Pitch discrimination in the cat through electrical stimulation of the terminal auditory nerve fibers

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Four cats were chronically implanted with electrodes in the scala tympani of the cochlea. Results support frequency following as a pitch-conveying mechanism, suggesting that electrical stimulation of the terminal auditory nerve fibers on a rate basis produces a sensation comparable to that previously discriminated in an equivalent pure-tone acoustic pattern.

The encoding of pitch, which varies as a function of the physical dimension of frequency, has long been of interest to psychologists. While in the past the problem has been tackled primarily at a psychophysical level (Békésy, 1968), it is important to also investigate the basic physiological mechanisms involved.

One way of exploring the frequency following as a pitch-conveying mechanism is to directly stimulate the terminal auditory nerve fibers on a rate basis and use behavioral evidence to evaluate the results. Clark, Nathar, Kranz, and Maritz (1972), using an avoidance conditioning paradigm and electrodes placed in the basal and apical turns of the cochlea, found cats generalized from pure tones to electrical stimulation when presented on a rate basis. Difference limen and frequency-modulated stimulus experiments conducted by Clark, Kranz, and Minas (1973) have been used to support the contention that electrical stimulation on a rate basis produces a sensation of pitch which forms the basis for the observed stimulus generalization abilities of the animals. The difference limens for electrical stimulation were found to be similar to acoustic difference limens obtained by Shower and Biddulph (1931) at 0.1 and 0.2 kHz, although not at higher frequencies, while the modulation experiments showed that the cats could detect a 100% modulation of a 1,600-pulse/sec signal. As these results were obtained after cochlear irradiation, electrophonic hearing effects could be excluded. Experiments by Johnsson and Hawkins (1972) have demonstrated that hair cells are destroyed with mycifradin sulfate (neomycin), and this treatment, employed in the present study, is therefore a useful alternative for eliminating possible electrophonic hearing effects

brought about by the electrical stimulation initiating vibrations in the basilar membrane by a capacitance effect and stimulating residual hair cells (Simmons & Glatke, 1972).

It can be argued that the experiments described above do not preclude the possibility that some other nonspecific aspect of the electrical stimulus, rather than a perception of pitch, is being used as a basis for the judgments made by the animals. The present study used stimulus patterning which required more complex judgments of a comparative nature to be made than these previous experiments, where the judgments required could be described purely in terms of same or different. This study required the animal to make comparative judgments on the basis of whether or not a stimulus was higher or lower than a reference, and it was considered that such a judgment was likely to be based on a pitch-like sensation.

The theory of signal detectability provides the basis for psychophysical measures which are independent of motivational levels, hence response variability is not a problem, given that the actual stimulus dimensions are the same over trials and that the actual sensitivity of the subject to the stimulus is invariant. Responses are scored as hits, misses, false alarms, and correct rejections. A receiver operating characteristic (ROC) curve is usually derived for each experimental subject for a particular discrimination task by plotting hit against false-alarm rates under a number of varying manipulated motivational conditions. Each of the individual sets of points defining the ROC curve thus represents a different criterion for responding but the same stimulus discriminability. The area under this curve, $P(A)$, thus can provide a useful nonparametric measure which may be used to compare subjects under varying motivational levels.

With animal experiments, it is impracticable to produce a number of motivational levels. McNicol (1972), Norman (1964), and Pollack, Norman, and Galanter (1964) have described a method of deriving the area under an estimated ROC curve, $P(\bar{A})$, from a single set of hit and false-alarm rate points. This single plot of hit and false-alarm rates must lie at a

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point (i) on the ROC curve. If an animal alters its response bias so that hit rates and false alarm rates increase by a proportional amount, x , then misses and correct rejections will decrease by the same amount but actual sensitivity stays constant. Similarly, if the response bias alters so that misses and correct rejections increase by some proportional amount, y , then hit rates and false-alarm rates must decrease by this same amount. By plotting a number of positive and negative values of x and y , projecting from point i , the upper and lower extremities of the possibilities of obtaining hit and false-alarm rates due to changes in response bias but equal sensitivity are described. These are thus the upper and lower possible limits of the ROC curve, and the mean of the areas under these two curves is the measure $P(\bar{A})$. These areas of $P(\bar{A})$ s can then be used as an index of discrimination which is independent of motivational levels so that inter- and intra-animal comparisons of discrimination abilities under varying conditions can be made. Pursell, Sanders, and Haude (1973) have shown that the area under the ROC curve provides a more sensitive measure of sensory discrimination than a measure expressed in terms of percentage correct.

