. At threshold, discharges appear seemingly at random during tone presentation and, as they are aperiodic, they are indistinguishable from spontaneous discharges except that no spikes occur in the initial period after stimulus onset.

How long can the latency be? Cells whose discharges are phase-locked and hence discharge periodically (periodic cells) provide an unequivocal answer to this question.

Figure 4C shows the distribution of initial spike latencies for a neuron responding to its best frequency stimulus of 0.6 kHz. A tonal signal 20 dB above threshold and 100 ms in duration was presented with an exceptionally long rise time of 30 ms. Discharges grouped about integral multiples of the stimulus period and the first distinct mode occurred after about 19 ms. Of immediate interest is that even at 20 dB above threshold, initial discharges of this neuron were evoked by every consecutive stimulus cycle for at least 80 ms after stimulus onset and for about 50 ms after the signal reached the steady-state amplitude.

Figure 5E presents data for another periodic neuron responding to 0.22 kHz. The tone burst was 220 ms in duration. The 45-dB SPL was only slightly above threshold since the 40-dB stimulus evoked but one spike in 100 trials and only 364 trials of 500 were effective at 45 dB SPL. All discharges were presumably evoked since all occurred about integral multiples of the stimulus period. The earliest discharges were grouped about 16.5 ms. Thereafter, nearly every stimulus cycle was effective in producing at least one initial discharge.

We conclude then that the initial discharge at threshold may occur, except for an early time segment, throughout the entire duration of the stimulus regardless of whether the cell is periodic or aperiodic.
It follows that the duration of the stimulus is a parameter in determination of both mean latency and threshold if the latter is defined as that SPL at which 50% of the trials are effective. (A trial is defined as effective if at least one evoked discharge occurs during stimulus presentation.) Figure 3B illustrates this statement. Four latency-intensity curves are shown based on the same data sets, but the sampling times were successively 20, 30, 40, and 50 ms. The values for mean latencies are substantially different for the different sampling times and the threshold is, respectively, very nearly 34, 32, 31, and 30 dB SPL. All curves, of course, join the 50-ms plot when all trials become effective. Clearly, the threshold is unequivocally defined only if stimulus duration is specified.

**EFFECT OF RISE TIME AT THRESHOLD.** Before proceeding, we shall consider the effect of rise time on the latency. All latencies given in this paper include the acoustic delay of 0.2 ms and are measured from the onset of the tonal stimulus which had (with one exception) a rise time of 6 ms in order to minimize spectral spread.

Since the slope of the rising portion of the stimulus envelope increases as stimulus intensity is increased, the minimal discharge threshold level for a given cell must be crossed earlier and earlier as SPL is increased. What this implies for the latency of the initial discharge is difficult to evaluate. One could suppose that at threshold the measured latency could be longer than the true latency by as much as the entire rise time, that at 20 dB above threshold the maximal lengthening effect could be as much as 0.1 of the rise time, while at 40 dB the effect of rise time would be negligible. On the basis of such considerations one could introduce a correction to the latency values which would compensate for the apparent latency lengthening due to stimulus rise time. It may be observed that the shape of the latency-frequency function would not change, since any correction would involve only a subtraction of a particular constant.
from each data point on a given iso-intensity profile. The data just presented indicate that to make a useful correction requires a precise knowledge of threshold and that even the maximal correction has a relatively small effect when a near-threshold stimulus is relatively long. Thus, when the steady-state amplitude of the stimulus is such that 50% of the trials are effective, the time of occurrence of the initial discharge is, as already stated, primarily a function of stimulus duration. If the initial discharge occurs with nearly every stimulus cycle during a tonal pulse of 220 ms, as is the case for the data shown in Fig. 5E, it matters but little whether during the first 6 ms the stimulus was entirely ineffective since the corrected mean latency would be shorter by 6 ms, which is only 10% of its value.

It is, however, not justifiable to subtract the entire rise time from the mean latency since the lengthening of tone duration as measured by lengthening the sampling time causes a decrease of threshold (Fig. 3B). As long as this is true it necessarily follows that some portion of the rise time of the stronger tone must have a stimulating effect for it contains amplitudes that are equal to or larger than the steady-state amplitude of the weaker tone that now reaches threshold intensity.

