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NEURAL ENCODING OF SOUND SENSATION EVOKED BY ELECTRICAL STIMULATION OF THE ACOUSTIC NERVE

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SUMMARY–A series of psychoacoustic experiments was conducted in subjects implanted with a permanent intracochlear bipolar electrode. These experiments were designed to reveal the nature of the sensation evoked by direct sinusoidal electrical stimulation of the acoustic nerve. A series of single unit experiments in the inferior colliculus of cats was then conducted, using intracochlear stimulus electrodes identical to those implanted in human subjects in all respects except size, and using identical stimuli. These physiological experiments were designed to reveal how sounds evoked by intracochlear electrical stimulation in humans are generated and encoded in the auditory nervous system. Among the results were the following: 1) The sensation arises from direct electrical stimulation of the acoustic nerve. It is not "electrophonic" hearing arising from electro-mechanical excitation of hair cells. 2) While sounds are heard with electrical stimulation at frequencies from below 25 to above 10,000 Hz, the useful range of discriminative hearing is limited to frequencies below 400-600 Hz. 3) There is no "place" coding of electrical stimuli of different frequency. Tonal sensations generated by electrical stimulation must be encoded by the time order of discharge of auditory neurons. 4) The periods of sinusoidal electrical stimuli are encoded in discharges of inferior colliculus neurons at frequencies up to 400-600 Hz. 5) Both psychoacoustic and physiological evidence indicates that the low tone sensations evoked by electrical stimulation are akin to the sensations of "periodicity pitch" generated in the normal cochlea. 6) Most cochlear hair cells are lost with intracochlear implantation with this electrode. Most ganglion cells survive implantation. Implications of these experiments for further development of an acoustic prosthesis are discussed.

There have been several attempts to reestablish hearing in subjects with profound sensorineural deafness through direct electrical stimulation of the remaining acoustic nerve.[1-8] In one reported series, Michelson[8,9] permanently implanted a bipolar electrode within the scala tympani in three deaf patients. Because these patients have a stable functioning unit, it has been possible over the past 18 months to more completely determine what they hear with simple intracochlear electrical stimulation of the acoustic nerve.

Given these basic psychoacoustic data, a series of physiological experiments was conducted in cats designed to reveal how these auditory sensations are generated and encoded in the auditory nervous system. The stimulating electrodes used in cats were identical to those implanted in human subjects in all respects except size; stimuli employed in the two sets of experiments were nearly identical. In these physiological

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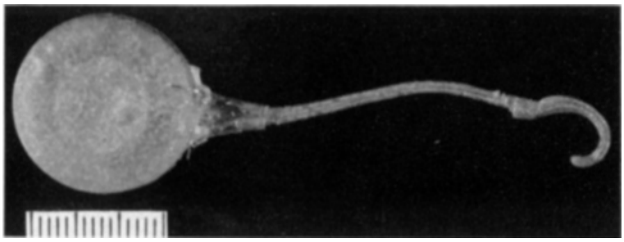

Fig. 1. Implanted electrode-receiver system. The receiver (at the left) is embedded in methylmethacrylate; the electrode leads are embedded in Silastic®. The Silastic® is molded to fill the scala tympani in the basal cochlea. The electrode implanted in cats is similar to that shown in all respects except size: it extended 9 mm into the scala tympani in the basal coil. Small scale divisions are 1 mm in length.

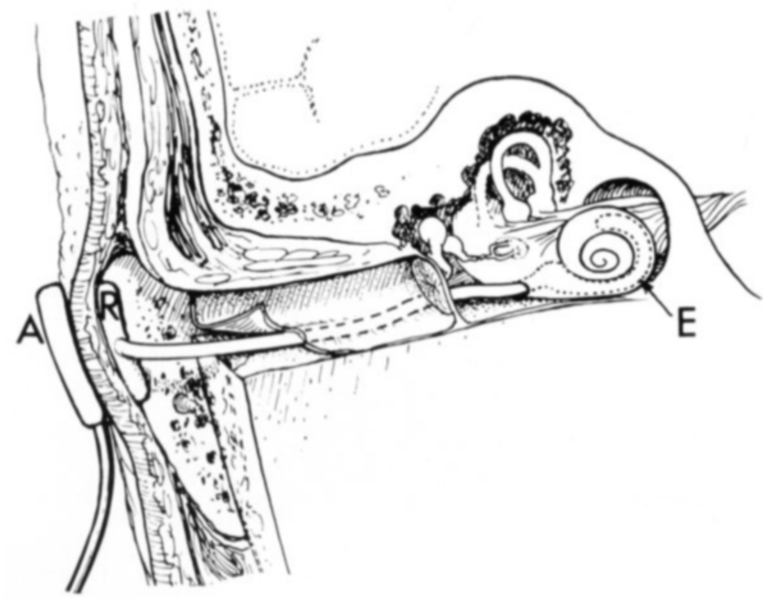

Fig. 2. Diagrammatic representation of the implanted electrode-receiver. The electrode (E) extends about 11 mm into the scala tympani in the basal coil; it is inserted via the round window. The receiver (R) and electrode leads are fastened into position with methylmethacrylate. The receiver is driven (across the skin-subcutaneous gap) by the transmitter antenna (A) worn much like a bone conduction hearing aid.

investigations, the response properties of single neurons in the inferior colliculus (IC) of the cat have been chosen for study for two reasons: First, binaural properties of neurons of IC allow for a direct comparison of their response to sound stimulation (ipsilateral) and electrical stimulation (contralateral). Second, neurons in the colliculus are normally driven from approximately the same site in each cochlea, and there is a highly systematic representation of the cochlea within the nucleus.[10,11] Therefore, it is possible to monitor the effect of electrical stimulation along the length of the cochlear basilar membrane. Thus, the cochlear "place" representation of simple electrical stimuli can be determined by monitoring the response of neurons within the IC.

With this physiological and psychoacoustic data, and with evidence from earlier studies of the response to electrical stimulation in humans and animals, especially those of Simmons,[7]

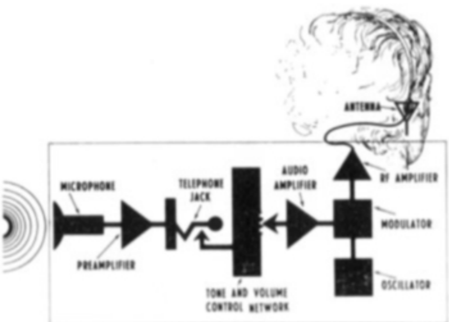

Fig. 3. Schematic diagram of the patient transmitter. In psychoacoustic experiments, electrical stimuli were fed directly to the transmitter via an input jack ("telephone jack"), thereby bypassing (and decoupling) the microphone.

Kiang and Moxon[12,13] and Clark et al.,[14] we can understand how the sensation heard by these patients is generated and encoded in the auditory nervous system up to the level of the inferior colliculus. We can also understand how it relates to the normal hearing mechanism. This provides an objective evaluation of acoustic nerve stimulation procedures and suggests how substantial improvement of stimulating systems might be effected. Relevance of these data to questions of normal encoding of sound sensation is discussed. A preliminary report of these experiments has been presented elsewhere.[15,16]

METHODS AND MATERIALS

Psychoacoustic Experiments. Four patients implanted with intracochlear stimulating electrodes by Michelson were studied. The preoperative hearing status of three of these patients has been described earlier.[8,9] Audiometric testing before and after implantation in a fourth patient (profoundly deaf as an apparent consequence of neomycin treatment) revealed no measurable hearing in either ear. No hearing of sound stimulation in the implanted ear could be demonstrated in any of these four subjects, as determined postoperatively by use of conventional audiometric procedures.

