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Protective Effects of Patterned Electrical Stimulation on the Deafened Auditory System

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ABSTRACT

This Quarterly Progress Report presents a summary of results from electrophysiological studies conducted in primary auditory cortex (AI). These studies were conducted in three groups of experimental animals: "normal" animals that were implanted as adults; "passively stimulated" cats that were neonatally deafened and received chronic stimulation with a meaningless, stereotyped electrical stimulus (80 pps or 300 pps pulse trains amplitude modulated with a 30 Hz sinusoid) for approximately 6 months; and "behaviorally trained" cats that received initial stimulation through a model speech processor, and when mature enough, were behaviorally trained to detect and respond to a variety of electrical signals. The passively stimulated and behaviorally trained groups consist of the same experimental animals for which we have previously presented morphological, psychophysical and inferior colliculus electrophysiology data.

In these cortical studies, high resolution maps of AI were made by making multiple microelectrode penetrations at closely-spaced intervals, and systematically determining response thresholds at each location. Results in normal animals show that stimulation of an individual intracochlear bipolar electrode pair produces a dorsal to ventral "ridge" of higher sensitivity, lower threshold in AI. This ridge is located caudally for apical electrodes, and it shifts progressively more rostral with excitation of more basal electrode pairs on the cochlear implant. These preferential threshold locations for different intracochlear electrodes are consistent with the known tonotopic organization of AI demonstrated by acoustic stimulation, indicating that tonotopic organization, or "tuning" also occurs with electrical stimulation. In contrast, neonatally deafened animals that received chronic electrical stimulation through a cochlear implant showed much poorer electrode specificity and degraded tuning. In the passively stimulated animals, electrode specificity appears to be weaker than normal, and although tuning may be present, it appears to be broader than in normals. Results in behaviorally trained animals were particularly striking. In this experimental group, many of the response threshold distributions were nearly flat and lacked any spatial selectivity whatsoever. These results indicate that electrical stimulation of a bipolar intracochlear electrode pair initially produces a preferential, spatially selective response in primary auditory cortex, but after chronic stimulation with such electrodes, this selectivity or tuning is lost. The equalization of all thresholds across a broad region of AI is particularly impressive because absolute threshold is typically very low in these behaviorally trained animals, suggesting *an increase in sensitivity* of neurons throughout the cortex. These results are interpreted as indicating that chronic stimulation, particularly with behaviorally relevant signals, can result in profound functional alterations or reorganization of auditory cortex.

Alterations in Response Threshold Distributions in Primary Auditory Cortex Following Chronic Electrical Stimulation: Preliminary Results.

Many cortical sensory fields, including AI, have been shown to exhibit representational plasticity of their functional organization under a variety of stimulus and behavioral conditions. That is, cortical receptive fields dedicated to specific regions of peripheral sensory input can be enlarged or usurped, depending upon the sensory experience occurring over the lifetime of the animal. One of the intriguing possibilities for reorganization in the auditory system may be found in the phenomenon that deaf children, including congenitally or early deafened children, who are electrically stimulated using cochlear prostheses, are typically unable to understand speech in the first hours, weeks, or months of stimulation. However, with daily stimulation of their prostheses over a prolonged period of time and some directed auditory training, many young patients eventually acquire the ability to discriminate some speech. The goals of the cortical studies presented here were: to investigate the representation of peripheral electrical stimulation in primary auditory cortex; to evaluate whether AI representations in neonatally deafened animals undergo consistent reorganization following chronic stimulation with a cochlear implant; and ultimately, to determine whether or not the behavioral relevance of the chronic stimulation plays a role in inducing such changes in cortical representations. The premise for the present investigation was to use the known acoustic physiological response topographies in AI as a template against which to compare neuronal responses to peripheral electrical stimulation. In this report, the focus will be on threshold distributions and what is referred to as spatial "tuning".

1. Experimental Animals; Methods

The animals in which cortical studies have been conducted include three groups of adult cats. The "normal" group included both completely normal and acutely deafened adult cats that were implanted shortly before the electrophysiological experiment. Table 1 shows the stimulation histories for the other two groups of animals: the "passive stimulation" group that were neonatally deafened, chronically implanted and passively stimulated until the time of the terminal electrophysiological experiment, and the "behaviorally trained" group that was neonatally deafened, chronically implanted, and initially received passive stimulation until animals were mature enough to undergo behavioral training (approximately 3 months of age). Behavioral training continued for many weeks in duration, and during this time, detection thresholds were determined for a variety of pulsatile and sinusoidal electrical stimuli. In this report, cortical threshold data are presented for eight animals in the normal group, four animals in the passive stimulation group, and four animals in the behaviorally trained group.

The cochlear implant devices were always implanted in the left scala tympani and consisted of multiple electrode arrays with a variable number of near-radial bipolar pairs. The individual contacts of each electrode pair were separated by approximately one millimeter with a 1.5 to 2 mm separation between pairs. In the second group of animals, those that were passively stimulated, stimulation was initiated at 6.4 to 10.5 weeks of age. Animals were stimulated 4 hours per day, 5 days a week, with stimulation delivered over a period 25.5

weeks on average. Stimulus intensity was set at 2 dB above the EABR threshold for each animal and stimulus currents ranged from 80-400 µA with a pulsed stimulus (biphasic, 200 µsec/phase) at a frequency of 80 Hz (K83) or 300 Hz amplitude modulated with a 30 Hz sinusoid (all other cats). It should be noted that two of these cats, K83 and K91, also received brief periods (3.5 weeks and 6 weeks, respectively) of behavioral training to determine detection thresholds for the chronic stimulus. These short behavioral training sessions were followed by a return to the passive stimulation paradigm for periods of 6 weeks (K83) and 13 weeks (K91) which continued until the time of the cortical experiments. Thus, although these 2 cats received a modest period of behavioral training, they are included in the passive stimulation group because the great majority of their stimulation was passive and because long periods of passive stimulation immediately preceded the electrophysiological experiments.

The third group of animals, those that received both passive stimulation and prolonged behavioral training were stimulated as follows: Passive stimulation was accomplished using a backpack speech processor generating an analogue electrical stimulus encoding ambient environmental sounds picked up by a portable microphone and delivered directly to the animal's connector for 3-4 hours per day, 5 days per week with stimulus currents ranging from 30-400µA. Animals were behaviorally trained using a variety of electrical stimuli, including: 100 Hz, 300 Hz, 500 Hz, and 1000 Hz sinusoids; 30, 100 and 300 Hz pulses (pulse duration respectively 0.2 -5.0 ms/phase, stimulus duration 0.03-2 sec). The training paradigm was one of conditioned avoidance in which threshold was determined using a descending method of limits and a 50% avoidance criterion. In addition to the mean passive stimulation time of 21.3 weeks, the mean period for behavioral training was 21.9 weeks. In some cases, passive stimulation time overlapped behavioral training time for a short time. In others, the passive stimulation was discontinued when behavioral training was initiated. The mean total stimulation time period over which this group received stimulation was 36.5 weeks (range 35-48 weeks).

At the conclusion of passive stimulation or behavioral training, acute electrophysiological experiments were conducted. It should be noted that results from these same chronically stimulated animals have been presented in previous Quarterly Progress Reports, including behavioral threshold data, morphometric data from the cochlear spiral ganglion, and data from inferior colliculus electrophysiological studies. After completion of the interior colliculus studies in these animals, a second craniotomy was performed on the right side to expose the primary auditory cortex contralateral to the cochlear implant, and the AI cortical mapping study was then conducted. In normal animals, identical acute electrophysiological experiments were conducted either immediately following implantation or after two to three week recovery periods. Cortical responses were elicited by electrical stimuli delivered to the various bipolar pairs of electrodes on the cochlear implant device. Stimuli were either capacitively coupled, charged balanced, biphasic square wave pulses (200 µs/phase) delivered at 1-2 pps or 1-3 cycles of a 100 Hz sine wave. A number of parameters were measured, but only the threshold results will be presented here. Multiple microelectrode penetrations were made at closely-spaced intervals across AI, and response thresholds were determined at each location.