The above remarks are meant to emphasize that the effect of the rise time on the initial latency at threshold is not easily
LATENCY INTENSITY FUNCTIONS. As the intensity of the stimulus was raised above threshold, the initial discharges of aperiodic cells started to group around a central latency value, which decreased continuously with each intensity step (Figs. 1C and 3A). The distributions were approximately normal and the variability around the mean decreased continuously with increasing SPL. Figure 6 illustrates these relationships, typical for an aperiodic cell, in first-spike latency histograms.

Examples of intensity-latency relations for periodic cells are shown in Figs. 4 and 5. At threshold or at moderate SPL above it, the distributions of the initial spikes were always polymodal. As the intensity increased the early stimulus cycles became associated with an increased probability of an initial discharge. Consequently, the number of peaks diminished as did, thereby, the variance about the mean latency. However, even at the highest SPL, the distributions of the latencies in response to 0.6 kHz were still polymodal (Fig. 4).

Data for neuron 71-213-1 (Fig. 5) indicate that the distributions of the initial spikes may become unimodal when the period of the stimulating frequency is sufficiently long. As observed before, the distributions were polymodal at near-threshold intensity at 45 dB SPL (Fig. 5E). Already at 50 dB SPL there were only four peaks (the last not shown since it consisted of only three spikes, Fig. 5A). For 60, 80, and 100 dB SPL the distributions were unimodal (Fig. 5B–D). At 50 dB SPL the main mode centered around 16 ms. At 60 dB there was a shift in mean latency by one stimulus period and the distribution centered around the 11.41-ms value; at 80 dB there was still another shortening by one stimulus period and the distribution centered about 7.5 ms. At 100 dB SPL the effective half-cycle remained the same as at 80 dB, though mean latency decreased by 0.41 ms. The distribution became narrower as the total dispersion around the mean for 500 values was not more than ± 200 μs. At 80 dB SPL the distributions for neuron 71-213-1 were unimodal also for 0.1 and 0.16 kHz. Two modes were present for a 0.38-kHz tone, though one of them was small.

In summary, we conclude that the latency behavior of the periodic and aperiodic cells seems in principle similar, even though the shortening of the latencies occurs con-
continuously for the aperiodic cells and in quanta1 jumps, equal to stimulus period, for the periodically discharging neurons. We shall consider some implications of this finding in the discussion.

ANATOMICAL LOCATION AND SOME DISCHARGE CHARACTERISTICS OF LATENCY PRECEDENCE NEURONS. With few exceptions all cells encountered in AVCN were latency precedence neurons. However, such cells occur frequently also in PVCN, at least in the anterior portion. Whether they occur in other regions as well is an open question. The posterior division of PVCN was not examined and the small sample of DCN neurons permits no conclusion, though no neuron which was definitely known to have been located in DCN qualified as a latency precedence cell.

Spike-count response areas, as exemplified in Figs. 1A and 2B, were nearly always simple, that is to say, the spike counts were a monotonic function of SPL and the best frequency was typically the most effective stimulus at any SPL below saturation rate.

Discharge patterns, as defined by distribution of discharges in poststimulus time histograms (PSTH) at best frequency and moderate SPLs, were of several types. Most common were: 1) phase-locked patterns, produced by periodic cells, where the time between successive peaks was equal to the stimulus period; 2) chopper patterns (17), produced by aperiodic neurons, which also display several peaks in the PSTH but the interval between them is not related to the stimulus period; 3) adaptive patterns produced by some aperiodic cells without prominent multiple peaks in the PST histograms. Onset patterns at best frequency were rare in our material, but some latency precedence neurons were essentially onset cells.

Our sample is biased regarding spontaneous activity because, as stated in METHODS, we usually restricted our latency studies to neurons which were silent or nearly silent when not stimulated. However, some studies of highly spontaneous cells suggest that the latency behavior of such neurons may be an orderly function of frequency and intensity, at least when the stimulus levels are moderate or high.

EFFECT OF STIMULUS CADENCE ON LATENCY. However stable the latency may be for a given stimulus configuration, the latency of the initial spike is affected easily by a change in stimulus cadence, that is, by variations in stimulus duration and rest period. Figure 7 presents data from one relevant study. The stimulus was always a 10.0-kHz tone (best frequency) at 78 dB SPL (50 dB above threshold). The duty cycle is plotted against the latency to the first spike for several constant values of the rest period. Duty cycle expresses the stimulus duration as a percentage of the repetition period. Hence, duty cycle % = (stimulus duration × 100)/(stimulus duration + rest period).