A photograph of the intracochlear electrode implanted in these subjects is shown in Figure 1. The platinum-rhodium bipolar electrode is mounted in Silastic® molded to precisely fill the scala tympani. The implantation procedure has been described.[8] The exposed electrode surfaces lie along the basilar membrane over approximately half the basal turn (Fig. 2). The electrode derived its input from a small radio frequency receiver (demodulator) embedded within a shallow, circular depression in the mastoid cortex with methylmethacylate.

The receiver was driven by a microphone/amplifier/tone control/transmitter system, outlined schematically in Figure 3. The transmitter antenna was positioned and held in place over the receiver (across the skin gap) by a headband. The impedance and some input-output characteristics of the receiver-electrode were determined in situ during the implantation procedure. In all psychoacoustic experiments, voltage levels were initially estimated through the use of a test receiver identical to that implanted in these patients.

The envelopes of sinusoidal electrical stimuli arising from oscillators* were shaped by tone switches. The output level of the two switches was controlled by calibrated attenuators. Timing of electrical and sound stimuli was controlled by a series of six programmable timers and a preset counter. These timers were also used to trigger synchronization (sync) mark generators, to introduce measured delays, and to control timing of lamp drivers. The electrical stimuli were fed directly (through a safety limiter) into the amplifier in the subject's transmitter system, thereby decoupling the microphone. Sound stimuli used in several experiments arose from headset speaker phones** mounted within a metal can with the speaker diaphragms facing upward into a small cavity. Sound was delivered to a standard ear mold via a hollow tube sealed into this cavity.

Among the psychoacoustic experiments which have been conducted are the following: A) Threshold determinations derived through a method of adjustment. B) Pitch scaling determinations derived through a category scaling procedure.[17] C) Pitch discrimination determinations, derived through a method of adjustment. D) Magnitude estimation experiments.[17] E) Pitch matching experiments, conducted with a method of adjustment. Relevant details about methods employed in these experiments will be given in the appropriate figure legends. All experiments were conducted in an IAC sound room. In all experiments except those in which acoustic stimuli were used, only the electrical signal was fed into the room.

Physiological Experiments. An electrode identical to those implanted in human subjects in all respects except size was implanted in

* Model 1309-A, General Radio Co., Concord, Mass.

** Model 61470-07 10 OHM, Telex Communications Division, Minneapolis, Minn.

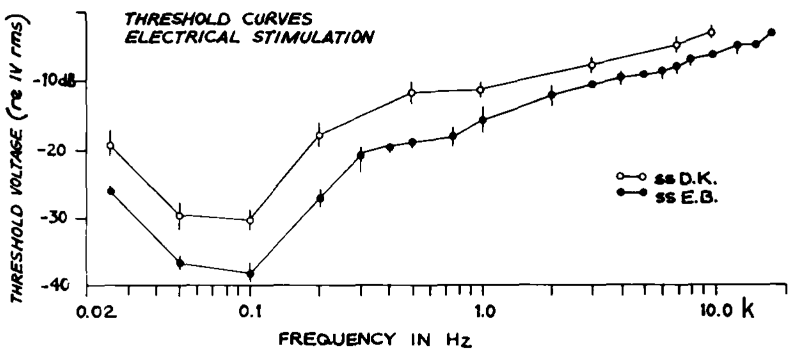

Fig. 4. Threshold curves for sinusoidal electrical stimulation in two subjects derived through use of a method of limits. Subjects moved a lever by which they controlled the voltage of sinusoidal electrical stimuli. They set the level at which the stimulus was just audible. Stimulus envelopes were trapezoidal in form with a rise and a fall time of 5 msec. Stimuli were 800 msec in duration, repeated once/two sec. Stimuli of different frequency were delivered in random order in this and in following experiments. Points represent the mean of three stimulus repetitions. Vertical lines represent the total range of response at each stimulus frequency.

the scala tympani in an identical manner in 17 adult cats. An acute neurophysiological experiment was conducted from 5 to 136 weeks after electrode implantation. Two animals were treated with heavy doses of neomycin (100 mg/kg) for 14 successive days, several months prior to the acute experiment.

In acute experiments, animals were anesthetized and maintained at a surgical level of anesthesia with Nembutal®. Following craniotomy, the contralateral occipital forebrain was aspirated, directly exposing the dorsal surface of the inferior colliculus. Single colliculus units were recorded with platinum-plated, glass-coated platinum-iridium microelectrodes employing conventional micro-electrode recording techniques.

Contralateral electrical stimuli were generated in the system described earlier; stimuli were identical to those used in psychoacoustic experiments. Ipsilateral acoustic stimuli were fed to the ear via a hollow ear bar sealed into the outer ear canal. This hollow ear bar was connected into a small cavity, with the diaphragm of the calibrated audiometric drivers facing into it.

At the termination of each experiment, the cochlea was perfused through the round window with Heidenhain-Susa or formol-saline fixative. It was later decalcified in EDTA, embedded in celloidin, sectioned in the midmodiolar plane and stained with hematoxylin and eosin (H. and E.). The brain was fixed by immersion in formol-saline in several experiments. After embedding in celloidin, 30 μ sections were cut in the plane of the electrode penetrations and stained with thionin. These histological controls verified that at least the great majority of neurons from which data were obtained lay within the central nucleus of the inferior colliculus.[18]

The neural spike record was recorded on magnetic tape, along with sync marks signaling stimulus onset and sine wave zero crossings. Data from isolated neurons was "digitized" off line, using a spike level discriminator. The output of the discriminator represented precisely the time order of discharge of isolated colliculus neurons. This digitized signal was fed (along with sync marks) to special purpose counters, to a raster display generator and to an averaging computer. Histograms were plotted on an XY plotter.*

RESULTS

PSYCHOACOUSTIC EXPERIMENTS

Threshold Curves; Qualitative Description Of Sensation Arising From Simple Electrical Stimulation. Threshold functions for two subjects derived with use of sinusoidal electrical stimulation are shown in Figure 4. Curves derived for the other two subjects (not shown in Fig. 4) are similar. All subjects detected sinusoidal electrical stimulation at stimulus levels of 1 V rms (volt-root mean squared) or less across a frequency range extending from below 25 Hz to above 10 kHz. The sensation was described as "buzzing" in quality at lowest stimulus frequencies

* Models 7100 and 7590 AR, Nuclear-Chicago, Des Plaines, Illinois.