2. Organization of Primary Auditory Cortex (AI)

In order to place the electrical stimulation data from the cortical mapping experiments in appropriate context, it is first necessary to review some of the features of AI organization and neuronal response properties to acoustic stimulation. Although the exact role of the auditory cortex in the processing of complex acoustic signals remains unknown, early work by Merzenich and colleagues (1975) and Reale and Imig (1980) showed the existence of isofrequency bands in which neurons with similar characteristic frequencies (CF) are found in bands that run dorsal to ventral across the extent of AI. More recent work by Schreiner and colleagues has revealed that neurons in AI demonstrate differential physiological response characteristics that are systematically organized across both the dorsal-ventral and caudal-rostral extents of AI. These findings have demonstrated that AI can be preliminarily divided into three distinct areas along the axis that is orthogonal to the isofrequency domain: a dorsal area, a ventral area and a central area that lies between them. Detailed studies of response distributions have revealed that neurons in the central area consistently demonstrate significantly sharper tuning, lower thresholds, shorter latencies, high non-monotonicity and contain a relatively larger number of excitatory-inhibitory neurons (EI) as compared to neurons in the adjacent dorsal and ventral areas (Schreiner and Mendelson, 1990; Schreiner, et al., 1992; Schreiner and Sutter, 1992). Moreover, single neurons and neuron clusters in dorsal vs. ventral AI respond in a systematic and differential way to signal intensity (Sutter and Schreiner, 1995).

Figures 1-3 illustrate three-dimensional distributions of some of these acoustic parameters across AI. In Figure 1, the small diagrams at the left illustrate the recording region in normal cat primary auditory cortex, with each dot representing the location of a microelectrode penetration site. At the right of the figure is an isofrequency contour map which shows the spatial distribution of CF to contralateral acoustic tonal stimuli as derived from those recordings. Each of the small, vertical lines corresponds to an individual penetration site, and the elevation corresponds to the CF at that site. A clear and relatively smooth CF gradient is seen, demonstrating the low (≈ 4 kHz) to high (≈24 kHz) frequency distribution that runs from caudal to rostral across AI. The lines connect recording locations with similar CF, defining the well-known isofrequency bands of AI, which run parallel to the dorsal-ventral axis of AI. The sharp change in CF at the ventral end of the map is attributed to recordings made in an adjacent cortical field (AII) with a separate frequency organization.

As mentioned previously, in addition to this orderly CF distribution, AI also appears to be organized on the basis of other specific physiological response characteristics, into three distinct areas running orthogonal to the isofrequency domain. Compared to neurons in the dorsal and ventral areas, those in the central region demonstrate several different functional properties such as sharper tuning and lower thresholds when tested using acoustic tone burst stimuli. In Figure 2, the left plot shows that there is a central area of high Q values, meaning that there is a restricted, central area where neurons demonstrate sharper tuning, whereas neurons demonstrate broader tuning in both the ventral and dorsal areas. The right plot in Figure 2 illustrates the acoustic threshold distribution. The data show a central area of low threshold that corresponds to the locations of sharpest tuning seen in the left plot, bounded by dorsal and ventral regions of higher threshold. On the basis of an extensive body of work confirming the fundamental observations summarized above, it can be concluded that AI is segregated into distinct response areas in which any neuron can be characterized as bearing a number of specific functional behaviors. Whether or not these neurons are, therefore, "combination selective" remains to be seen pending further investigation of the representations of complex signals.

This functional organization of AI demonstrated with acoustic signals forms the theoretical context for the present studies of cortical responses to electrical stimulation of the cochlea. Therefore, we were interested not only in the specific behavior of isolated cortical neurons, but also in the distribution of responses across the dorsal-ventral and caudal-rostral extents of AI. Comparing the distributions of electrical responses with those already known for acoustic stimulation is believed to be a logical first step in understanding the fundamental mechanisms of electrical stimulation of the auditory system. Moreover, such a comparison might provide important information concerning normal cortical physiology and might ultimately shed some light on the reasons for the varying success in different cochlear implant patients and with different signal processing strategies.

Figure 3 shows an example of the threshold distribution for a 20 kHz acoustic signal. On the left is a 3D plot of the CF distribution in AI with the dark line defining the dorsal to ventral isofrequency line for 20 kHz. On the right is shown the threshold distribution for this frequency that demonstrates a fairly sharp, location-specific, ventral to dorsal "ridge" of high sensitivity or low threshold. This demonstrates what is referred to as "spatial tuning." That is, AI is spatially tuned to pure tones such that higher frequency signals result in rostral ridges and lower frequency signals produce progressively more caudal ridges, as a straightforward expression of the clear tonotopic organization of AI.

3. AI Distributions of Response Thresholds to Electrical Stimulation.

For direct comparison, Figure 4 shows the threshold distribution for four radial bipolar intracochlear electrode pairs and one longitudinal pair, stimulated with biphasic pulses in a normal animal. Pair 1,2 is the most apical electrode pair, positioned in the scala tympani at a location corresponding to roughly 5 kHz; the other electrode pairs are located at progressively more basal sites, with pair 7,8 corresponding to about 15 kHz. These cortical threshold data demonstrate a clear caudal to rostral "ridge" of high sensitivity running ventral to dorsal which shifts in position from a caudal location for pair 1,2 to progressively more rostral locations for the more basal stimulating electrode pairs. These data demonstrate that tuning also occurs with electrical stimulation, in that there are electrode-specific areas of high sensitivity that are appropriate for the tonotopic organization of AI (i.e., lower frequency electrodes are represented caudally and progressively higher frequency electrodes are represented in more rostral locations.) It is clear, however, that the ridges are not smooth and continuous dorso-ventrally as they are using acoustic pure tone stimuli, but rather have peaks and troughs that may reflect underlying differential parametric acoustic response distributions as discussed above. It is also interesting to note that stimulation using the longitudinal electrode pair 1,8 (which subtends a broad range of frequencies in the cochlea), does not produce a preferential threshold location.

Another method of evaluating tuning is to measure thresholds in a single line of data points across the caudal-rostral extent of AI. This has been a very useful methodology because it provides a simpler depiction of actual data points, and also because these experiments can take up to 60 hours to complete and recording single lines of penetrations is more efficient. The data points are typically 0.5 mm apart, and we refer to a single line of data points as a "slice." Several rows of caudal-rostral penetration sites are used to develop the tuning profile. An attempt is made to place these rows so that they are representative of the entire AI, with at least one row in the dorsal region, one in the ventral region and one in the central region.

Our working definition of spatial tuning for slice data requires that two criteria be met: 1) that there is a preferential, spatial locus of best response for different electrodes, and 2) that the threshold profile has at least a broad, U- or trough-shaped threshold configuration with a relatively clear preferential locus. Specifically, for a slice to be classified as tuned, the spatial tuning curve must have a well-defined minimum and a width at 10 dB above minimum threshold of less than 3 mm. Sharply tuned spatial tuning curves are defined as those with widths < 2mm. Broadly tuned slices are defined as those that have a less well-defined minimum with a width between 2 and 3 mm. This implies that the threshold configuration in all tuned slices shows increases in thresholds on both the caudal and rostral sides of the profile. In contrast, slices with an absence of tuning or a flat configuration are those that show no preferential spatial locus of best response for any radial pair and do not show threshold increases of more than 10 dB on both the caudal and rostral sides of the threshold profile.

Figure 5 shows the slice distribution for the same data that were illustrated in Figure 4. That is, single lines of data points were extracted from the whole data set. There is a clear spatial separation between threshold minima for each bipolar pair with the apical-most pair 1,2 having its lowest threshold on the caudal side of the plot and the basal-most pair 7,8 having its threshold minima on the rostral side. It can also be seen that there is an absolute threshold difference across pairs with pair 1,2 having the poorest response or highest minimal threshold. Again, Pair 1,8 shows no tuning or no preferential response location.

In Figure 6 another example of slice data is shown from a cat (CH637) that was acutely deafened and implanted. In contrast to the previous figure, data in this animal were collected for stimulation with both pulses (p) and sinusoids (s). Although tuning appears to be considerably broader in this cat, preferential spatial response locations are still clearly present for the two stimulated electrode pairs and their threshold minima are tonotopically appropriate. Thresholds are lower and tuning is sharper for sinusoidal stimuli, a finding which is common across all experiments.

These results in normal adult cats suggest that: 1) there are electrode-specific positions of minimum threshold to electrical stimulation in AI that are appropriate for the tonotopic organization as defined by acoustic stimulation; and 2) this tuning can be relatively selective (≈ 1-2 mm wide).

4. AI Response Threshold Distributions in Chronically Stimulated Cats.

Figures 7 and 8 show examples of slice data for the two cats that were neonatally deafened, implanted, and passively stimulated over periods of approximately 6 months. The data in Figure 7 are from an animal (K89) that was passively stimulated with an invariant pulsatile electrical signal (300 Hz pulse train, amplitude modulated at 30 Hz), over a period of 26.5 weeks. The solid lines show the threshold distributions for pulse stimuli delivered by two near-radial bipolar electrode pairs. Note that these functions show very broad tuning with spatial tuning curves that have a poorly defined minimum. With sinusoidal stimuli, the spatial selectivity or tuning is somewhat better in that there does appear to be a U-shaped threshold function. However, the minimum threshold region is still quite broad with a 10 dB width that is greater than 2 mm. These results suggest that the spatial tuning in this cat, if present at all, is broader than that seen in normal cats.

