7th Quarterly Progress Report
April 1, 1996 to June 30, 1996

Fundamental Neurosciences Contract N01-DC-4-2143

Protective Effects of Patterned Electrical Stimulation on the Deafened Auditory System

Submitted by:

Patricia A. Leake, Ph.D.
Gary T Hradek, M.S.
Stephen J. Rebscher, M.A.

Epstein Hearing Research Laboratories
Department of Otolaryngology, Room U490
University of California, San Francisco
San Francisco, Ca 94143-0526

ABSTRACT

The current focus in chronic electrical stimulation experiments is to define specific stimulation parameters and/or features that are critical in maximizing the protective effects on the auditory nerve. Studies have been initiated to evaluate effects of intracochlear stimulation with higher frequency stimuli that are designed to be temporally challenging to the central auditory system. In a previous Quarterly Progress Report (QPR #3, April 1, 1995 to June 30, 1995, Contract N01-DC-4-2143), spiral ganglion morphometric data were presented for the first 9 neonatally deafened kittens in these new intracochlear series. Data from an additional group of 4 neonatally deafened cats are presented in this QPR. These animals are the first group to be chronically stimulated with the new "wing" feline electrode design. Data on electrode positions documented significantly deeper insertion of these electrodes, which consistently positioned the most apical electrode at about 4.5 kHz as compared to an average of 6.7 kHz with the older design. Since the basal electrode pair remained in about the same frequency position, the new design provides greater frequency separation between bipolar channels. Two of these most recent cases showed a striking protective effect of electrical stimulation resulting in maintenance of about 20% more of the spiral ganglion neurons; one cat had unusually high neuronal survival in the contralateral cochlea (and thus showed no significant difference between sides), and the final cat was not deafened prior to implantation. Histologic and morphometric results in these cats are compared and contrasted with the findings from the previous groups.

Histologic and Morphometric Results with Higher Frequency Temporally Challenging Stimulation

Initial studies conducted under a previous Contract and completed during the initial months of this Contract demonstrated that chronic electrical stimulation (delivered via both intra- and extracochlear electrodes) using passive and invariant 30 pps stimuli induced a significant protective effect, partially preventing the degeneration of spiral ganglion cells in neonatally deafened animals. Subsequently, additional experiments were initiated in which the signals used for chronic electrical stimulation have been varied in order to begin to define specific parameters that are critical in maximizing the protective effects on the auditory nerve. In a previous Quarterly Progress Report (QPR #3, April 1, 1995 to June 30, 1995, Contract N01-DC-4-2143), spiral ganglion morphometric data analyses were reported for 9 neonatally deafened cats from these new intracochlear series. This group included 2 animals (K83, K85) that received chronic passive intracochlear stimulation using continuous pulse trains at 80 pps (200 µsec/phase pulses), three cats (K89, K91, K92) that were chronically stimulated with pulse trains (biphasic, 200 µsec/phase) at 300 pps, and 100% amplitude modulated at 30 Hz, and four additional cats (K84, K86, K93, K94) that received temporally- and intensity-varying stimulation through a single channel speech processor which transduced environmental sounds into an analogue electrical signal (these animals also received extensive behavioral training to determine psychophysical thresholds to selected electrical stimuli). The daily stimulation periods were 4 hrs/day, 5 days/week. The intensity of stimulation was set at 2 dB above EABR threshold for pulsed stimuli and at a dynamic range of 0 to 6 dB above EABR threshold for the processors. The individual stimulation levels and duration of stimulation are shown for each animal in Table 1. The mean stimulation period for the 9 animals comprising the first 2 groups of animals was 12.5 weeks and the mean age at study was 41.8 wks. All these animals were stimulated with the apical bipolar pair of electrodes (E1 and 2), which were positioned in the scala tympani at ~43 and 39% basilar membrane distance from the base of the cochlea (represented frequency of 6.7 and 8.5 kHz, respectively; see Table 2).

Since histological findings and morphometric data documenting spiral ganglion cell survival in these nine cats were reported in detail previously, results are only summarized here for direct comparison to data obtained during this past quarter from 4 additional cats receiving chronic intracochlear stimulation with the new "wing" feline electrode.

The data for the first group of 5 cats (K83-K89) demonstrated impressive increases in neuronal survival as a consequence of chronic stimulation. The volume ratio (density) for each cochlear segment (from base to apex) in the left, chronically stimulated cochlea was compared w the paired data from the contralateral deafened, unstimulated ear of each individual cat. Figure summarizes the morphometric data for these 5 cats showing the mean stimulated less control *difference* in spiral ganglion cell density, expressed as percentage of normal. Mean spiral ganglic cell survival was 30-40% higher over the basal one-third of the cochlea. When averaged over al cochlear sectors, the mean difference in neuronal density was 22% in this group.