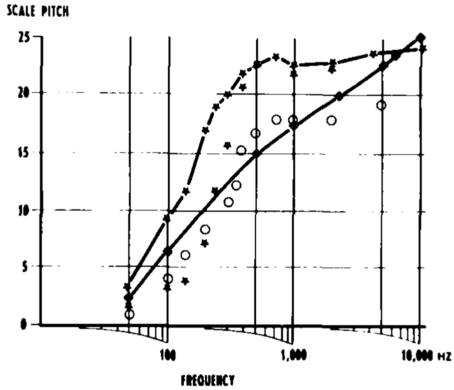

Fig. 5. Apparent "pitch" of sinusoidal electrical stimuli as a function of stimulus frequency in three subjects. Stimuli were 800 msec in duration, repeated once/five sec. Subjects were instructed to place the "notes" on a scale having 25 divisions. All stimuli were of matched intensity. Each point represents the mean of 30 stimulus repetitions at each frequency for Subject E.B. (filled stars); 25 repetitions for Subject J.G. (open circles); and 15 repetitions for Subject D.K. (open stars). A function derived for a normal hearing subject using sound stimulation and following a similar experimental procedure is represented by the broken line.

(below about 100 Hz) in all subjects. At higher frequencies, the sensation was described as having a tonal quality. The region of transition from "buzz" to "tone" was described differently by different subjects. Subject E.B. described the sensation as having a tonal quality from about 100 Hz; she described the sensation as "bell-like" at frequencies above about 150-200 Hz, up to about 1 kHz. At still higher frequencies of electrical stimulation, the sensation was described as tonal in quality, but changes in timbre were clearly described; there, the sound was "thin" or "tinny." In the other three subjects, the sensation was described as having a tonal quality at frequencies above about 100 Hz, but the tone was not described as being "clear" or "bell-like" until a frequency of 200-450 Hz was reached. In the intermediate range, the sensation was often described as a "buzzing tone." Again, at frequencies above about 1 kHz, changes in timbre were noted. The sensation was usually described as tonal at frequencies up to at least several thousand Hz. Interestingly, subjects described stimulation with continuous electrical noise as sounding like noise (e.g., "sounds like rushing water"). All subjects stated upon repeated inquiry that the sensation evoked by electrical stimulation arose from the stimulated ear.

"Pitch" Scaling. All subjects described changes in "pitch" of the sensation evoked by sinusoidal electrical stimulation as a function of stimulus frequency from below 50 to above 500 Hz. The apparent "pitch" heard as a function of stimulus frequency derived through use of a category scaling procedure is illustrated for three subjects in Figure 5. In this experimental task, subjects placed equally loud "notes" of randomly ordered frequency upon a "scale;" the higher the "note" the higher its placement on the scale. Inquiry after the experiments indicated that subjects probably detected differences in rate of stimulation at the lowest frequencies (below 100 Hz), and differences in tonality over the intermediate range (above 100 Hz to 500-1000 Hz). At frequencies above about 500-600 Hz, the apparent pitch of sinusoidal stimuli changed little. This pitch scaling with electrical stimulation can be compared with the function for category scaling of pitch using sound stimulation in a normal hearing subject, represented by the tilted square in Figure 5.

Other experiments were conducted with Subject E. B. using a MEL scaling procedure[17] for determination of the change of apparent pitch as a function of electrical stimulation frequency. Results were consistent with those seen in Figure 5.

"Pitch" Discrimination. Results of "pitch" discrimination experiments closely paralleled those of scaling experiments. That is, subjects could detect relatively small differences in stimulus frequency at frequencies up to 300-600 Hz (Fig. 6). For Subject E.B., for example, the dF* at 100 Hz was

* Variant tone frequency minus invariant tone frequency.

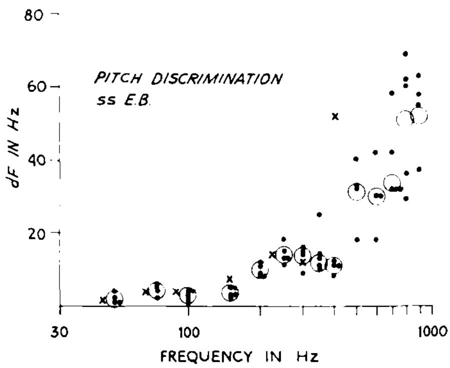

Fig. 6. "Pitch" discrimination in two subjects derived through use of a method of limits. Subjects were stimulated with alternating variant and invariant tones. Both were 800 msec in duration, and each was repeated in alternate sec once/two sec. The tone control network in the transmitter was adjusted so that the stimulus loudness was constant across the tested frequency range. The subject adjusted a knob controlling the frequency of the variant tone, setting the variant tone frequency at which he could just detect a noticeable difference in "pitch." Variant tone frequency minus invariant tone frequency = dF. Open circles represent the mean of 4 or 5 repetitions at each frequency value; dots represent individual trial values. X = mean of three values at seven tested frequencies for Subject J.G.

about 2 Hz; at 200 Hz, 7 Hz; at 500 Hz, 9 Hz and at 900 Hz, 60 Hz. Subjects were required in pitch discrimination experiments to indicate by hand signal which was the higher and which the lower pitch in the alternating stimulus sequence. This was accomplished without error at frequencies up to 500-1000 Hz. No reliable data was obtained for any subject at frequencies much above 1 kHz. There, dF values set by the method of adjustment employed in these experiments (Fig. 6) commonly were set at more than an octave higher than the invariant stimulus sinusoid, and errors in signaling the higher and the lower pitch in the alternating stimulus sequence were common.

Additional Experiments. Magnitude estimation experiments were conducted with three patients. Magnitude functions rose more steeply than with sound stimulation in all cases. The exponent of the power function describing the growth of loudness[17] was about 1.5.[15] In both Subjects D.K. and J.G., functions derived at each of several stimulus frequencies were nearly parallel.

Pitch matching experiments were conducted in three subjects, taking advantage of the limited residual hearing available for matching comparisons in their unimplanted ears. In all cases, subjects had difficulty in precisely matching the pitch of tonal stimuli heard in the unimplanted ear with the "tones" heard in the electrically stimulated ear. Subject E.B. matched very low frequencies (below about 100 Hz) relatively accurately, although making many octave errors. She matched frequencies over the middle range with the fundamental of the stimulus, within about 50 Hz. As frequency of electrical stimulation rose to 400-500 Hz and above she mismatched it to a relatively low-frequency tonal stimulus, consistent with pitch scaling experiments. The task was performed with much less precision by both Subjects D.K. and J.G.