Figure 8 shows data from another animal (K92) that was passively stimulated with the same stimulation protocol and 300 pps/30 Hz complex signal as in the previous cat. The representative slice profile shown in these data includes threshold data for both the apical (1,2) and basal (3,4) cochlear electrode pairs, and for both pulses and sinusoidal stimuli. These functions are all quite flat, indicating no tuning or preferential spatial responses for this animal with either pulses or sinusoidal stimuli. These data are representative of the data from the four cats in this group. The results suggest that passive chronic electrical stimulation of the cochlea degrades the location-specific responses and spatial selectivity in AI; although tuning may be present, it is broader (2-3 mm wide) than in normal animals.

Figures 9 and 10 show slice data for two exemplary behaviorally trained cats (K84, K86). These two neonatally deafened animals were initially stimulated with a speech processor generating an analogue electrical stimulus in response to ambient environmental sounds with this stimulation period continuing for 21 and 15 weeks, respectively, until the animals were judged to be sufficiently mature to undergo behavioral training. The subsequent behavioral training periods extended for 10 weeks in K84 and for almost 6 months in K86. Figure 9 shows slice data for K84, including threshold data for both pulses and sinusoids and for the two intracochlear electrode pairs 1,2 and 3,4. The functions are extremely flat in this cat, with no evidence of spatial selectivity or tuning for either cochlear electrode pair. Figure 10 shows the slice data from K86. Although there may be some weak, location-specific responses, there is no clear U-shape to any of the threshold functions, and no indication of preferential locations for the apical and basal cochlear electrode pairs. The cortical threshold data shown in Figures 9 and 10 are representative of all four cats in this experimental group (Table 1). That is, neither stimulation with pulses nor with sinusoidal stimuli resulted in any clear location specific responses or tuning, with nearly flat threshold functions over broad regions of the AI. These data indicate that in this group of neonatally deafened animals after chronic electrical stimulation and behavioral training there is no electrode specificity and no clear tuning in AI.

Figure 11 shows a summary of the incidence of tuning across the three groups of animals. For this analysis, all the slices from each cat were classified as either tuned or not tuned, based upon the presence or absence of a U-shaped threshold function and preferential loci of specific cochlear electrode pairs that were appropriate to the AI frequency organization (see above). Figure 11 shows the percentage of slices that demonstrated tuning (dark bars) or the lack of tuning (hatched bars) with data pooled from each of the three experimental groups. Results are shown for both pulsed stimuli (top graph) and sinusoidal stimuli (bottom graph). It should be noted that when the percentage of tuned slices was determined for each individual animal and averaged across all animals, the percentage of tuned slices shows nearly this same distribution of tuned vs. not tuned slices. This indicates that the prevalence of tuning is not influenced by differences in the number of slices per animal.

The data show that both tuned and untuned slices are observed in all the groups, however, there are clear differences between the three conditions. The number of tuned slices is considerably greater for normal animals than either passively stimulated or behaviorally trained animals, and passive stimulation appears to result in a greater number of tuned slices than those found for behaviorally trained animals. In fact, the behaviorally trained animals demonstrate a marked predominance of slices that lack any demonstrable tuning or spatial selectivity. This finding holds for both pulsatile and sinusoidal stimulation

5. Discussion and Conclusions

These results support the notion that electrical stimulation of an intracochlear bipolar electrode pair initially results in a preferential, location-specific response in AI that appears to undergo profound degradation or reorganization after some period of chronic electrical stimulation and behavioral training. That is, with such peripheral electrical stimulation, the preferential spatial response in AI that is very apparent in normal, unstimulated animals, can disappear. The near-total lack of tuning seen in animals that have undergone behavioral training, may be viewed as an equalization of all distributed thresholds, or an increase in sensitivity of all neurons to equality. Of particular significance in this regard is the fact that the absolute thresholds have generally been very low in these trained animals.

It should be noted that during behavioral training, the actual exposure to electrical stimulation amounts to only minutes per day. Thus, although the total number of weeks of stimulation is longer in many cats that have been behaviorally trained as compared to the passively stimulated animals, the passively stimulated animals generally received more total stimulation exposure than the behavioral animals. This suggests that it is not simply the longer time period over which stimulation is administered that accounts for the marked lack of tuning in the behaviorally trained animals, but rather the nature of the stimulation that induces the observed changes in AI. Specifically, the variations in frequency and intensity of stimulation through the speech processor and in the behavioral testing paradigm, and/or the behavioral relevance of the stimuli may be important for these cortical alterations.

With respect to cochlear implant patients, if these findings reflect actual cortical effects of chronic stimulation that occur in patients, then it appears that implant patients would have lost one of the fundamental attributes of AI, i.e., location-specific responses suggestive of the discrete basilar membrane stimulation found in normal hearing. However, instead of patient performance deteriorating over time, performance frequently improves. There are a number of possibilities that might account for this finding. First, it is possible that speech information is carried primarily in the temporal signal, and that the tonotopic spatial selectivity is less important for the function of the implant. If this were the case, it would mean that the improved performance reflects an improvement in the temporal resolution of the central auditory system that is independent of the normal tonotopicity. Alternatively, it is important to remember that the present results reflect the effects of stimulation of only a single channel of information via activation of a single intracochlear electrode pair; if two or three channels were stimulated nearly simultaneously and in competition with one another, this might result in maintenance of more normal preferential, location-specific responses. Future experiments using more sophisticated stimulation paradigms such as multichannel stimulation and complex signals with less temporal coherence will attempt to address some of these questions.

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Work Planned for the Next Quarter

1) Two adult-deafened cats have recently been implanted with the new model UCSF cat electrode and EABR thresholds have now stabilized at acceptable levels. During the next quarter, there animals will be chronically stimulated using a temporally challenging (but passive and invariant) electrical stimulus (300 pps amplitude modulated with a 30 Hz sinusoid). These animals will eventually be studied in acute electrophysiological experiments to evaluate spatial selectivity (STC widths) in the inferior colliculus and AI and thus to determine in functional alterations observed after chronic stimulation in neonatally deafened cats are also observed in adult-deafened subjects. Moreover, studies of spiral ganglion cell survival and cochlear nucleus morphology should allow us to determine whether the protective effects of chronic electrical stimulation previously observed in neonatally deafened cats are dependent upon critical periods of development or, alternatively, can also be induced in animals deafened as adults.

2) One neonatally deafened kitten was also implanted during this past quarter and two more will be implanted during the next quarter. Chronic stimulation in the first kitten has been initiated using an operational prosthesis which consists of a single channel speech processor that responds to sounds in the animals' environment and generates an analogue electrical signal delivered to the intracochlear electrode. One objective in this new series is to initiate behavioral training as early as possible in these animals.

3) Morphometric evaluation of spiral ganglion survival has now been completed for our last series of cats stimulated with temporally challenging electrical stimuli (300 pps amplitude modulated with 30 Hz sinusoid or "speech" processor responding to environmental sounds). These data will be presented in the next QPRs.

4) Histological processing of the cochlear nucleus specimens has been completed for for several chronically stimulated cats in a group that showed marked protection of the spiral ganglion as a consequence of chronic electrical stimulation. Morphometric analyses including volume of individual subdivisions of the cochlear nucleus, neuronal cell density and cross-sectional area of large spherical cells in the AVCN has been initiated and will be continued throughout the next quarter.