Table 1. Higher Frequency, Temporally Challenging Stimulation

Cat #	Neomycin mg/kg/days	Age at Initial Stimulation	Stim Current	Stim Period	Stim Frequency	Age at Sacrifice
K83	60/19	10.5 wks	125 µA	21 wks*	80 Hz	32 wks
K84	60/19	10 wks	200-400 µA	35 wks	SP beh	45 wks
K85	60/19	10 wks	125 µA	42 wks	80 Hz	52 wks
K86	60/19	9 wks	30-160 µA	44 wks*	SP beh	55 wks
K89	50-60/19	10.5 wks	80-100 µA	26.5wks	300/30 Hz	37 wks
STIMULATION DAMAGE SERIES						
K91	60/17	6.4 wks	100-400 µA	31.5 wks	300/30 Hz	38.5 wks
K92	60/17	6.4 wks	150 (310) µA	23 wks*	300/30 Hz	31 wks
K93	60/21	8 wks	40-400 µA	36 wks	SP beh.	44 wks
K94	60/21	8 wks	40-500 µA	34 wks	SP beh	42 wks
"WING" ELECTRODE SERIES						
K96	60/17	7 wks	50-160 µA	36 wks*	SP "yoked"	44 wks
K98	60/20	7 wks	50-100 µA	32 wks	SP beh	39 wks
K99	60-70/25	8 wks	32-100 µA	40 wks	300/30 Hz beh	49 wks
K100	[illegible]	8 wks	125 µA	37 wks	300/30 Hz "yoked"	45 wks

Table 1. Individual histories of the 9 animals for which histological results were previously presented, and the 4 additional cats implanted with the new "wing" electrodes, for which histological results are presented in this report. Animal #K96 was "yoked" to K98 during the final 7 weeks of the stimulation period and K100 was "yoked" to K99 for the final [illegible] weeks of stimulation.
(*Device failed during chronic stimulation and animal was reimplantated.)

As reported previously (QPR #3, April 1, 1995 to June 30, 1995) this first group of 5 cats that demonstrated stable thresholds during chronic stimulation and striking maintenance of spiral ganglion neurons, presented a striking contrast to the next group of 4 cats denoted "Stimulation Damage Series" in Table 1. The 4 cats in this group exhibited elevations in thresholds during their chronic stimulation periods, as reflected by the final stimulation levels shown in Table 1. EABR thresholds are determined periodically throughout chronic stimulation for each cat, and chronic stimulation levels are adjusted accordingly. Two animals (K91 and K93) had final chronic stimulation levels of 400 µA and one animal (K94) had a final chronic stimulation level of 500 µA. In K92, although the final stimulation level was 150 µA, at the time of the final electrophysiology experiment in this animal the EABR threshold had shifted up to

INCREASED SPIRAL GANGLION SURVIVAL WITH TEMPORALLY CHALLENGING STIMULATION (K83-89)

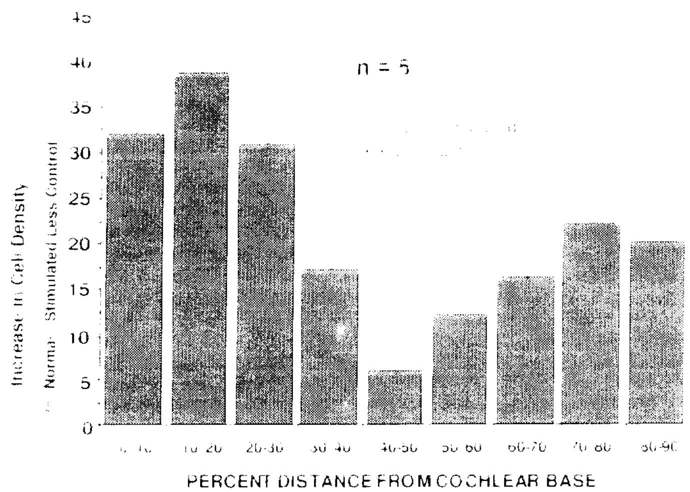

Figure 1. Striking increase in spiral ganglion survival induced by chronic intracochlear electrical stimulation in neonatally deafened cats. The data shown are pooled from 5 animals (K83-K89). The mean stimulated less control values for spiral ganglion cell density are expressed as percent of normal values for each cochlear sector and thus represent % *increases* in neuronal survival in the stimulated cochleas. The increased survival was offset by insertion damage which occurred near the tip of the electrode in the 40-50% sector in all five cases. Overall spiral ganglion cell density was increased by about 22%, and this difference was highly significant (P< 0.001, Student's paired t-test).