PHYSIOLOGICAL EXPERIMENTS

More than 200 neurons have been studied quantitatively within the central nucleus of the IC in 17 cats. Most neurons isolated in the most superficial aspect of the central nucleus could be excited by ipsilateral sound but not contralateral electrical stimulation at levels below 1 V. Neurons in this most superficial aspect of the nucleus have relatively low best frequencies to sound stimulation, i.e., they derive their input from the most apical sector of the cochlea. Responses to sinusoidal electrical stimulation at 1V or lower stimulus strength were usually first encountered with neurons with best frequencies to ipsilateral sound stimulation in the high hundreds or low thousands. The threshold to electrical stimulation dropped dramatically in every animal studied across the frequency range from about 2 to 6 kHz (Fig. 9), and most if not all neurons deriving their input from this cochlear region down to the extreme base were affected by electrical stimulation. Across this range (about 4-20+ kHz) the threshold of

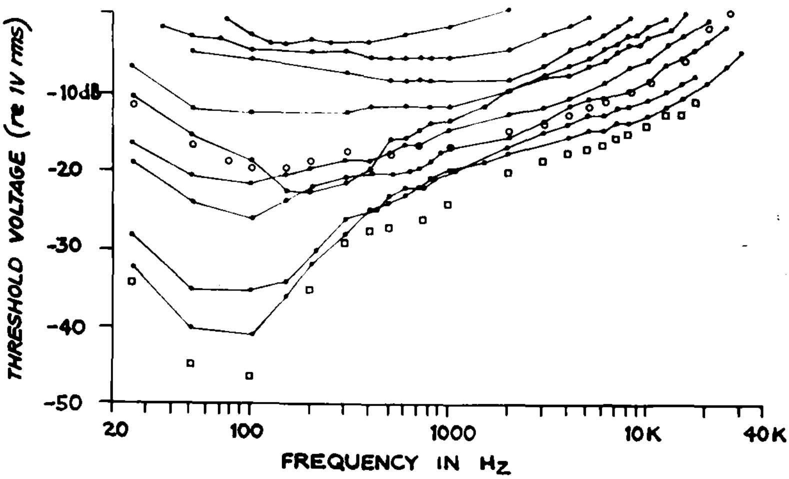

Fig. 7. Threshold tuning curves of 11 isolated colliculus neurons to sinusoidal electrical stimulation. Each point represents the voltage level (ordinate) at that frequency (abscissa) at which the neuron just responds. A tuning curve derived in a neomycin deafened animal is represented by the open circles. The psychophysical threshold curve for Subject E.B. (scaled on the ordinate; see Fig. 4) is represented by the open squares.

driving was relatively constant. Sensitivity in this broad sector of IC was 20-40 dB greater than for neurons deriving their input from the apical cochlea.

Response Patterns of Colliculus Neurons Excited By Electrical Stimulation. Response patterns of colliculus neurons driven by electrical stimulation are similar to those seen for colliculus neurons driven by normal sound stimulation.[10] Two classes of responses were encountered. One class of neurons was excited continuously by sinusoidal electrical stimulation. Response patterns of two neurons of this type are shown in Figures 12 and 13. With these nerve cells, a heavy continuous response lasting throughout the duration of the electrical stimulation was seen across the frequency range over which the cells responded. Thus, the heavy response of the neuron in Figure 13 excited at 5 kHz is very similar to the response at 500 Hz. Continuous responses have been recorded from several neurons of this type at frequencies of 10 kHz or higher. Some of the neurons of this class were also driven continuously by ipsilateral sound stimulation. The response of most of these neurons was a sharply nonmonatonic function of stimulus voltage level (Fig. 14). At higher stimulus intensity levels, the spontaneous discharge of most of these cells was inhibited, and there was a characteristic heavy poststimulus discharge.

A second large population of colliculus neurons was driven continuously by electrical stimulation at very low frequencies; but at frequencies ranging from about 50 to 250 Hz (different with different neurons) and at all higher frequencies, these neurons responded only in relation to the stimulus onset. These neurons often responded to ipsilateral sound stimulation; when they did, only an onset response was seen.

Threshold Tuning Curves. Threshold tuning curves for contralateral sinusoidal electrical stimulation have been derived for more than 100 colliculus neurons. The curves of 11 isolated IC cells are shown in Figure 7. As in the acoustic nerve,[12,13] tuning curves were relatively flat with greatest sensitivity in the range from about 75 to 1000 Hz. All neurons can be driven at all stimulus frequencies (up to at least 10 kHz) given adequate stimulus intensity, and the threshold curves of different neurons are roughly parallel. Differences

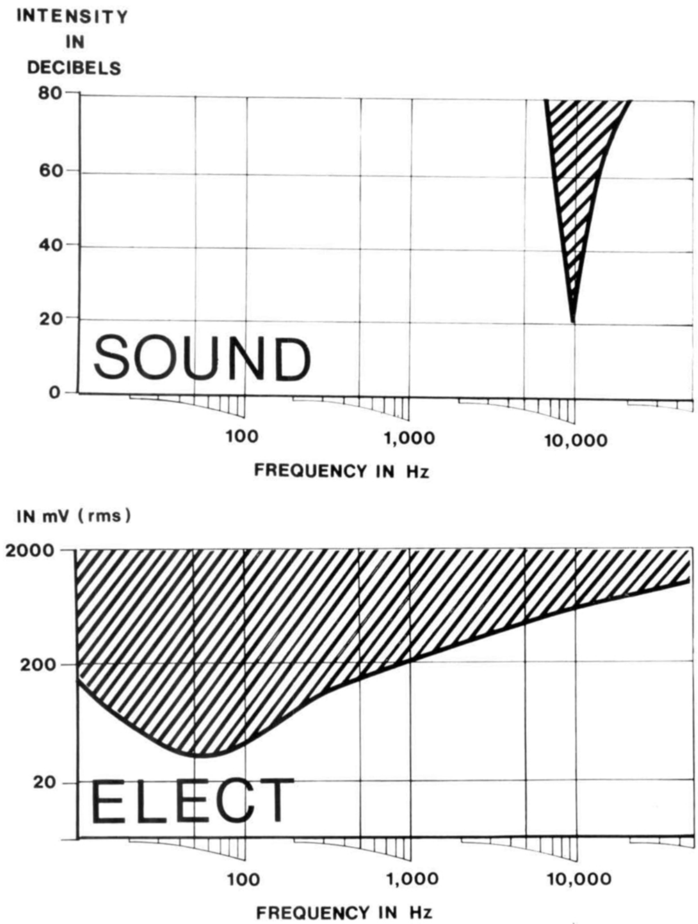

Fig. 8. Diagrammatic representation of the frequency response characteristics of a typical colliculus neuron to electrical and sound stimulation. The response area of the neuron (frequency-intensity domain over which it responds) for contralateral sinusoidal electrical stimulation is represented in the lower graph. The response area of the same neuron for ipsilateral sound stimulation is shown in the upper graph.

in overall sensitivity of different neurons are apparently related to the proximity of the electrode to the cochlear nerve fibers driving inferior colliculus neurons via the cochlear nucleus and superior olive. That is, neurons deriving their input from the apex have much higher thresholds than neurons deriving their input from a broad basal sector nearer and in apposition to the electrode. In the animal from which the nine tuning curves illustrated in Figure 9 were derived, for example, no neurons with best frequencies below about 2 kHz could be excited by electrical stimulation. Thresholds to electrical stimulation were 20-40 dB lower in the sector from about 6 to 12+ kHz than at the 2.7 kHz position. The threshold curves for human subjects paralleled the curves of the most sensitive colliculus neurons (Fig. 7). As illustrated by example in Figure 7, threshold curves for neurons in neomycin deafened animals paralleled those defined in other cats in this experimental series.