TABLE 1

INTRACOCHLEAR ELECTRICAL STIMULATION HISTORY & CORTICAL PHYSIOLOGICAL RESULTS

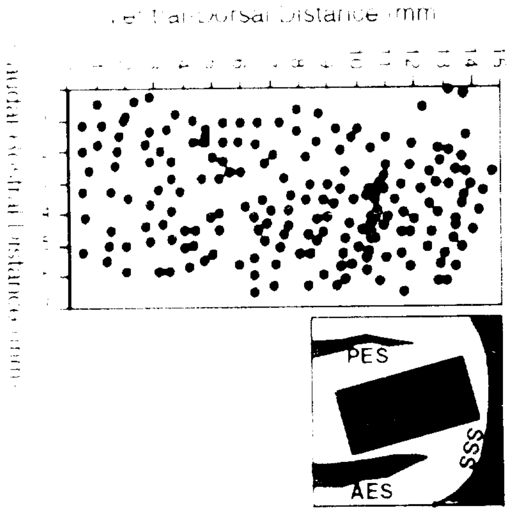
NEONATALLY DEAFENED, PASSIVELY STIMULATED ANIMAL

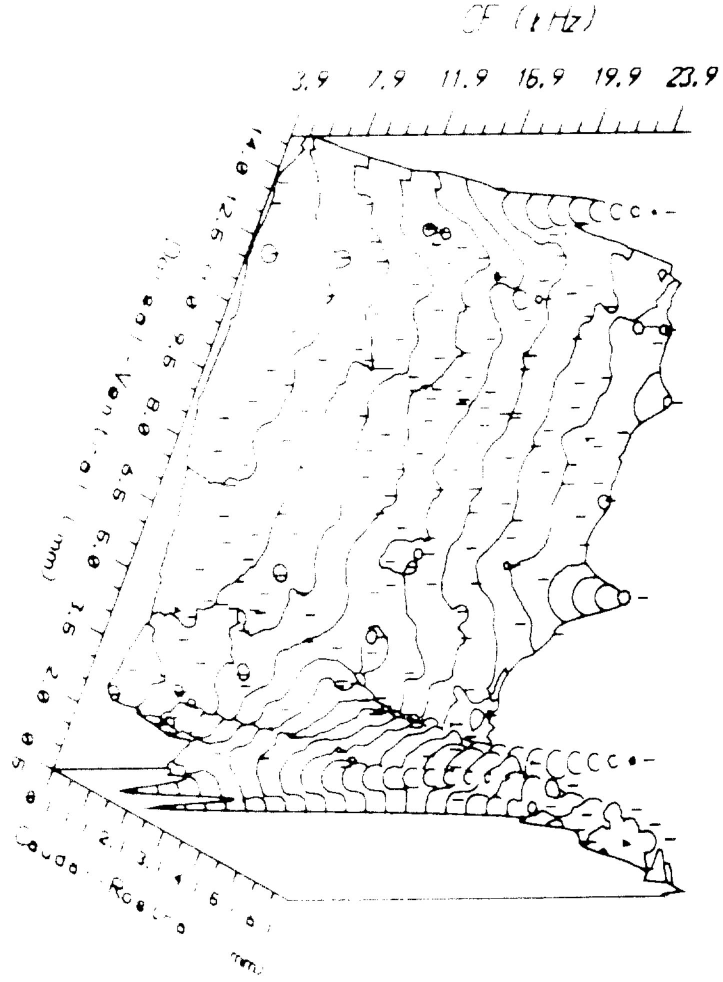
										Tuning			Tri-Sector			
CAT #	*Age-Impl.*	*Age-Init. Stim.*	*Stim. Current*	*Stim. Period*	*Pass. Stim.*	*Beh. Training*	*Beh. Stimulus*	*Stim. Dur*	*Beh. Sig. Dur*	*C-R Slices*	*P vs S*	*B vs M*	*V-D Slices*	*P vs S*	*B vs M*	*Age Sac*
K83	6 weeks	10.5 weeks	125μA	21 weeks	80 pps	(3.5 weeks)	80Hz Pulses	2 seconds	0.2 ms/phase	S1-FLAT	P & S	B & M	S1-CHT	P & S		32 wks
K89	6.5 weeks	10.5 weeks	80-100μA	26.5 weeks	300pps/30Hz					S1-FLAT	P	B	S1-CHT	S & P	B	37 wks
										S1-BTUNED	S	B				
K91	6.5 weeks	7.5 weeks	100-400μA	31.5 weeks	300pps/30Hz	(6 weeks)	300/30Hz Pulses	1 second	0.2ms/phase	S1-FLAT	P & S	B	S1-FLAT	P & S	B	38.5 wks
										S2-BTUNED	P & S	B	S2-FLAT	P & S	B	
										S3-BTUNED	P & S	B	S3-FLAT	P & S	B	
										S4-BTUNED	P & S	B	S4-FLAT	P & S	B	
K92	6 weeks	6.4 weeks	150μA	23 weeks	300pps/30Hz					S1-FLAT	P & S	B & M	S1-FLAT	P	B & M	31 wks
										S2-FLAT	P & S	B & M	S1-CHT	S	B & M	
										S3-FLAT	P & S	B & M	S2-FLAT	P	B & M	
										S4-TUNED	P	M	S2-CHT	S	B	
										S4-FLAT	P & S	B	S2-FLAT	S	M	
										S3-FLAT	P & S	B & M				
										S4-FLAT	P & S	B & M				

NEONATALLY DEAFENED, PASSIVELY STIMULATED AND BEHAVIORALLY TRAINED ANIMALS

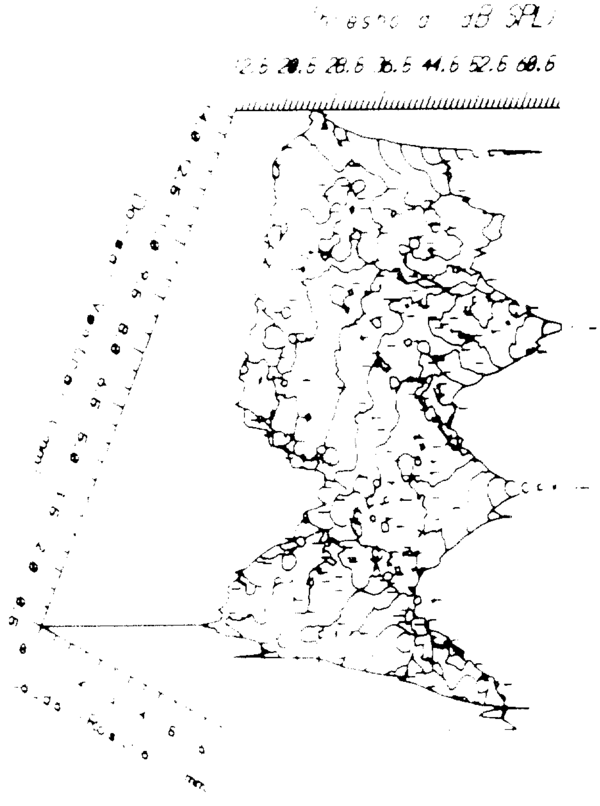
PASSIVE						**BEHAVIORAL**				Tuning			Tri-Sector			
CAT #	*Age-Impl.*	*Age-Init. Stim.*	*Stim. Current*	*Pass. Stim. Per*	*Pass.Stimulus*	*Beh. Train Per*	*Beh. Stimulus*	*Beh Stim Dur*	*Beh Sig. Dur*	*C-R Slices*	*P vs S*	*B vs M*	*V-D Slices*	*P vs S*	*B vs M*	*Age Sac*
K84	7.5 weeks	10 weeks	200-400μA	25 weeks	Spch Process	10 weeks	100Hz S/P	2 seconds	0.2/5ms/phs	S1-FLAT	P & S	B & M	S1-FLAT	P&S	B & M	45 wks
K86	6 weeks	9 weeks	30-160μA	15 weeks	Spch Process	23.5 weeks	30HzP;100 1KS	0.03-2s	0.2ms/phase	S1-FLAT	P & S	B & M	S1-FLAT	P & S	B & M	55 wks
										S2-FLAT	P & S	B & M	S2-FLAT	P & S	B & M	
										S3-FLAT	P & S	B & M	S3-FLAT	P	B & M	
										S4-FLAT	P & S	B & M	S3-CHT	S	B & M	
													S4-FLAT	P & S	B & M	
K93	7 weeks	8 weeks	40-400μA	22.5 weeks	Spch Process.	28.5 weeks	30/2P,100-1KS	1sP;0.3 1sS	0.2 5ms/phs	S1-BTUNED	P & S	B & M	S1-FLAT	P & S	B & M	45 wks
										S2-FLAT	P & S	B & M	S2-FLAT	P & S	B & M	
										S3-FLAT	P & S	B & M				
										S4-FLAT	P & S	B & M				
K94	7 weeks	8 weeks	40 200μA	22.5 weeks	Spch Process.	25.5 weeks	30/2P,100-1KS	1sP,0.3 1sS	0.2-5ms/phs	S1-FLAT	P & S	B & M	S1-FLAT	P & S	B & M	42 wks