Behavioral thresholds to pulses were also determined in 3 of these animals (K91, K92 and K93) during chronic stimulation periods, and these thresholds were also unusually high in these animals compared to previous intracochlear experimental series.

Histological evaluations of the implanted and stimulated cochleas from this group of animals also presented some highly unusual findings. In K91 severe hemorrhage was observed in the modiolus along with total degeneration of spiral ganglion cells in Rosenthal's canal over a 1.5 mm region directly adjacent to the stimulating electrodes. Extensive ectopic bone formation was also observed at more basal locations along the electrode carrier. New bone formation was also severe in two other cats in the group. In K92 ectopic bone was observed over a region of approximately 7 mm in relation to the electrode carrier, primarily under the spiral ligament and adjacent to the modiolus. In K93, massive new bone formation was noted not only in the scala tympani but also partly occluding the scala vestibuli in the region directly above the stimulating electrodes. In the final cat in the series, K94, the cochlear histopathological findings also included some osteoneogenesis, although it was less extensive and did not appear to displace or insulate the stimulating electrodes from the spiral ganglion cells in Rosenthal's canal. However, there was notable insertion trauma in this cochlea, with a fracture of the osseous spiral lamina in the region and an obvious reduction in spiral ganglion cell survival adjacent to the apical electrode pair (1,2).

Figure 2 summarizes the morphometric data in this group of 4 cats, showing the mean stimulated less control increases in spiral ganglion cell density. The mean difference in neuronal density (averaged over all cochlear sectors) was only 8%. Particularly striking is the complete lack of spiral ganglion maintenance in the region 30-50% from the base of the cochlea, in the region of the stimulating electrodes. In comparison to the data shown in Figure 1, these data provide a striking contrast to earlier results. Both the unusual, severe nature of the histopathology observed in the stimulated cochleas and this obvious drop in spiral ganglion survival near the stimulating contacts, strongly indicated to us that stimulation-induced damage had occurred in the regions nearest to the stimulating electrodes.

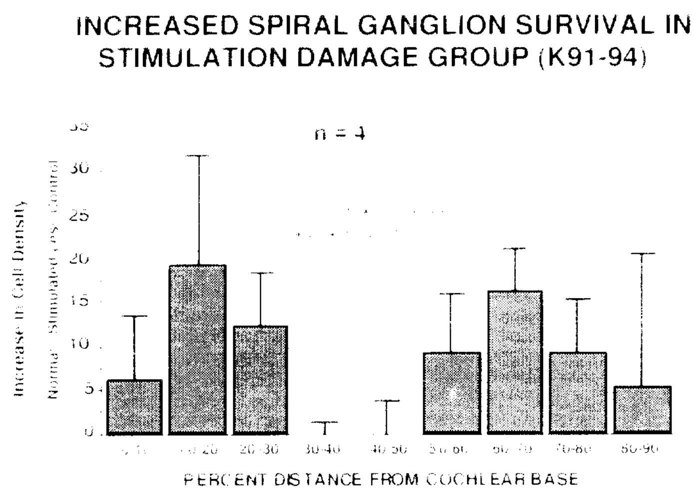

Figure 2. Spiral ganglion morphometric data from the group of 4 neonatally deafened cats that showed elevated thresholds and severe histopathology (K91, K92, K93, K94) following chronic intracochlear electrical stimulation. The mean difference (stimulated less control values) in spiral ganglion cell density are shown as percent of normal values for each cochlear sector. Overall spiral ganglion cell density was increased by only 8%. Note the lack of increased survival in the 30-50% sectors (See text).