"Place" Representation Of Electrical Stimuli. As pointed out in the important study of Kiang and Moxon,[13] the flat threshold curves derived with electrical stimulation are in striking con-

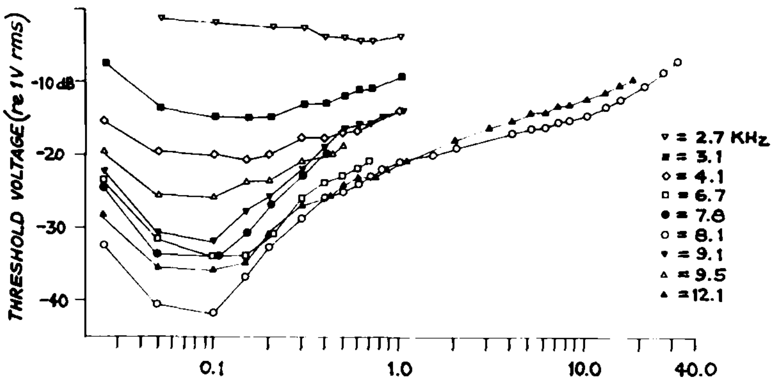

Fig. 9. Threshold tuning curves of nine colliculus neurons studied within a single experiment. Each point represents the voltage level (ordinate) at a given frequency in kHz (abscissa) at which the neuron just responds. The best frequency of each neuron to ipsilateral sound stimulation is indicated.

trast to the sharply-tuned frequency-specific response characteristics of sound-stimulated neurons.[10,19-22] A direct comparison of the response of a colliculus neuron excited by ipsilateral sound and contralateral electrical stimulation (Fig. 8) illustrates this point. With sound stimulation, a "best frequency" of about 10 kHz was sharply defined, and the neuron responded only over a restricted frequency-intensity domain. With electrical stimulation the same neuron responded across the entire audible range of stimulus frequencies. No best frequency could be defined. Greatest sensitivity was seen at lowest stimulus frequencies and all neurons studied had parallel curves. The frequency-specific response character of individual neurons in the auditory system is thus completely lost with electrical stimulation.

The mechanical resolution of frequency components by the normal cochlea excited by sound is also obscured in a second way (Fig. 10). In the acoustic nerve excited electrically with this electrode configuration, probably more than half of the neurons of central auditory nuclei are excited at relatively modest stimulus levels at any frequency across the normal audible range. The central "place" representation of stimuli (the population of cells engaged by stimuli) changes little as a function of frequency, and the cell population excited at any given electrical stimulus frequency is not the same population that signals sound sensation at that frequency.

By contrast, with sound stimulation a frequency-specific response is generated in a restricted population of acoustic nerve fibers, and this response is fed forward to a restricted, specific population of colliculus neurons. Different frequency components of sound are represented in different, restricted, frequency-specific central loci. Thus, a simultaneous representation of the different frequency components of sound can be realized.

Time Order Of Discharge Of Colliculus Neurons. The periods of low frequency sinusoidal electrical stimuli are encoded in the discharge of many colliculus neurons. That is, neural discharges occur over a restriced region of stimulus phase (Fig. 12, right column; Fig. 13, middle column) and interspike intervals correspond with integral multiples of the stimulus period (Fig. 11; Fig. 12, middle column; Fig. 13, right column; Fig. 14). For most neurons continuously driven by sinusoidal electrical stimuli, this representation of stimulus frequency was seen at frequencies up to 400-700 Hz (Figs. 11-14). It was never seen at frequencies higher than about 1 kHz. Commonly, there was a 1:1 spike discharge/cycle at

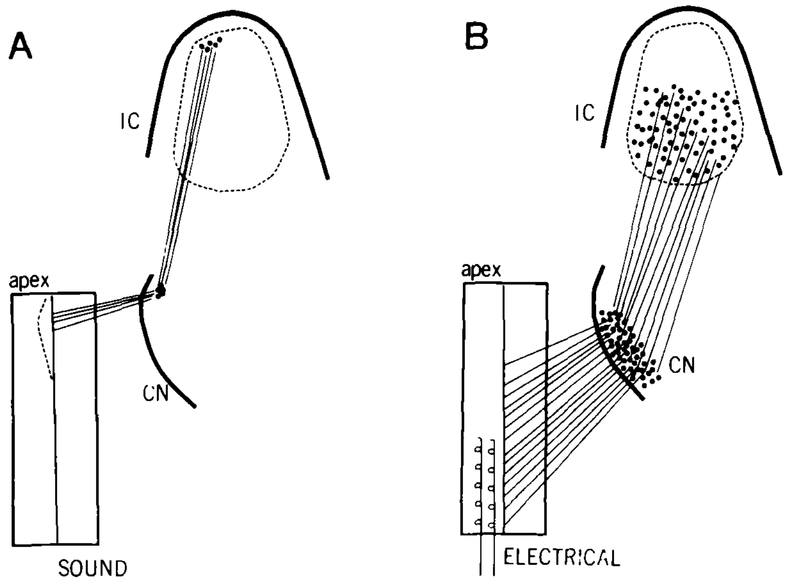

Fig. 10. Diagrammatic representation of the cochlear and inferior colliculus response to: A) Low frequency normal sound stimulation, and B) Low frequency intracochlear electrical stimulation with this electrode. With sound stimulation at a given low frequency, the response arises from a restricted segment of the nerve ending in the apical cochlea, effecting stimulation of a small population of neurons in the superficial aspect of the central nucleus of the inferior colliculus. With electrical stimulation at the same (or any other) frequency, the response arises from direct excitation of a broad segment of the nerve and there is a consequent excitation of a very large population of colliculus neurons. Sensitivity is greatest in the basal cochlea and in a deeper, broad sector of the inferior colliculus.

lowest frequencies (e.g., at 100 Hz; Fig. 13). Multiple discharges/cycle were seen in some but not all neurons at optimal intensities at lowest stimulus frequencies. As a rule, the response was locked to stimulus phase at low frequencies at intensities little above threshold (Fig. 14). Most neurons were effectively driven only over a narrow range of stimulus intensities from about 5 to 30 dB above threshold (Fig. 14). Responses in neomycin deafened animals were indistinguishable from those in other implanted animals.

Site of Generation of Response. The response of colliculus neurons was completely lost after section of the acoustic nerve of the implanted ear, at the end of two acute experiments. Colliculus response to electrical stimulation was not demonstrably affected by section of the opposite nerve innervating the normal cochlea. Binaural interaction between ipsilateral sound and contralateral electrical stimulation was seen in many colliculus neurons. An example is shown in Figure 15. The response of this cell and of several other IC neurons studied was a sensitive function of interaural time delay. The response of most neurons with low best frequencies in the normal sound-stimulated colliculus was similarly a function of interaural delay.[23,24] The response of many other neurons studied was a function of interaural sound and electrical stimulus intensity balance.

These data, with localization of the response in human subjects to the stimulated ear, indicate that the responses described arose solely from the electrically stimulated cochlea.