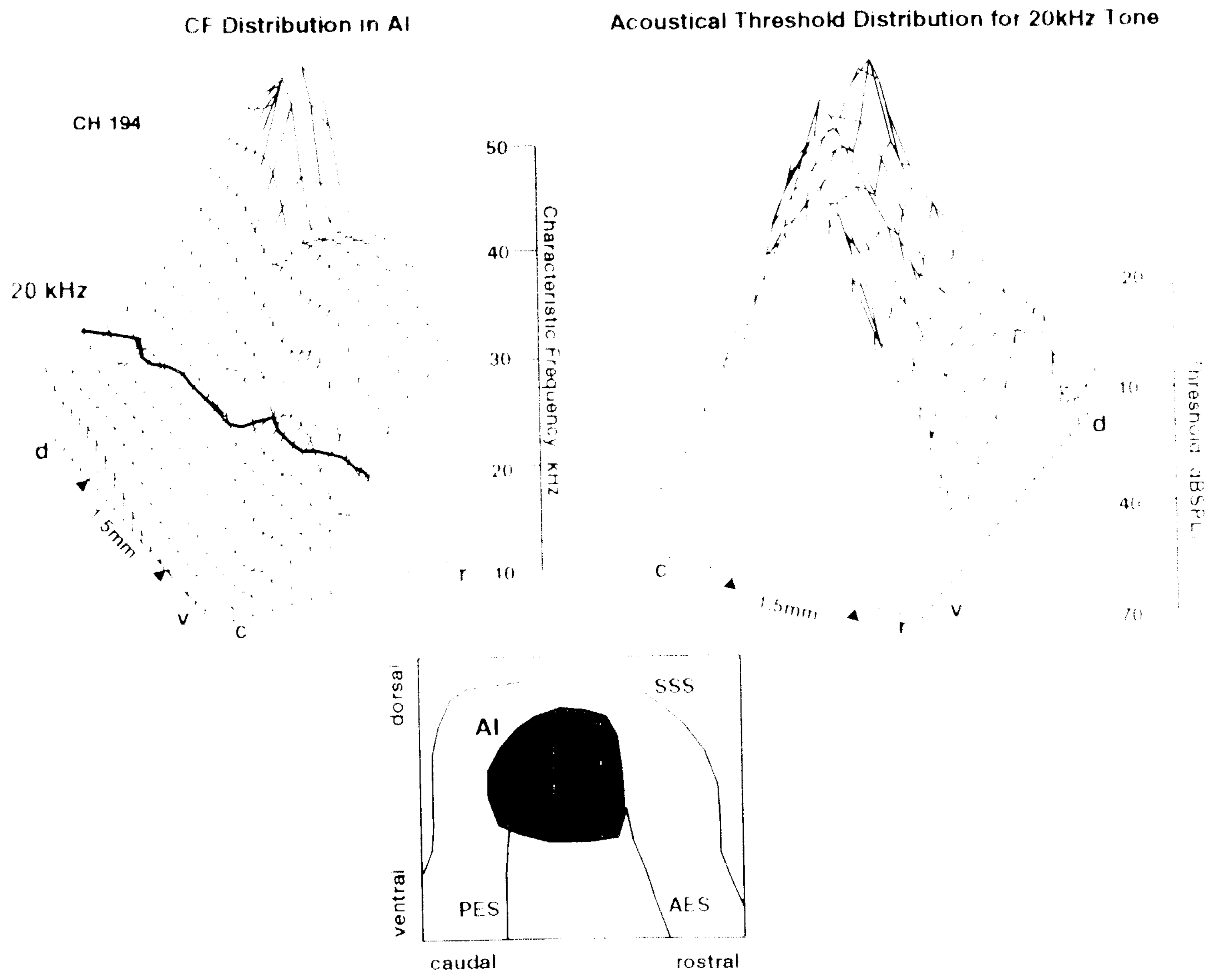
C-R = Caudal-Rostral
V-D = Ventral-Dorsal
P = Pulse
S = Sinusoid
B = Bipolar
M = Monopolar
S1-4 = Slice Designation
Tuning Designations = flat, broadly tuned, variable configuration
Tri-Sector Designations = flat, central area of high threshold (CHT)


Ventral-Dorsal Distance (mm)
Caudal-Rostral Distance (mm)
PES
SSS
AES


CF (kHz)
3.9
7.9
11.9
16.9
19.9
23.9
14.0
12.5
9.6
8.0
6.5
6.0
3.5
2.0
Ventro-Dorsal (mm)
2
3
4
5
6
Caudo-Rostral
mm


0 10dB
0.8 1.8 2.8 3.8 4.8 5.8 6.8 7.8


Threshold (dB SPL)
12.6 20.6 28.6 36.6 44.6 52.6 60.6



CF Distribution in AI

Acoustical Threshold Distribution for 20kHz Tone

FIGURE 3

Influence of Cochlear Stimulation Position on Cortical Threshold Response Distribution