METHOD

Subjects

The left ears of four cats were chronically implanted with bipolar pairs of enameled stainless steel wire (Nilstain) electrodes with 0.2-mm tip separation. Three cats received apical and basal electrode pairs, and one cat, a basal pair only. Basal electrodes were introduced through the round window (RW) in two cats (1 and 3) and directly in the other two. In each instance, the tip of the most basalward electrode was placed 4 mm from the RW in the scala tympani. The distance of the drill holes from the RW for the directly implanted electrodes was measured with a specially made measuring device. All apical electrodes were implanted directly. Each electrode wire was joined to a Teflon-coated multistranded wire just outside the bulla, which then extended under the skin to a Plessey 7-point socket attached to the skull over the frontal sinus cavity. Surgery was performed under general anesthesia. Animals were premedicated with chlorpromazine hydrochloride (2 mg/kg IP). Maintenance of anesthesia was obtained with a specially designed closed circuit apparatus which is a rebreathing technique

that enabled stable anesthesia to be maintained with methoxyflurane and halothane (Komesaroff, 1973).

After completion of the experimental series, the cats were anesthetized and perfused intra-arterially with normal saline followed by 10% Formalin. The temporal bones were removed, decalcified, and for Cats 1 and 4 embedded in low viscosity nitrocellulose and for Cats 2 and 3 in paraffin. The blocks were serially sectioned at a thickness of 30 μ , and 1 in 10 sections were stained with hematoxylin and eosin.

Apparatus

Figure 1 is a block diagram of the equipment setup used for the experiments. A specially designed conditioning box (CU) for presenting a milk reward was used. A solenoid valve allowed the appropriate discrete quantity of milk to be dispensed and a light source and photosensitive cell triggered this when the cat made the correct response of lowering its head through a narrow black padded oval opening to the milk dish. All stimulus parameters, both acoustic and electrical, as well as activation and deactivation of the reward apparatus were under computer control. The acoustic stimuli were produced by a Datapulse 410 sweep function generator (FG), shaped by a Grason-Stadler 829E electronic switch (ES) and 471-1 interval timer (IT) and presented to a Plessey C80/2/CAG speaker system (S) through a matching transformer (T). The 2100A Hewlett-Packard computer was interfaced to the sweep function generator and the duration of tone burst, intertone interval, frequency, and intensity were under program control and could be varied manually through a switch register. Variations in sound pressure level produced by the speaker for different frequencies were compensated for under program control. Sound levels were taken with a Bruel and Kjaer Model 4134 condenser microphone placed in the position of the cat's head in the conditioning box, the animal being simulated by a cloth and board bundle of similar bulk size, and weight. A Bruel and Kjaer measuring amplifier was used. The electrical stimulation was produced by a similar setup to that described for the acoustic stimuli. Constant-current stimulation was maintained by converting the constant-voltage stimulator into a constant-current device by inserting a 20 K Ω resistance in series with one of the leads connected to the stimulating electrode. A Grass micro electrode dc amplifier (PA) was used to amplify the current to enable reading of the current level from the cathode ray oscilloscope (CRO) and to trigger the analog-to-digital converter of the computer (CPU). The computer was used to sample the current level at the beginning of each higher or lower presentation and to correct the level of current to that of the reference if the deviation was more than 5%.

Stimulus Parameters and Behavioral Procedure

All training and experimental trials were carried out in an electrically shielded sound-attenuated room. Using reward conditioning and a "no-error" paradigm after Terrace (1963), all animals were first trained in an acoustic discrimination task. Terrace claimed that this technique was superior to other methods for conditioning animals, not only for the superior discrimination performance, but also in preventing or reducing emotional behavior usually associated with making errors. Animals were maintained on a 23-h liquid-deprivation schedule. A series of 32 random tones, each higher (FH) than an alternating reference tone (FO), provided the "go" stimulus, and a similar series, each lower (FL) than the same FO tone and also alternating with it, formed the "no-go" stimulus (Figure 2). Tone pulses were presented for a 320-msec period with a 160-msec intertone interval at 70 dB SPL for all animals and all acoustic trials. When discrimination level had reached an asymptote of at least 80% after misses and false alarms were subtracted from the number of go presentations, training was considered complete and the first experimental series (Series 1) was begun using identical auditory stimulus patterning and parameters. The FO was 1.2 kHz, FH ranged from 1.42 kHz to 1.58 kHz, and FL ranged from 0.82 to 0.98 kHz. The stimulus pattern was then replicated electrically (Series 2). Bipolar stimulation between basal