The graph indicates that the absolute duration of the rest period is of obvious significance for the latency of the initial discharge. With a rest period of 1,500 ms, even a 50% duty cycle was tolerated easily. On the other hand, with a rest period of 80 ms, even a light duty cycle of 20% already affected the latency.

Broadly speaking, the shorter the rest period, the lighter the duty cycle must be if it is not to affect the latency to the first spike. It follows that the cadence of the stimuli can greatly affect the latency of the initial discharge.

Neurons whose discharges are affected by inhibitory events

There is, as a rule, no reason to invoke inhibitory interactions to explain the behavior of latency precedence cells, though the onset discharge patterns produced by a few of them, in response to best-frequency stimuli, may be an exception to the rule. By contrast, there exist cells in the cochlear nuclear complex, primarily in DCN, where the reaction of the cell leaves little doubt that excitatory and inhibitory events intertwine. It is noteworthy that Evans and Nelson (8) found the excitatory cells to be located in AVCN and PVCN while the inhibitory cells were present in DCN.

We shall not analyze here the responses of DCN neurons for their behavior is often very complex and our relevant sample is small. We thought it useful, however, to present a few samples of cell behavior which differ greatly from the reactions of latency precedence cells, both to set apart more clearly the different cell groups and to illus-
rate how different the latency behavior may be when inhibitory events intervene.

Figure 8 shows the spike-count response area of a neuron whose discharge rate was a nonmonotonic function of SPL; the threshold was less than 10 dB. Discharge rate rose monotonically for each intensity step and reached a maximum at 25–35 dB SPL. Thereafter, the rate declined systematically with each increase of stimulus strength. Table 1 assembles the mean latencies to the first discharge. As SPL increases there is, for most frequencies, first a systematic decrease of the latency values, then a minimum, and finally a systematic increase. The marginally effective frequencies show only the initial latency decrease, probably because at 75 dB SPL they were less than 25 dB above threshold. Standard deviations (not shown) follow the general rule that the larger the mean, the greater the variability. One can conclude that at higher intensity levels when the discharge rate is declining systematically, the latency to the first discharge behaves, at least for some nonmonotonic cells, as if successively weaker stimuli were presented.

Entirely different behavior is shown by a set of "buildup" discharge patterns of neuron 70-154-3 (Fig. 9). The main feature is that the firing rate increased slowly to a maximum which was maintained throughout the stimulus duration. The latency of the initial discharge seems hardly a relevant parameter. The mean latencies were always long though they decreased with increase of
stimulus strength. The actual mean had a value of about 150 ms for the near-threshold condition at 47 dB SPL and about 63 ms at 77 dB SPL.

Individual buildup neurons differ greatly in latency of their initial discharges. However, even the shortest latencies are still longer than those of the latency precedence cells of comparable best frequency. The rate functions are often monotonic, but nonmonotonic functions also occur. The buildup neurons are common in our DCN sample, but no such cell is present in the much larger collection of AVCN neurons.

Finally, Fig. 10 presents data for a neuron where the latency to the first spike cannot have the usual meaning since the cell responded only with inhibition of spontaneous activity. When the response area is plotted in an inverted manner, with low discharge rate at the top of the ordinate and higher rates toward the abscissa, it is evident that the discharge rate varied parametrically with both frequency and intensity. There is a best frequency for suppression of spontaneous activity at 2.5 kHz and the amount of suppression increased with increasing stimulus levels. The entire response area resided either within or below the range of spontaneous activity. We have

TABLE 1. Mean latencies of initial discharge of neuron 70-376-1

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Latencies, in milliseconds, are shown as a function of frequency and intensity of the stimulus; rate response area is shown in Fig. 8.
FIG. 9. Buildup neuron 70-154-3. Dot discharge patterns for best-frequency stimulus at 7.0 kHz at indicated SPL. Each dot represents a spike in 20 consecutive stimulus presentations. Note the increase of discharge frequency with time and a seemingly erratic latency behavior at the tone onset. Stimulus: tone burst 1,000 ms in duration. Rate: 1/2 s. Cell located in DCN.

only two such cells in our sample and both were located in DCN.