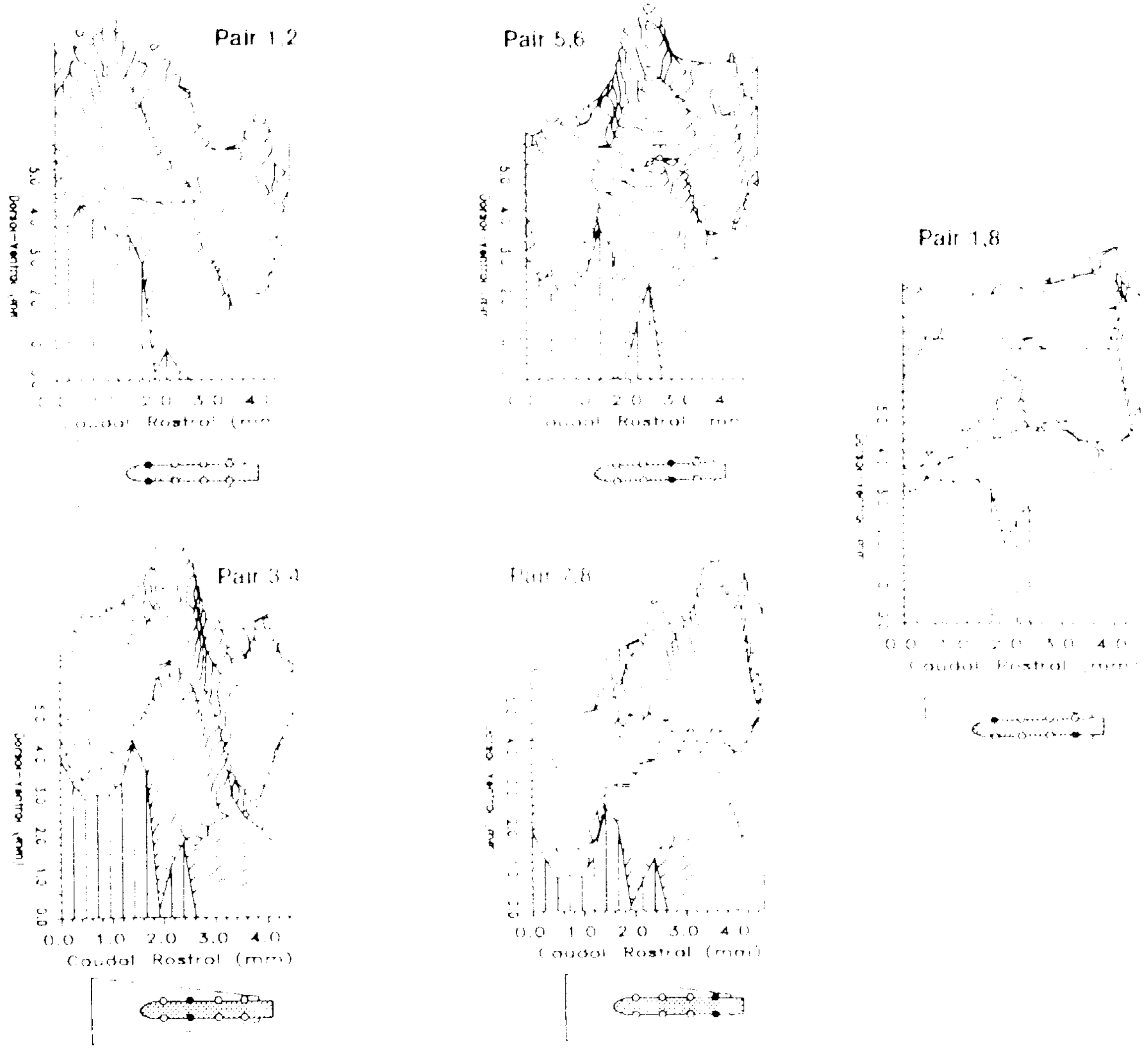


FIGURE 4

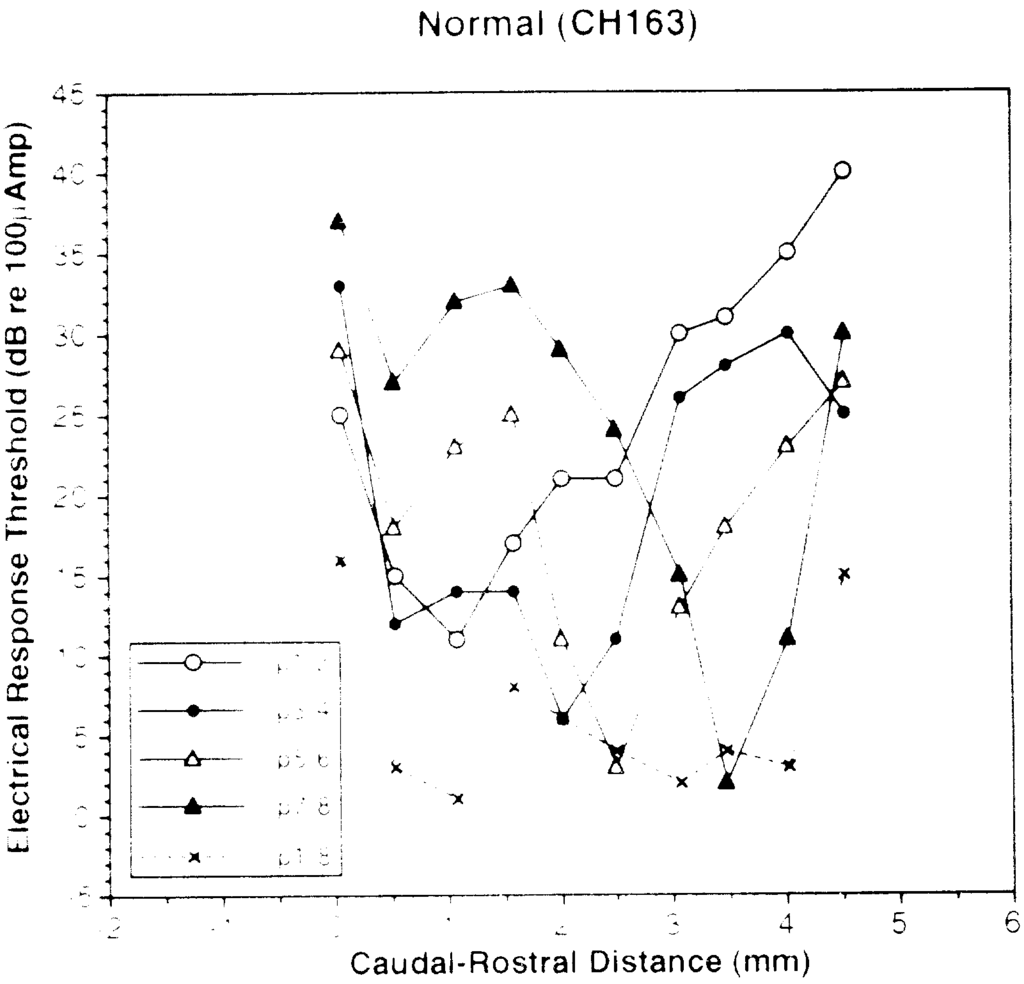

Normal (CH163)
Electrical Response Threshold (dB re 100μAmp)
45
40
35
30
25
20
15
10
5
0
-5
-2
-1
0
1
2
3
4
5
6
Caudal-Rostral Distance (mm)
p1 2
p3 4
p5 6
p7 8
p1 8

FIGURE 5

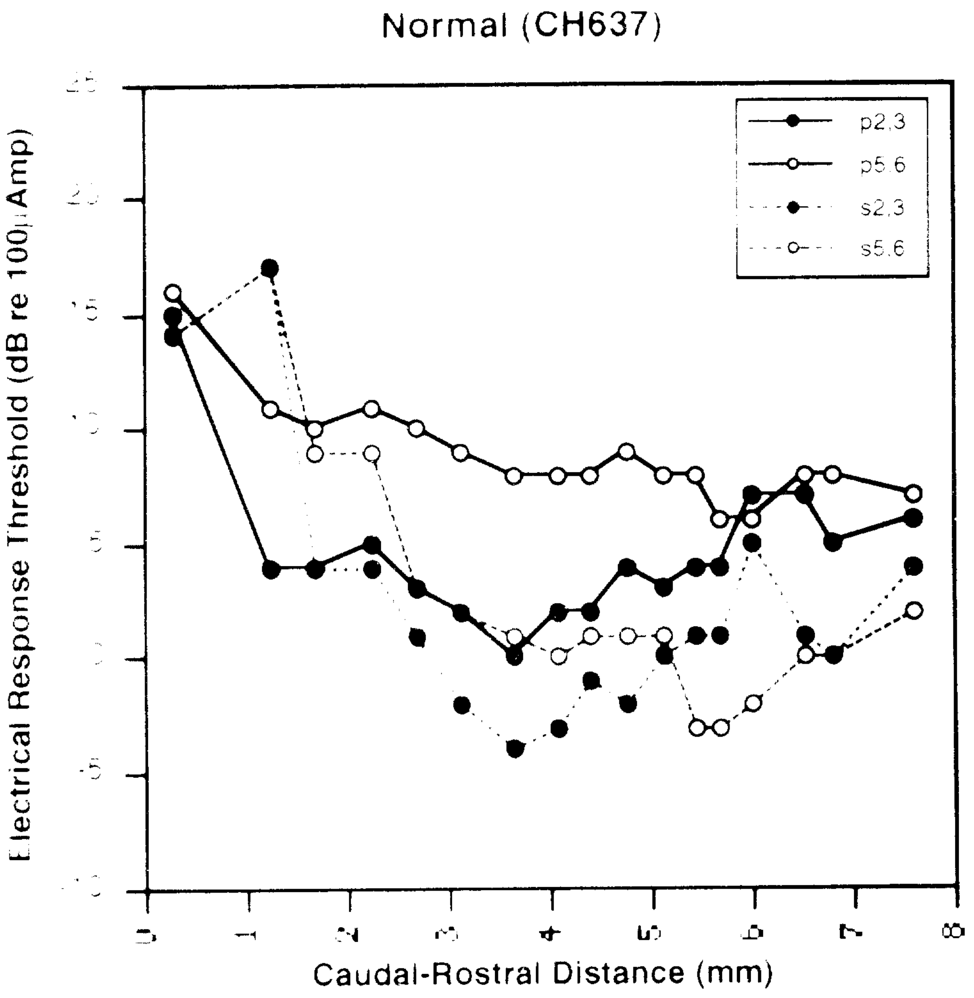

Normal (CH637)
Electrical Response Threshold (dB re 100µAmp)
25
20
15
10
5
0
-5
-10
0
1
2
3
4
5
6
7
8
Caudal-Rostral Distance (mm)
p2,3
p5,6
s2,3
s5,6