POSTIMPLANTATION STATUS OF THE ORGAN OF CORTI AND ACOUSTIC NERVE

Temporal bones from six implanted cats studied experimentally have been examined at this time. Postimplantation

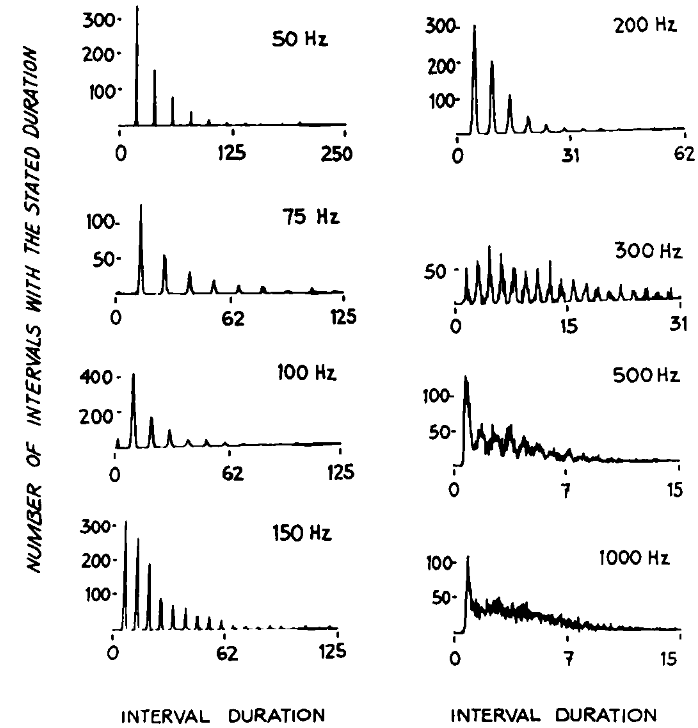

Fig. 11. Interspike interval histogram for an isolated colliculus neuron driven by contralateral sinusoidal electrical stimulation. Each histogram is constructed from 50 stimulus repetitions. All histograms are 400 bins in width. Stimuli were 1 sec in duration, repeated once/2 sec. Stimuli were −8dB (re 1V) at 50 Hz and −11 dB at all other frequencies. Best frequency of the neuron to ipsilateral sound stimulation was about 10 kHz.

times ranged from about six weeks to more than one year. Cochlear hair cells were lost in the basal cochlea as a consequence of implantation of this electrode. Some supporting cells were also lost in the basal cochlea. Some hair cells and supporting cells were present in the middle and apical turns in at least some animals. The spiral ganglion appeared to be normal in the middle and apical turns, but there was some evidence of degeneration (loss of cells) in the extreme base in examined cochleae. The degeneration of the organ of Corti and nerve appeared to be similar to that described for another electrode configuration, by Simmons.[25] Complete evaluation of the histopathological consequences of implantation of this electrode within the scala tympani will be the subject of a later report from this laboratory.

Survival of the acoustic nerve in human subjects is manifested by the apparently unchanging auditory responses with electrical stimulation over time periods of more than four years in the series reported by Michelson.[15]

DISCUSSION

With these data and with information from earlier studies of electrical stimulation in man and animals, a series of conclusions can be drawn as to how sounds heard by patients in this study are generated and encoded in the auditory nervous system.

1. *The sensation arises from direct intracochlear stimulation of the acoustic nerve.* Several points of evidence appear to establish that the sensation arises from the stimulated cochlea. First, sensation in implanted patients is re-

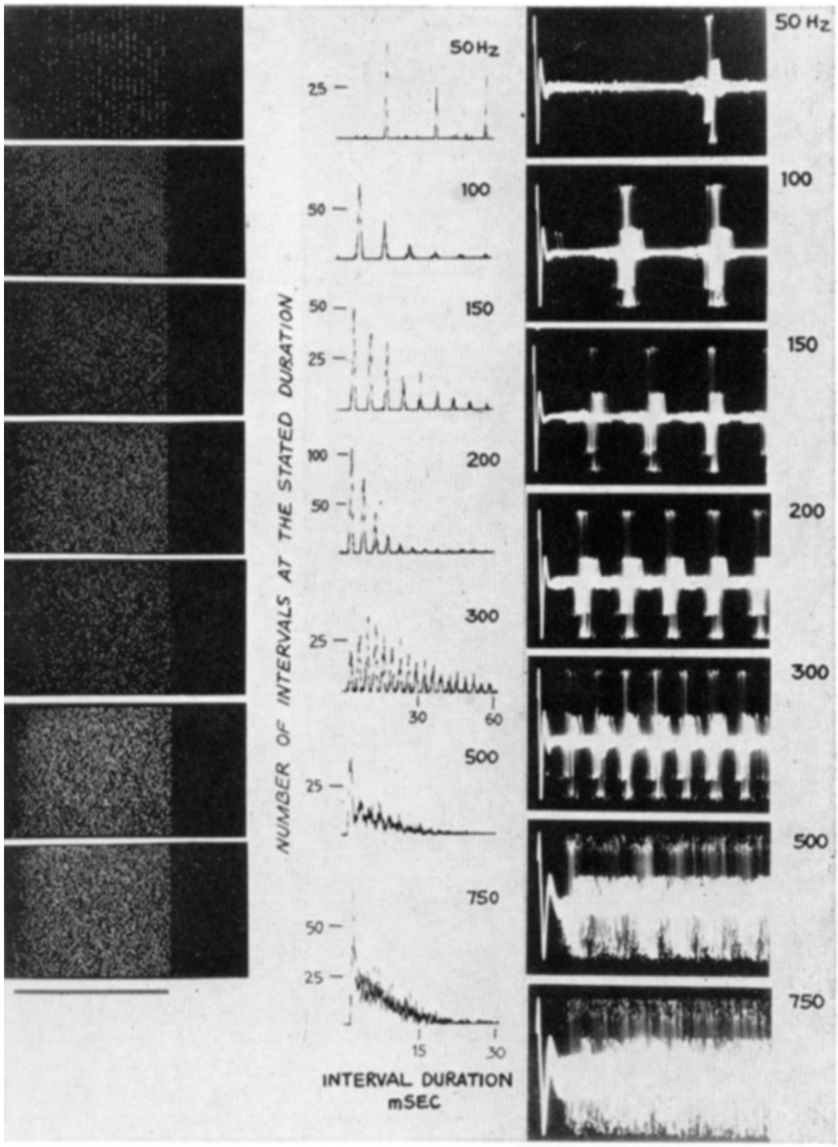

Fig. 12. Left Column: Firing patterns of a colliculus neuron to contralateral sinusoidal electrical stimulation at 50, 100, 150, 200, 300, 500 and 750 Hz. In these "dot displays" and in others in this paper, stimulus onset is at the extreme left of the display. The occurrence of an action potential is indicated by a dot. Stimulus duration is indicated by the black line below each column of dot patterns. In this series, stimuli were 500 msec in duration and were repeated once/sec. There were 50 stimulus repetitions at each frequency. Best frequency of this neuron to ipsilateral sound stimulation was about 9 kHz. Center Column: Interval histograms from the series shown at the left. Histograms are 400 bins in width. Right Column: Photographs of neural spike discharges illustrating the representation of the stimulus period (1/frequency) in the neural discharge of the same colliculus neuron. The oscilloscope sweep is triggered at a fixed position in the action potential, and thus the location in time of subsequent discharges is demonstrated. Each display was derived from 5 sec of electrical stimulation. There is a 2X increase in the time base in the displays at 500 and 750 Hz.