Some measurements on population of latency precedence cells

MEAN LATENCY AND THRESHOLD. If response latency is primarily a function of the effective amplitude of the stimulus, no relationship would be expected between response latency and threshold for stimuli exceeding threshold levels by a constant number of decibels. On the other hand, if the stimulus is at a constant absolute level, we would expect the latency of the responses of low-threshold neurons to be shorter than the response latency of higher threshold cells since the lower threshold cells would be driven by an effectively greater amplitude signal than would cells with higher thresholds. Data in Fig. 11 are in accord with these expectations.

Mean response latencies of 72 cells are related in Fig. 11A to cell threshold. The stimuli were at best frequency, 30 dB above threshold. The coefficient of correlation ($r = 0.16$) is not statistically significant. Thus, there is no evidence that the latency of response to stimuli that exceed threshold by a given amount depends on cell threshold.

Figure 11B illustrates the relation between mean latency and threshold when best-frequency tones were presented at a level between 60 and 69 dB SPL. It was not possible to select the same stimulus level for all neurons since the levels used during data collection were chosen according to the initial estimates of threshold for each individual neuron and were usually by 10.220.33.1 on November 3, 2016 http://jn.physiology.org/ Downloaded from

FIG. 10. Inhibitory response area for neuron 71-25-6. Suppression of spontaneous activity as a function of frequency and intensity of the tone. Note that the lowest ordinate values are plotted at the top of the ordinate. Solid line indicates mean value of spontaneous activity; dashed lines are the minimal and maximal values. Stimulus: tone burst 500 ms in duration. Rate: 1/2 s. Each data point based on 10 presentations. Cell located in DCN.
increased in 10-dB steps. Some of the variability around the line of best fit is due to the 10-dB range of stimulus levels and to the inaccuracy of the estimate of threshold. Nevertheless, a positive correlation ($r = 0.61$) exists between cell threshold and the latency of response and the result is highly significant ($t$ test, $P < 0.001$).

It appears then that, for a given stimulus level, low-threshold cells tend to respond at a shorter latency than do neurons with higher thresholds.

ESTIMATE OF TRAVEL TIME OF MECHANICAL DISTURBANCE ALONG COCHLEAR PARTITION. Broadly speaking the latency of the initial spike is the sum of two sets of components (11). The first consists of transmission delays, presumably invariant for a given neuron; the second set involves delays that occur at the hair cell-nerve fiber junctions and at the synapses in the cochlear complex. It is the latter delays which result in variation in latency with stimulus intensity. The transmission delays include the neural conductions, the acoustic and middle ear delays and, what is of particular interest here, the mechanical travel time, that is, the delay due to propagation of the mechanical disturbance along the basilar membrane.

If the stimulus is set at a specified number of decibels above threshold, the delays due to stimulus strength could be expected to be approximately the same for the different cells in the sample. The transmission delays may be also assumed to be about constant except for the mechanical travel time which should vary systematically as a function of best frequency. This is expected because best frequency indicates the locus on the basilar membrane whose motion activates the neuron, and this locus lies closer to the apex of the cochlea the lower the best frequency. Thus, the variations of latency with best frequency for a population of neurons should provide an indication of the time required for propagation of the mechanical disturbance.

Figure 12A shows, for 73 latency precedence cells, the relation between best frequency and the mean latency to the first spike when the best frequency stimulus was 30 dB above threshold. A higher stimulus level was not used because the required SPLs often could not be generated at the higher frequencies. There is an obvious inverse relation between latency and best frequency.

In order to obtain an estimate of the mechanical travel time we fitted a power function to the data points using the Box algorithm (3). The equation for the curve is: $L = A F^B + C$, where $L$ = mean latency in milliseconds, $F$ = best frequency in hertz, and the constants as determined by the fitting program are: $A = 27.4$, $B = -0.284$, and $C = 2.35$. The constant $C$ can be taken as a measure of those transmission delays which are independent of frequency. Hence, travel time is approximated by subtracting $C$ from each latency value.