FIGURE 6

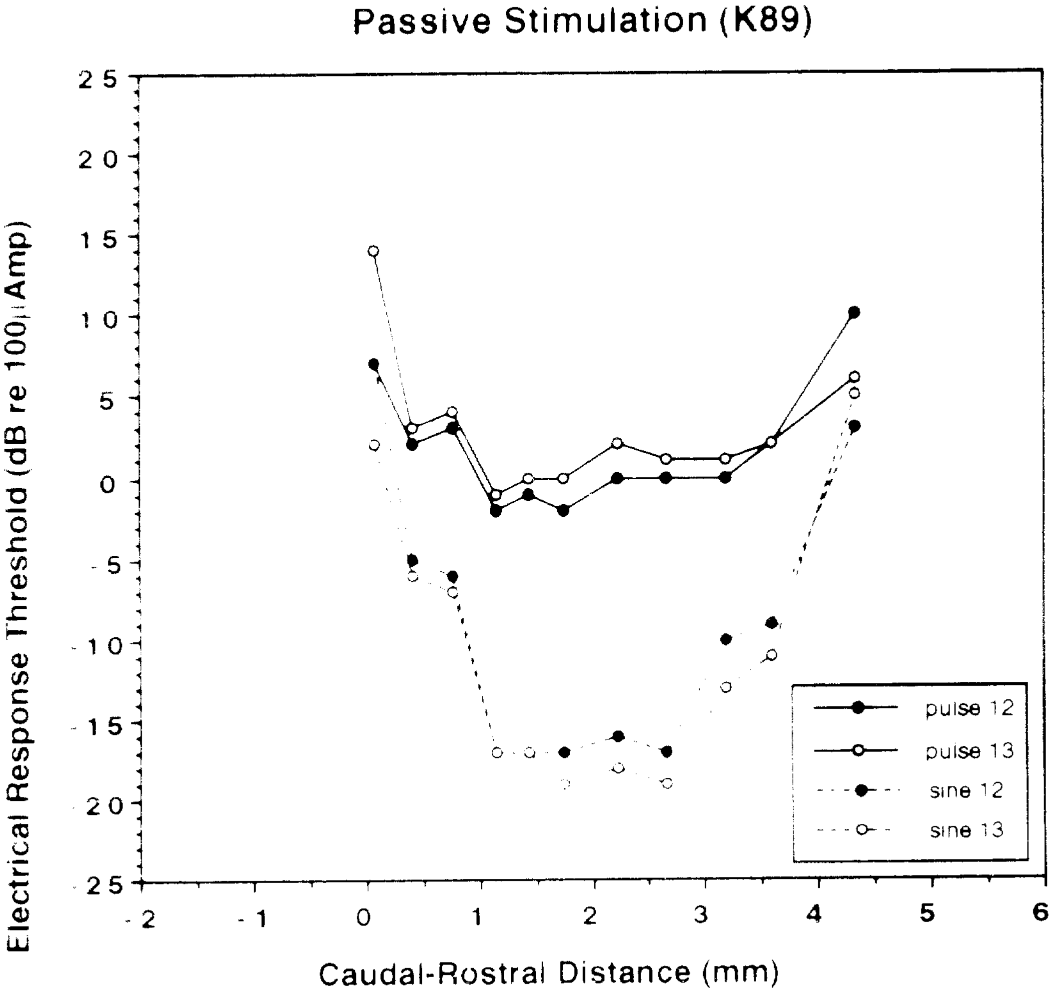

Passive Stimulation (K89)
Electrical Response Threshold (dB re 100μAmp)
25
20
15
10
5
0
-5
-10
-15
-20
-25
-2
-1
0
1
2
3
4
5
6
Caudal-Rostral Distance (mm)
pulse 12
pulse 13
sine 12
sine 13

FIGURE 7

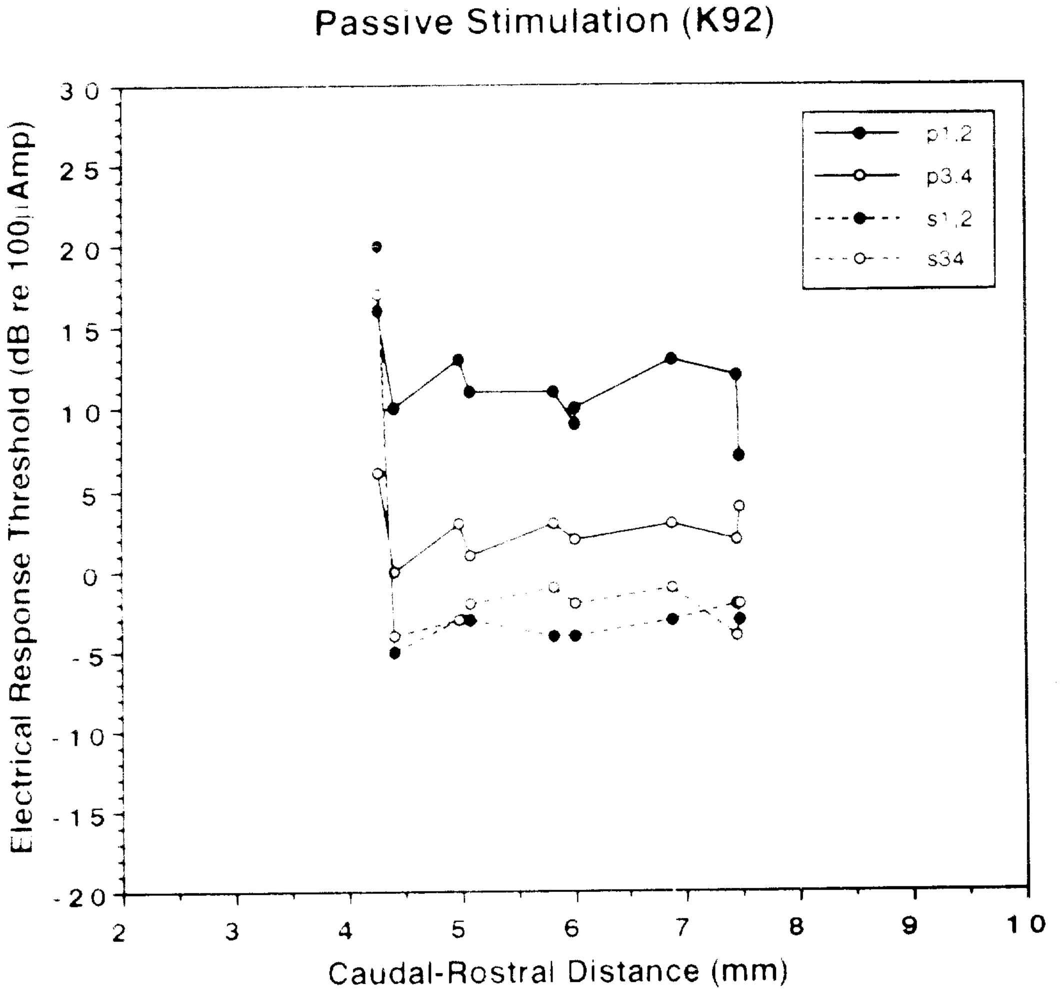

Passive Stimulation (K92)
Electrical Response Threshold (dB re 100μAmp)
30
25
20
15
10
5
0
-5
-10
-15
-20
2
3
4
5
6
7
8
9
10
Caudal-Rostral Distance (mm)
p1,2
p3,4
s1,2
s34

FIGURE 8

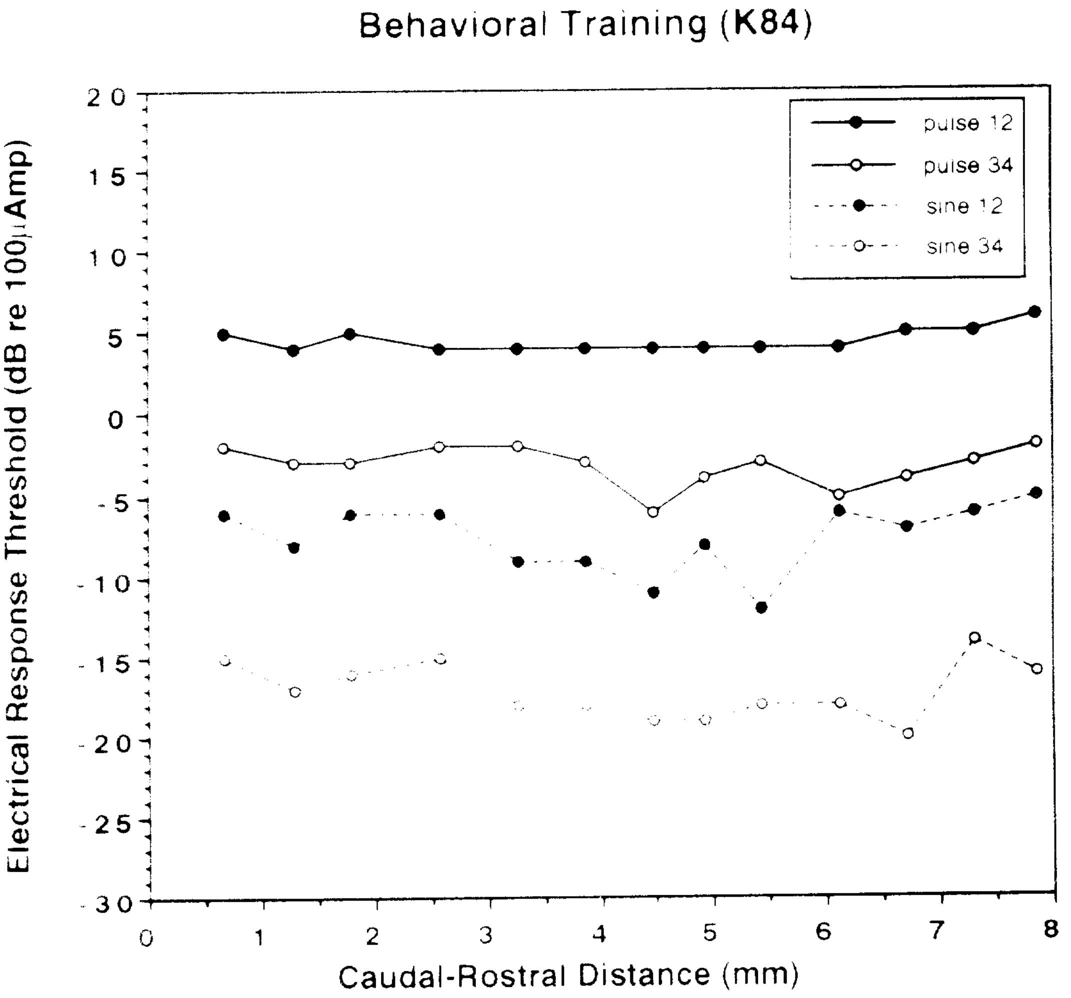

Behavioral Training (K84)
Electrical Response Threshold (dB re 100μAmp)
20
15
10
5
0
-5
-10
-15
-20
-25
-30
0
1
2
3
4
5
6
7
8
Caudal-Rostral Distance (mm)
pulse 12
pulse 34
sine 12
sine 34