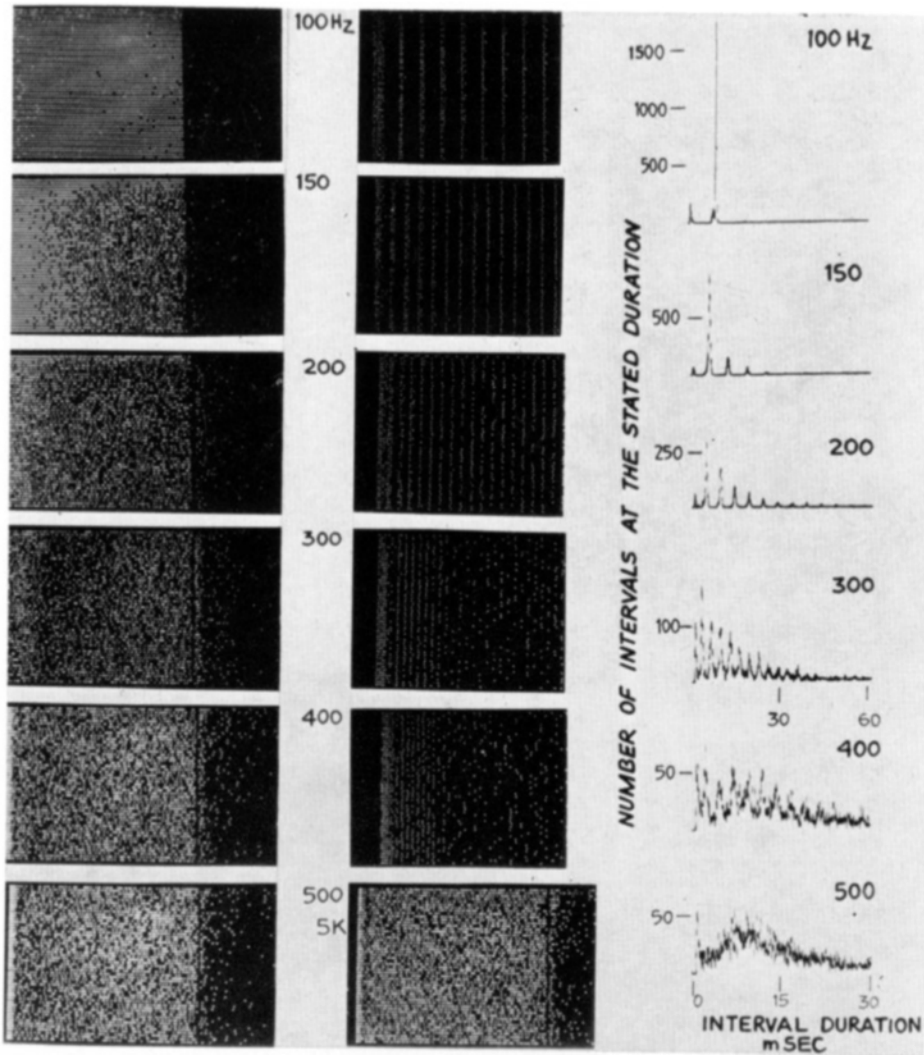

Fig. 13. Left Column: Dot displays showing firing patterns of a colliculus neuron to contralateral sinusoidal electrical stimulation at 100, 150, 200, 300, 400 and 500 Hz. The response at 5 kHz is shown at the bottom of the center column. Stimuli were 500 msec in duration and were repeated once/sec. There were 50 stimulus repetitions in each display. Center Column: Expanded time representation of the first 100 msec. Right Column: Interval histograms from the series shown at the left. Histograms are 400 bins in width.

ferred to the stimulated ear. Second, no sensational evidence of stimulus spread to the brain stem (e.g., facial twitching, dizziness) has been recorded in human subjects. Third, the central auditory neural response is lost with section of the nerve innervating the stimulated cochlea. Fourth, Kiang and Moxon[12,13] recorded responses of acoustic nerve fibers similar to those that were recorded in the IC.

It has been firmly established that the response does not arise from electromechanical excitation of hair cells, i.e., that it is not "electrophonic" hearing.[26-28] First, in two experimental animals in this series the cochlea lacked hair cells as a consequence of treatment

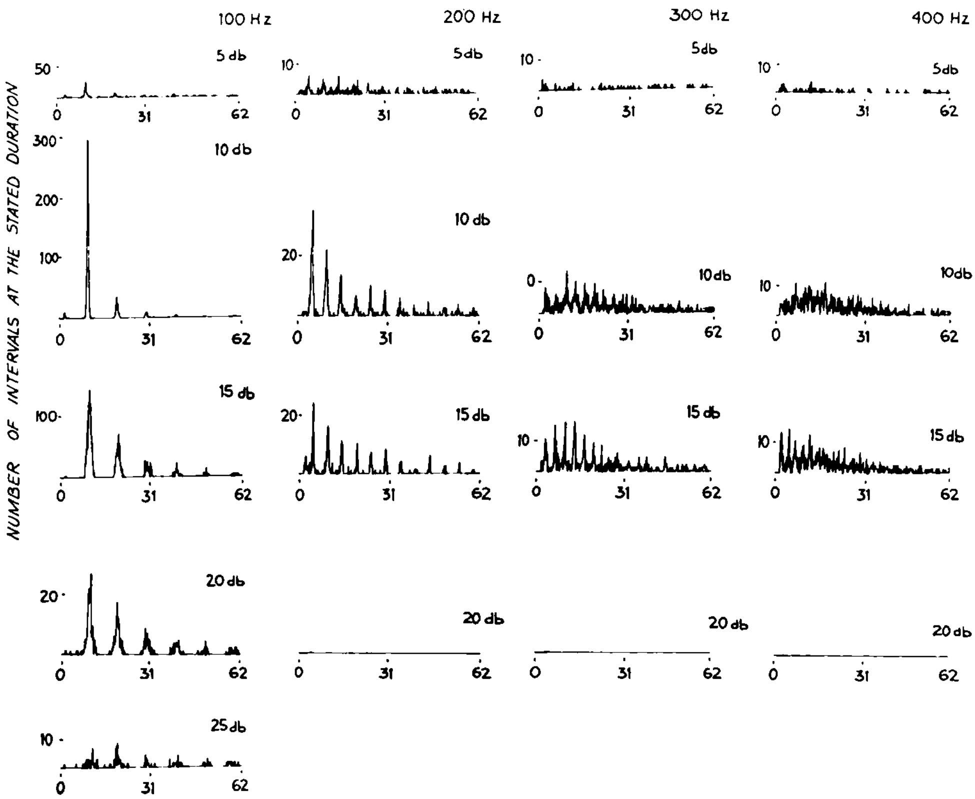

Fig. 14. Interval histograms illustrating the representation of the stimulus period and its multiples in the neural discharge at different intensities at four frequencies at which the neuron responded. Decibel values indicated = attenuation *re* 1V rms. Note that the response is a nonmonatonic function of stimulus intensity at all stimulus frequencies.

with neomycin. In other experimental animals, threshold curves and response properties of neurons deriving their inputs from a cochlear sector demonstrated histologically to lack hair cells, did not differ from those of neurons deriving their input from a cochlear sector in which hair cells may have been present. The correlation of physiological results in cats and psychoacoustic results in human subjects suggests that the input in humans is generated in the same way. Animals in Kiang and Moxon's series[13] were kanamycin deafened; their results correlate well with those reported. Second, on the basis of preoperative hearing tests in implanted subjects and physiological results it would appear unlikely that there are hair cells present in the cochlear sector excited by this electrode. Third, sound sensations evoked by electrical stimulation in a patient deafened as an apparent consequence of treatment with neomycin (with no measurable hearing in either ear) are the same as in other implanted subjects. Finally, the nature of the hearing sensation evoked in these subjects and of the encoding of electrical stimulation by the acoustic nerve in these experimental preparations is different from what is known or can be predicted about the electrophonic effect in many respects.[12,28]