Figure 12B shows the log-log plot for the data points after the subtraction. The straight line is the logarithmic transform of the fitting equation moved downward by the value of $C$. Since the sample is small and the scatter of the data points is great, the computed trend line must be viewed with considerable caution. Actually, the line of best fit intercepts the 10.0-kHz point at 2 ms and crosses...
the 0.3-kHz point at 5.42 ms. Thus, the travel time of the mechanical disturbance between these two frequency loci is estimated to be 3.42 ms on the basis of latency data. This value compares reasonably well with the 4.12-ms travel time between the two loci obtained by plotting the best frequency against the slope of cumulative phase shifts for AVCN cells (9). The latter sample is substantially larger (n = 149) but is of necessity restricted to cells which discharge periodically, a restriction which does not apply to the latency sample.

It is noteworthy that C (which is expected to represent the sum of all transmission delays except that due to travel time) is 2.35 ms for the latency data but only 1.51 ms for the phase sample (9). While it would be injudicious to argue what this difference may imply, the delays would be expected to be longer for the latency data. The phase data were gathered at high stimulus levels, whereas our latency analysis has been done at 30 dB above threshold, a level at which latency usually did not reach asymptotic values.

It may be mentioned that Anderson et al. (4) estimated the travel time to be 4.30 ms between the 10.0- and the 0.3-kHz points using phase data for auditory nerve fibers of the squirrel monkey. It seems that the travel time of the mechanical disturbance is similar for the squirrel monkey and the cat and that these three estimates are in fair agreement.

Our estimates of travel time of the mechanical disturbance are considerably longer than those of von Békésy (5) based on his work on a cochlear model and human cochleas. His determination of the propagation time of clicks in the cochlea indicates that the disturbance reaches the 0.5-kHz point after 1 ms. In the cat, Kiang et al. (14) noted a relation between the best frequency of an auditory nerve fiber and the latency of its response to clicks. Neurons whose best frequencies were above 2.0-3.0 kHz were said to respond almost synchronously, that is to say, no measurable latency difference was detected between about 20.0-kHz points and those at 2.0-3.0 kHz. On the other hand, fibers with best frequencies lower than 2.0 kHz responded with systematically longer latencies as the best frequency became lower. Kiang et al. did not attempt to establish an equation for travel time although they interpreted the longer latencies to be a consequence of longer travel times and felt that their results were in satisfactory agreement with the data of von Békésy. Recently, Bourk (6) plotted for a sample of anteroventral neurons the best frequency of the neuron versus latency of the click response. It is obvious that a relationship exists. Unfortunately, no trend line was calculated. Since there is a considerable scatter of the data points and relatively few pertain to best frequencies below 0.5 kHz, no detailed comparisons of Bourk’s and our results can be made. However, one can estimate from the graphs that the latency of the click response lengthens as the frequency becomes lower and that the
DISCUSSION

Latency precedence neurons

Our findings establish that there exists in the anteroventral cochlear nucleus and in the anterior division of the posteroverentral nucleus a large group of neurons whose initial discharge latency is a systematic function of the frequency and intensity of the tonal stimulus. We refer to such neurons as latency precedence cells because there is little doubt that it is this class of cells which transmits, in a hierarchical order, time information concerning the activation of the neuron. Since the response to a sustained tone is commonly only an onset burst in higher auditory centers, it is tempting to infer that the latency of the initial discharge is indicative of the influence a given neuron may exert on its synaptic targets. It is noteworthy that the latency to the initial spike is sensitive not only to the frequency and intensity of the tone, but also to the stimulus cadence.

There is a correspondence between the discharge-rate area of a neuron and its latency area. In general, the higher the discharge rate, the shorter the latency. Hence, the best frequency tends to produce responses with the shortest latencies at any SPL below saturation. In apparent contradiction is the observation that quite frequently at least one (the highest) stimulus level continued to produce responses of short latency for frequencies above best frequency, although the discharge rate was greatly diminished (Fig. 2). The longest tones examined in this connection lasted 220 ms. As intensity is raised the early stimulus cycles become rapidly more effective, and at high stimulus levels even the first relevant cycle may be always effective in triggering the initial discharge if the stimulus period is sufficiently long. The evidence is strong that aperiodic cells react, at any intensity level, in a manner similar to that of periodic cells, even though the shortening of the latency is a continuous function for aperiodic neurons while it occurs in steps equal to the stimulus period for periodic cells.