The degree to which this damage relates to the various specific conditions of stimulation is not clear. We believe the damage may have been caused by a few episodes when a stimulator went into oscillation during EABR testing in these animals. However, there was also one feature of the electrodes that was different in this group as compared to the previous series: slightly smaller electrode contacts (≈175 µm - 200 µm) were used to allow the fabrication of electrode arrays with greater numbers of contacts. These smaller contacts exhibited somewhat higher impedances initially and further increases over time, so that with the elevated thresholds in some cases the compliance voltage of the battery driven stimulators used for chronic stimulation in K 93 and K94 may have been exceeded. Exceeding the compliance voltage supply in these stimulators may have produced instability in the constant current driving circuits resulting in asymmetric, distorted output. We have also evaluated the possibility that safe charge limits may have been exceeded with these smaller electrode contacts. The reduction in contact diameter in these electrodes resulted in a reduction in real surface area of ≈ 50%. However, the charge densities produced at the electrodes during stimulation were still considerably below accepted safe limits. K91 and K92 were initially stimulated at 100 and 150 μA respectively; the 200 μsec/phase pulses used in their stimulation thus generated 55 μC/cm² and 82 μC/cm² respectively at maximum modulated intensity. At the completion of their stimulation periods, after increasing the level of stimuli to 400 and 316 μA to correspond to their elevated EABR thresholds, the charge density at the electrodes in these animals were 220 μC/cm² and 174 μC/cm² stimuli. Even these higher levels (which were not applied until after some earlier event resulted in an increase in the EABR threshold) should have been within safe charge transfer limits. Calculation of the actual charge densities for the animals receiving speech processor stimuli is more difficult because the charge accumulation is an integral function of the constantly varying frequency and intensity of these devices. During the next quarter we will attempt to better quantify the speech processor bandpass characteristics and maximum charge densities associated with stimulation using these processors. Our working hypothesis is that the damage in the K91-94 group is related either to the contact size or specific stimulation problems, and our strategy has been to replicate these same stimulation protocols (speech processors and 300 pps/30 Hz paradigm) while avoiding these problems.

Results From New Higher Frequency/Temporally Challenging Stimulation Series Using New "Wing" Feline Electrode.

In order to confirm the results seen in the initial higher frequency stimulation series, to further explore the effects of modulating specific parameters of electrical stimuli, and to confirm our hypothesis concerning the relationship of electrode size to the damage seen in the K91-94 series, additional neonatally deafened animals were implanted and chronically stimulated. The animals in this new series received newly designed feline "wing" electrodes, incorporating larger contacts (≈250 μm). We have now studied and completed initial data analysis for the first 4 cats (K96, K98, K99, K00) in this new higher frequency/temporally challenging chronic stimulation group using the new electrodes.

One specific goal of the design of the new "wing" electrodes was to permit deeper insertion and lower frequency positioning of the stimulating electrodes. Table 2 shows electrode contact positions observed with the older electrodes used in the 9 cats discussed above and compares them with the new "wing" electrodes implanted in the K96 - K00 series. To derive these data, the fixed temporal bone of each cat was dissected to remove the bone overlying the scala vestibuli. The metal electrode contacts, or at least pair 1,2 are usually visible through the basilar membrane in the dissecting microscope. If the electrodes are not visible from above due to ectopic bone formation or dense fibrotic connective tissue over the electrode, then the bone underlying the scala tympani is drilled out until at least the most apical electrode is visualized. The electrode locations are marked by a small notch (≈300 μm diameter) drilled in the bone adjacent to the spiral ligament. The electrode array is then removed and the temporal bone embedded in epoxy resin. When the surface preparation is made, the markers are visible and the precise location of each electrode is determined as percent of basilar membrane length, and the represented frequency can be calculated based on the known frequency map of the cat cochlea (Liberman, 1982, J. Acoust. Soc. Am. 72: 1441-1449).

All cats in these groups presented in Table 2 were stimulated with the apical bipolar pair (electrodes 1,2). With the previous electrodes in the first 9 cats, the mean position of electrode 1 was at 6.7 kHz, and electrode 2 was positioned at about 8.5 kHz. In the new "wing" electrode series, the mean position of electrode 1 shifted down to 4.5 kHz and electrode 2 averaged 5.7 kHz. It should be noted that the separation between the apical pair and the basal electrode pair was increased from 2 mm in the older electrodes to 4 mm in the new "wing" electrodes. Thus, the mean position of electrode 3 actually shifted to a slightly more basal higher frequency cochlear location (from 11.6 to 14.8 kHz) in the new electrodes.

Electrode Position Summary

Cat #	Bas. Mem. Length (mm)	E1 (% B.M.)	E2 (% B.M.)	E3 (% B.M.)	E4 (% B.M.)
K83	24.8	42	-	-	-
K84	23.7	45.6	-	--	--
K85	24	45.8	42.9	--	--
K86	23.2	43.5	37.9	31	-
K87	25.3	46.2	41.5	29.5	28.9
K91	23	36.9	31.5	25.2	20.9
K92	23.1	45.5	41.1	30.8	--
K93	23.7	40.1		--	--
K94	22	42.7	36.8	29.5	25
MEAN	**23.6mm**	**43.1 (6.7 kHz)**	**38.6 (8.5 kHz)**	**32.4 (11.6 kHz)**	**24.9 (16.8 kHz)**