2. *With a bipolar electrode implanted in the cochlear base, the useful range of discriminative hearing is limited to frequencies below 400-600 Hz.* A sound sensation can be evoked at stimulus frequencies extending from below 25 to above 10,000 Hz, but the apparent

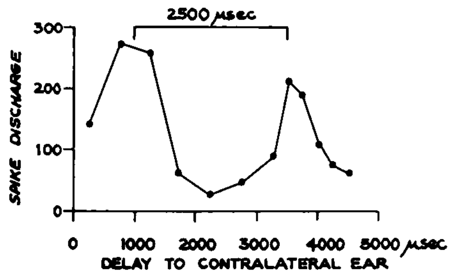

Fig. 15. Response to contralateral sinusoidal electrical stimulation and ipsilateral normal sound stimulation in a colliculus neuron, as a function of interaural stimulus delay. Number of discharges/20 repetitions of a 500 msec stimulus is plotted as a function of the delay (in μsec) of the time of arrival of the electrical stimulus to the contralateral ear. The curve was derived at the approximate best frequency of the neuron to sound stimulation = 400 Hz.

pitch changes as a significant function of stimulus frequency produced by a bipolar electrode implanted in the basal turn of the cochlea occurs only across this low frequency range. Clear tonal sensations can be evoked by low frequency electrical stimulation in these subjects, as in the patient of Simmons.[7]

3. *There is no "place" coding of tonal sensations heard by these subjects.* The frequency-specific responses characteristic of individual elements in the normal auditory system[10,19-22] are not seen with electrical stimulation. Individual neurons stimulated with sinusoidal electrical currents have relatively flat tuning curves that extend completely across the normal hearing range, given adequate stimulus intensity. Differences in sensitivity or in the form of tuning curves are related to proximity of the electrode to acoustic nerve fibers driving the IC neurons (via cochlear nucleus and superior olive).

In animal experiments, stimulation with this electrode favorably excites a broad sector of the acoustic nerve in the basal cochlea; it is probable that this is also the case in human subjects. Whatever the sector of the nerve excited in man, it is evident that all sensations arise from excitation of the same population of peripheral and central neural elements. There is no place coding of stimuli of different frequency. One corollary of this fact is that (as demonstrated in unreported experiments in patients), there can be no analysis of individual frequency components of complex signals in a single-channel stimulation system.

4. *Tonal sensations generated by electrical stimuli must be encoded by the time order of discharge of acoustic neurons.* As there is no place coding of stimulus frequency, the tonal quality of sensations described by these subjects must be encoded by the time order of discharge of auditory neurons. As indicated in earlier studies,[13,29] the periods of low frequency electrical stimuli are encoded in the discharges of neurons in the auditory system at frequencies up to 600-700 Hz. This correlates well with the frequency domain over which subjects can discriminate differences in the apparent pitch of the electrically evoked sensation. The time structure of discharges of colliculus neurons evoked by electrical stimuli resembles that of auditory neurons with low best frequencies excited by sound stimulation[20,30,31] in many respects, although the very low frequency responses in the former case occur over a much more restricted region of stimulus cycle phase.[13]

These experiments provide direct evidence that the tonality of low frequency stimuli can be encoded by the time order of discharge of auditory neurons.

5. *The low tone sensations evoked by electrical stimulation are akin to "periodicity pitch" generated in the normal cochlea.* It has long been appreciated that a low pitch sensation can be evoked through generation of a corresponding low frequency periodic neural input from the middle and high frequency ranges of the cochlea (up to 5-6 kHz). Such a low frequency periodic neural input can be generated with sound stimulation in several ways: 1) With addition of closely spaced higher harmonics, a pitch sensation corresponding to the fundamental of the harmonics and generated at the coch-

lear place of the harmonics can be evoked.[32-35] There is direct physiological evidence that with such stimulation, the period of the low frequency tone heard is represented in the discharge of acoustic nerve fibers innervating the place region of the harmonics[36,37] 2) A low pitch sensation can be generated by low frequency modulation or repetition of a band-limited high frequency noise or click.[38-40] With such stimulation, there is generation of a powerful beating input in the auditory system, with the modulation frequency represented in the discharge of elements deriving their input from the middle or high frequency sector of the cochlea.[41-43]

This low frequency pitch sensation arising from generation of a low frequency periodic neural input from a cochlear region normally signaling high tone sensation is termed "periodicity pitch."[32,44-46]

Sensations evoked by intracochlear sinusoidal electrical stimulation with this electrode apparently also arise from generation of a powerful low frequency periodic neural input from the middle-high frequency sector of the cochlea. It is not surprising, then, that descriptions of sounds heard closely parallel descriptions of "periodicity pitch" evoked by appropriate sound stimulation of the normal cochlea. Both sensational phenomena are evoked across the same range of low frequencies (up to 500-1000 Hz). Descriptions of changes in the quality of the sound as a function of frequency are very similar. In both cases the apparent pitch of the sensation evoked in the range above 500-800 Hz changes little as a function of stimulus frequency. Detailed comparisons of periodicity pitch and electrically generated pitch phenomena are beyond the scope of this report. Such comparisons shall be the subject of a later report from this laboratory, along with some further implications of electrical stimulation studies in humans and animals on normal mechanisms of coding of pitch.

6. *There are several practical implications of these experiments for further development of an acoustic prosthesis.* These experiments indicate what can be achieved with stimulation with a single bipolar electrode. While the range of discriminative pitch is narrow and alone cannot provide sufficient information for direct hearing of speech sounds, it should be used for encoding of the low end of the sound spectrum in the development of a more useful prosthetic system. Differences in sensation evoked in different subjects implanted with intracochlear electrodes probably can be largely accounted for by excitation of different sectors of the acoustic nerve (due, for example, to different degrees of loss of nerve in the basal cochlea). It has long been appreciated that there are differences in the clarity with which low tones are heard as well as differences in the upper limit of the low frequency range over which they are heard, consequent from generation of the low frequency periodic neural input from different cochlear sectors.[33,39] Thus, electrode placement is probably very important for generation of a clear low tone sensation across the widest possible frequency band, and it is possible that with optional placement and an appropriately restricted stimulator, a clearer and more useful sensation can be evoked from a single channel.

No analysis of frequency components of sound can be achieved with a single stimulus electrode. In order to hear different frequency components simultaneously, input must be generated in different populations of acoustic nerve fibers. As Kiang and Moxon[13] have emphasized, a multiple electrode system also will be required for generation of spectral input necessary for direct hearing and interpretation of speech sounds.

Finally, these experiments point out the value of the animal model and normal hearing model for further development of a prosthetic system. From experiments such as these, we can assess the spatial and temporal character of the neural code generated by any implanted electrode system. It should be possible to generate approximate corresponding temporal and spatial inputs in normal hearing subjects through use of appropriate sound stimuli. In this way, further development of a prosthesis can be greatly accelerated.

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