FIGURE 9

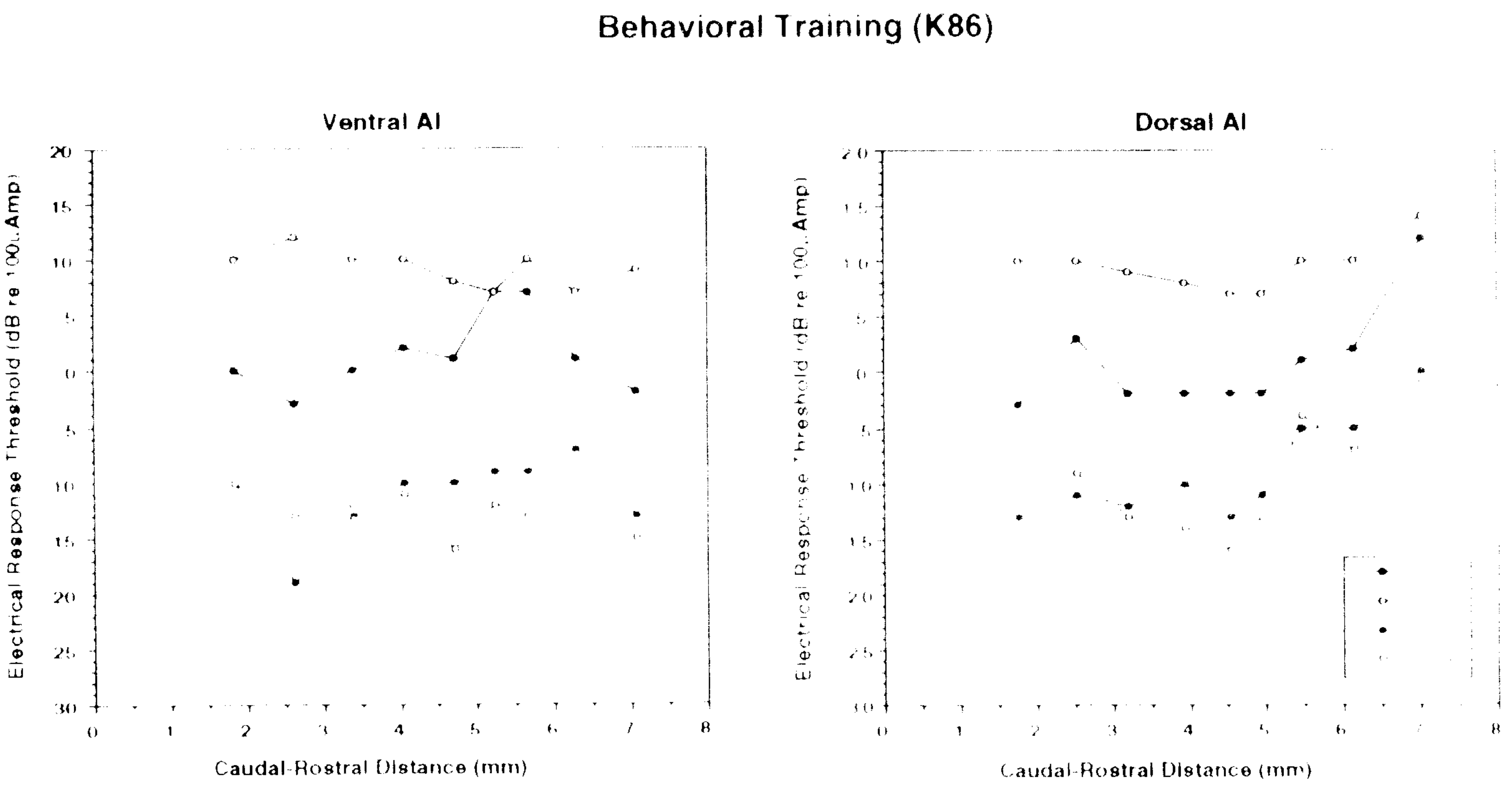

Behavioral Training (K86)
Ventral AI
Dorsal AI
Electrical Response Threshold (dB re 100. Amp)
20
15
10
5
0
5
10
15
20
25
30
0
1
2
3
4
5
6
7
8
Caudal-Rostral Distance (mm)

FIGURE 10

Effects of Cochlear Electrical Stimulation on Cortical Tuning

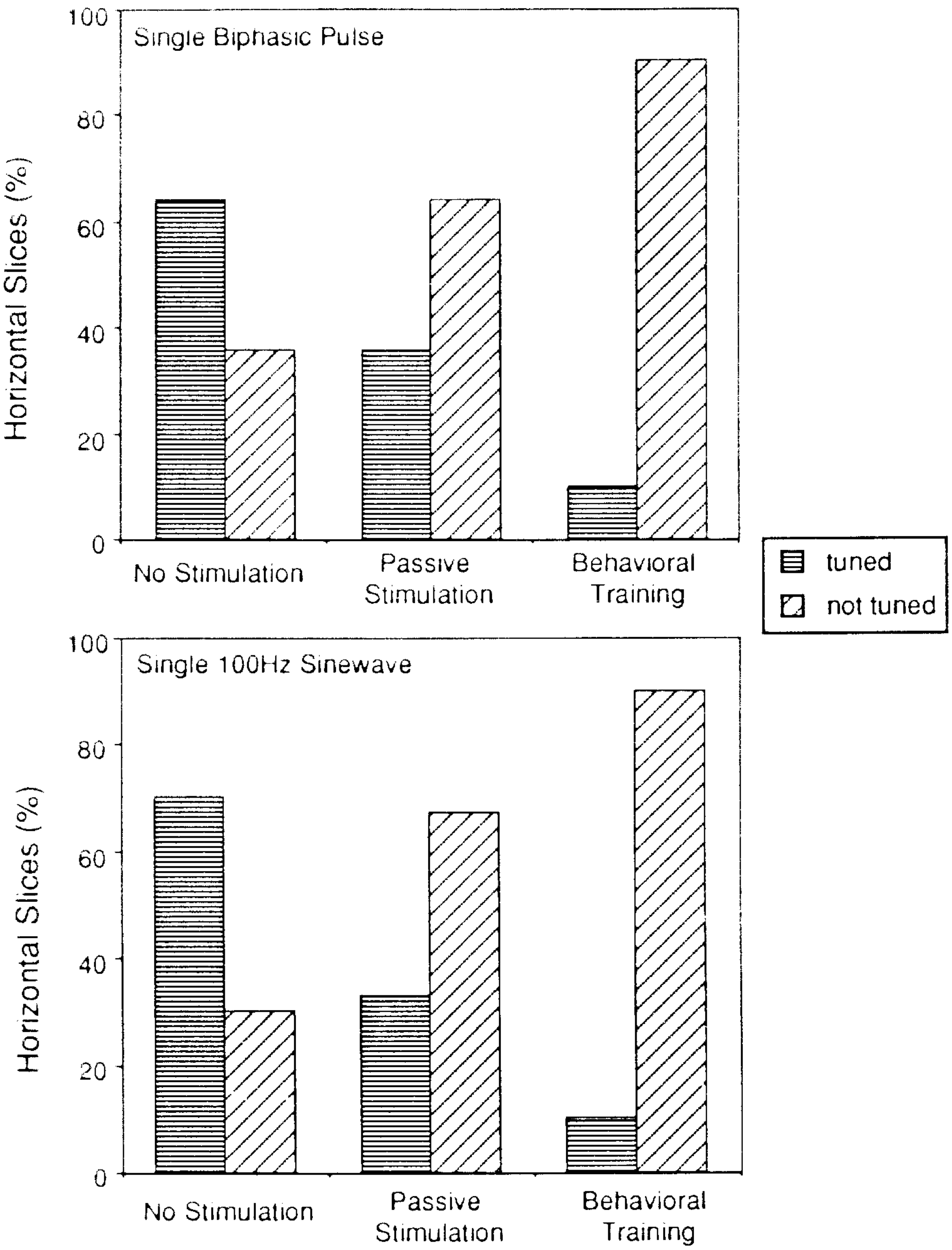


FIGURE 11