Figure 1

electrode pairs and between apical pairs in each animal was carried out using positive monophasic square pulses of 250- μ sec width and a fast rise-fall time. These pulses were chosen in preference to sinusoidal stimulation as, with the latter, the total charge per half cycle changes with frequency, thus giving rise to a greater likelihood of intensity increases with rising frequency. Narrow rectangular pulses allow time for the restoration of membrane properties between each pulse, thus greater probability of working in the constant coulomb characteristic of the strength duration curve. The pulse bursts were on for 320 msec and off for 160 msec, as in the acoustic presentations. Impedance was monitored throughout the series to ensure the integrity of the electrodes and/or the electrode-tissue interface. The current level for each trial for each animal was determined by watching for the pinna pricking and orienting responses of the animal as the level was raised, noting that value, and then raising the level further until the first sign of aversion occurred. The stimulating level was then set midway between these two values. A further acoustic series (Series 3) was then conducted. FO was .49 kHz. FH ranged from .616 to .784, and FL ranged from .306 to .390 kHz. These parameters were replicated with electrical stimulation (Series 4), as described above. Series 5 and 6 electrical stimulation stages of the experiment were conducted with these same parameters but followed the neomycin treatment (50 mg/kg IM daily). Series 5 was begun 2 weeks after completion of the 7 days of neomycin treatment for Cats 1 and 3 and Series 6 was begun 3 weeks after the second 7 days of neomycin treatment for Cat 3 and 3 weeks after the 14 days of neomycin treatment for Cat 2.

Each of the experimental series completed by the four animals consisted of between 6 and 10 trials of between 20 and 30 each "go" and "no-go" stimulus periods for each of their electrode pairs.

RESULTS

Table 1 shows the calculated $P(\bar{A})$ values for each animal for each series and mode of the experiment. These values are all 0.853 and above and are thus well above 0.5, which represents chance response level.

The index on the whole displays a regular pattern, with Series 1 having the highest discrimination index values and Series 6 the lowest. Discrimination for acoustic Series 1 was superior to acoustic Series 3. The Series 1/Series 2 acoustic/electrical stimulation comparison shows no such superiority. Series 5 and 6,

Figure 2

which were carried out after 7- and 14-day courses of neomycin, show a progressive deterioration in discriminability. A greater between-cat variation is apparent for electrical stimulation than for acoustic discrimination.

The temporal bone sections for Cat 4 (no neomycin treatment) revealed some hair-cell damage in the basal turn, very slight hair cell damage in the middle turn, and considerable damage to the apical turn, including some damage of the basilar membrane itself. There also appeared to be some very slight damage to the ganglion cells, but well over 90% appeared to be intact in the sections studied.

Cat 1 sections revealed evidence of very considerable infection in all turns. There were no hair cells or supporting cells. This cat was sacrificed when suffering a serious infection 3 weeks after administration of the neomycin treatment.

The sections studied for Cat 2 of both right and left temporal bones revealed complete loss of hair cells and atrophy of most supporting cells in all turns. The basal turn of the left scala tympani was filled with fine fibrous tissue, confirming the placement of the electrode there.

Although Cat 3 sections also showed complete loss of hair cells, the paraffin sections had led to some distortions of the soft tissue so that conclusive statements about the hair cells in this animal cannot be made.