The latency behavior of the latency precedence cells strikingly resembles the behavior of the auditory nerve fibers. Although we have only fragmentary data concerning the latency of the auditory nerve fibers there is little doubt that when the stimulus approaches threshold intensity, the latency of the initial discharge may be very long and may be measurable in tens of milliseconds (unpublished observations). Moreover, the behavior of periodic cells resembles the behavior of auditory nerve fibers responding with a train of spikes to a steady-state, low-frequency tone (19). As the stimulus approaches threshold intensity, long interspike intervals become more numerous and at near threshold, all stimulus cycles seem to cause discharges with a very low but similar probability. Hence, some speculations may be permissible. One way to account for our data is to assume that: 1) the hair cells are excited only by unilateral deflections of the basilar membrane; 2) the excitation produces a multitude of local excitatory events as a function of SPL; 3) such events sum during each favorable half-cycle of the stimulus and decay, not necessarily to zero, when the mechanical drive on the receptors is reversed.
If this were so, one could easily account for the behavior of a periodic cell of low frequency (such as shown in Fig. 5) since each cycle of the stimulating tone could be viewed as an essentially independent stimulus. One would expect, for high stimulus levels, all discharges to occur during the first favorable half-cycle, while at threshold each half-cycle would have the same probability of discharge. For the periodic cells of higher frequencies and aperiodic cells certain assumptions need to be made concerning the interactions of the excitatory and decay processes. However, we shall not elaborate further on the problem here since the matter can be approached experimentally and we intend to do so.

Our finding that the threshold is dependent on tone duration is in harmony with the well-known psychoacoustic observation that the threshold for a human observer is lowered when the tonal pulse is increased in duration (18, 21). The data of Plomp and Bouman (18) indicate that an increase in duration of a tonal pulse from 20 to 50 ms lowered the threshold by 4.2 dB (average for two subjects at 1.0 and 2.0 kHz). This value compares rather well with a 4 dB threshold shift obtained for neuron 74-73-2 (Fig. 3B) for the same stimulus durations. The threshold shift is usually thought to be due to temporal integration in the higher auditory centers (23). Our observations do not favor this view, for the effect is already manifest at the level of the cochlear nuclear complex and, we believe, reflects the way the action potential is generated by the auditory receptors.

Latency cue for sound lateralization

Shortening of latency caused by an increase of stimulus intensity may be a factor in the process of lateralizing sounds of high frequency since the lateralization of such sounds depends essentially on the intensity difference at the two ears, due principally to head shadows (15). According to Wiener et al. (22) the difference between the signal intensities at the two tympanic membranes in the cat is approximately 15 dB for a 4.0-kHz stimulus and about 20 dB for an 8.0-kHz signal when the sound is located 90° off midline, i.e., at the side of the head. A disparity of that magnitude would be likely to result in a significant difference in the discharge rates of the two relevant cell populations and, additionally, the less-intense responses would occur at longer latencies. A latency difference between the responses may thus be an additional cue for localization of a transient sound source. The magnitude of this cue could be expected to vary with SPL and be of the order of 1 to several milliseconds. Whether a differential latency cue is actually used in lateralizing a sound source is not known. We can recognize, however, that such a cue is available and its magnitude may well be physiologically significant.

Population measurements

Our measurements on cell population merit some comments. We found no relation between cell threshold and the discharge latency when the signal exceeded threshold by a specified number of decibels. The implication is that the effective amplitude of the stimulus may be invariant across different threshold values.

By contrast, there is a relation between cell threshold and mean latency for signals at a fixed SPL. Thus, in an ensemble of cells responding to an acoustic environment, the lower threshold cells will not only respond to weaker signals, but they will also tend to respond earlier to intense sounds than do neurons with higher thresholds.

The relation between best frequency and mean latency suggests that when other conditions are equal, the higher the best frequency, the shorter the latency of the response. What this systematic relation may imply for normal operation of the auditory system is not immediately apparent. Since the best frequency indicates locus along the cochlear partition, the relationship reflects, we believe, the different travel times of the mechanical disturbance along the cochlear partition as was considered in some detail in RESULTS.

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