Table 1
Index of Estimated Discriminability

Series	Mode and FL (Center Frequency) to FO/ FO to FH (Center Frequency)		Cat 1		Cat 2		Cat 3		Cat 4	
			Mean Currents $P(\bar{A})$ in μ Amps		Mean Currents $P(\bar{A})$ in μ Amps		Mean Currents $P(\bar{A})$ in μ Amps		Mean Currents $P(\bar{A})$ in μ Amps	
1	Acoustic (.9-1.2 kHz/1.2-1.5 kHz)		.966		.968		.958		.971	
2	Electrical (.9-1.2 kpps/1.2-1.5 kpps)	Basal-Bipolar	.928	423	.923	411			.935	286
		Apical-Bipolar			.953	183	.948	291		
3	Acoustic (.348-.49 kHz/.49-.7 kHz)		.925		.929		.921		.928	
4	Electrical (.348-.49 kpps/.49-.7 kpps)	Basal-Bipolar	.934	175	.917	215	.937	179		
		Apical-Bipolar					.934	189		
5	Electrical (.348-.49 kpps/.49-.7 kpps)	Basal-Bipolar	.916	452			.914	453		
6	Electrical (.348-.49 kpps/.49-.7 kpps)	Basal-Bipolar			.873	246	.854	500		
		Apical-Bipolar			.890	272	.853	433		

Note—kpps = kilo pulses per second

DISCUSSION

The aim of this experiment was to assess the ability of the cat to make relative pitch discriminations arising from electrical stimulation of the auditory nerve on a rate basis through electrodes implanted in the scala tympani of the cochlea.

The results suggest that all animals were able to perceive pitch in all phases of the experiment. The tendency for greater between-cat variation for electrical stimulation than acoustic stimulation can probably be explained in terms of very slight differences in actual electrode placements. The superior discrimination of Series 1 acoustic over Series 3 acoustic stimulation is in accordance with previous studies in cats where hearing acuity improves as frequency rises (Elliott, Stein, & Harrison, 1960; Neff & Hind, 1955). The results obtained for Series 2 electrical stimulation quite probably represented, to some extent, an electrophonic effect. Previous research has suggested that pitch discrimination achieved through electrical stimulation may have a top perceptible limit of .8 kHz or a little above (Clark et al., 1973). For Series 2, it seems likely that the pitch discrimination must have exceeded the FO of 1,200 pulses/sec in order for the animals to respond to the "go" stimulus. This suggests that either electrophonic hearing was occurring or the upper limit perceivable is higher than previous studies have suggested.

The comparison of Series 3 acoustic stimulation with Series 4 electrical stimulation shows very little difference in discrimination ability. Comparison of Series 2 and Series 4 electrical trials also reveals a similar sensitivity. For Series 5 and Series 6 of the experiment conducted after the neomycin treatment, the decrease in discrimination is quite clearly evidenced. This decrease is quite understandable if performance in trials prior to neomycin treatment had some electrophonic component affecting the results. As histological findings show hair cell destruction in Cat 2, we have concluded that the results of electrical stimulation in Series 2 and 4 were facilitated by an electrophonic effect but that the discriminations made by Series 6 can be attributed solely to the stimulation of the terminal auditory nerve fibers on a rate basis.

An alternative interpretation of the results is that intensity was used as the basis for the discriminations made by the animals. However, in the acoustic series, this possibility can virtually be excluded as intensity differences with frequency were very carefully controlled for. It can be argued that it is unlikely that the animals would have changed their basis of discrimination to another dimension of the stimulus when electrical stimulation was used.

Furthermore, the parameters of electrical stimulation were carefully chosen to reduce the possibility of changes in intensity with changes in rate

of stimulation. Square pulses of 250 μ sec duration were used, and the length of the pulse trains was 320 msec with a 160-msec break between trains. Thus, for the vital Series 4, 5, and 6, where the maximum rate used was 784 pps, the stimulation parameters should have fallen within the constant coulomb characteristic of the strength duration curve, and as suprathreshold stimulation was always used, firing of auditory nerve fibers could be expected to follow the rate of electrical stimulation.

Moxon (1967), using intensities three times threshold, has shown that with square pulses of 100 μ sec width, repetition rates up to 900 pps, and for periods exceeding the 320 msec of the pulse trains used in this experiment, auditory nerve fibers followed the rate of electrical stimulation. At the higher rates of stimulation used in Series 2, we cannot dismiss the possibility that some intensity difference with frequency may have occurred. Overall, however, it seems that by far the most likely basis for discrimination judgment made by the animals was that of the repetition rate, particularly for Series 4, 5, and 6, where the maximum rate of FH was 0.784 kpps.

The results would seem to support the conclusion that frequency following is a pitch-conveying mechanism for lower frequencies. They suggest that a pitch sensation may be produced by electrically stimulating auditory nerve fibers on a rate basis, either from the basal or the apical turn of the cochlea, and show the ability of cats to discriminate more complex stimulus patterning than previous electrical stimulation experiments have revealed.

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