"WING" ELECTRODE SERIES

Cat #	Bas. Mem. Length (mm)	E1 (% B.M.)	E2 (% B.M.)	E3 (% B.M.)	E4 (% B.M.)
K96	23.1	48.9	45.5	26	-
K98	25.1	55	49	--	--
K99	23.5	49.4	43.8	28.5	X
K00	23.1	50.9	47.6	28.1	X
MEAN	**23.7mm**	**51.1 (4.5 kHz)**	**46.5 (5.7 kHz)**	**27.5 (14.8 kHz)**	

Table 2. Data on placement of individual electrode contacts in the individual 9 animals with the older type electrodes, and the 4 additional cats implanted with the new "wing" electrodes. X: In K99 and K00 Electrodes E3 and E4 were oriented as a strictly radial pair so both E3 and E4 were positioned at the site indicated. -- indicates that electrode could not be visualized during dissection due to overlying bone or connective tissue.

Initial thresholds in the 4 animals implanted with the new electrodes were relatively low and stable throughout stimulation periods (Table 1). Two of these neonatally deafened cats (K99, K00) were chronically stimulated with pulses (biphasic, 200 µsec/phase) delivered in continuous trains at 300 pps and 100% amplitude modulated at 30 Hz. Two additional cats (K96, K98) were stimulated with operational speech processors which transduced environmental sounds to an analogue electrical signal; these animals also received extensive behavioral training to determine thresholds to selected electrical stimuli and thresholds for discrimination of the 300 PPS/30 Hz stimulus (See QPR #6). The daily stimulation periods (4 hrs/day, 5 days/week), intensity of stimulation (2 dB above EABR threshold for 300 Hz/30 Hz stimulation and a 6 dB dynamic range, 0 to 6 dB above EABR threshold for the processors) and duration of stimulation were matched as closely as possible to the earlier series (see Table 1). The mean stimulation period for the K83-K89 group was 34 weeks and age at sacrifice averaged 44 wks. Since the new experimental group (K96-K00) was stimulated at a younger age, the mean stimulation period was 2 weeks longer (36 wks) but mean age at sacrifice was identical to the first group (44 wks).

During the past quarter morphometric analyses of spiral ganglion cell survival were completed for these first 3 cats in this new higher frequency / temporally challenging chronic stimulation group using the new electrodes. The fourth animal in the group, K00, is included at this time only for the presentation of the data on electrode position. This animal was one of a litter of 4 solid black kittens, 2 of which were neonatally deafened for implantation. Due to an error, and unknown to the investigators, the animals were switched and K00 was a normal-hearing kitten that was implanted and chronically stimulated along with its neonatally deafened littermate. The interesting histological results from this cat will be presented in a subsequent QPR.

Figure 3 shows individual spiral ganglion cell data from the other 3 cats. Cell (somata) density is shown in the stimulated ears (dark data bars) and the control deafened/unstimulated ears (striped bars) for cochlear regions from base to apex. Two of the animals showed highly significant increased maintenance of spiral ganglion neurons in the stimulated cochlea. K98 (Fig. 3b) had a 17% increase in survival in the stimulated cochlea (38%) as compared to that in the control cochlea (21%), and in K99 (Fig. 3c) data showed an increase of 22% (54%) in the stimulated cochlea and 33% in the contralateral cochlea.

Histological findings in one of these 2 cats are illustrated in Figures 4 through 7. Figure 4 shows a light microscopic section from the basal cochlea of K99 in which a few myelinated neurons were observed coursing through the connective tissue over the electrode array in the scala tympani. These fibers apparently passed through the habenula perforata to reach the lower scala. Although there is no way to determine whether these fibers are afferent or efferent, their presence demonstrates that neurons in the stimulated cochlea are capable of sprouting. Figure 5 shows the difference in spiral ganglion survival demonstrated in K99, with a section through Rosenthal's canal in the stimulated cochlea shown on the left and the same region from the contralateral ear at the right. (Sections were taken from the region of maximum difference in neuronal survival in the basal cochlea (10-20%) where the density was 83% of normal in the stimulated cochlea and 35% of normal in the control deafened cochlea. Figures 6 and 7 illustrate histological findings at more apical regions. Figure n shows that the excellent preservation of spiral ganglion neurons in the stimulated cochlea of K94 was accompanied by the maintenance of substantial numbers of myelinated peripheral axons within the osseous spiral lamina. The insertion trauma caused by the tip of the electrode in this cochlea consisted by a small fracture of the osseous spiral lamina in the region about 50% from the base of the cochlea.

HIGHER FREQUENCY.TEMPORALLY CHALLENGING CHRONIC STIMULATION
(Speech Processor, 300 pps/30 Hz AM. Behavioral)

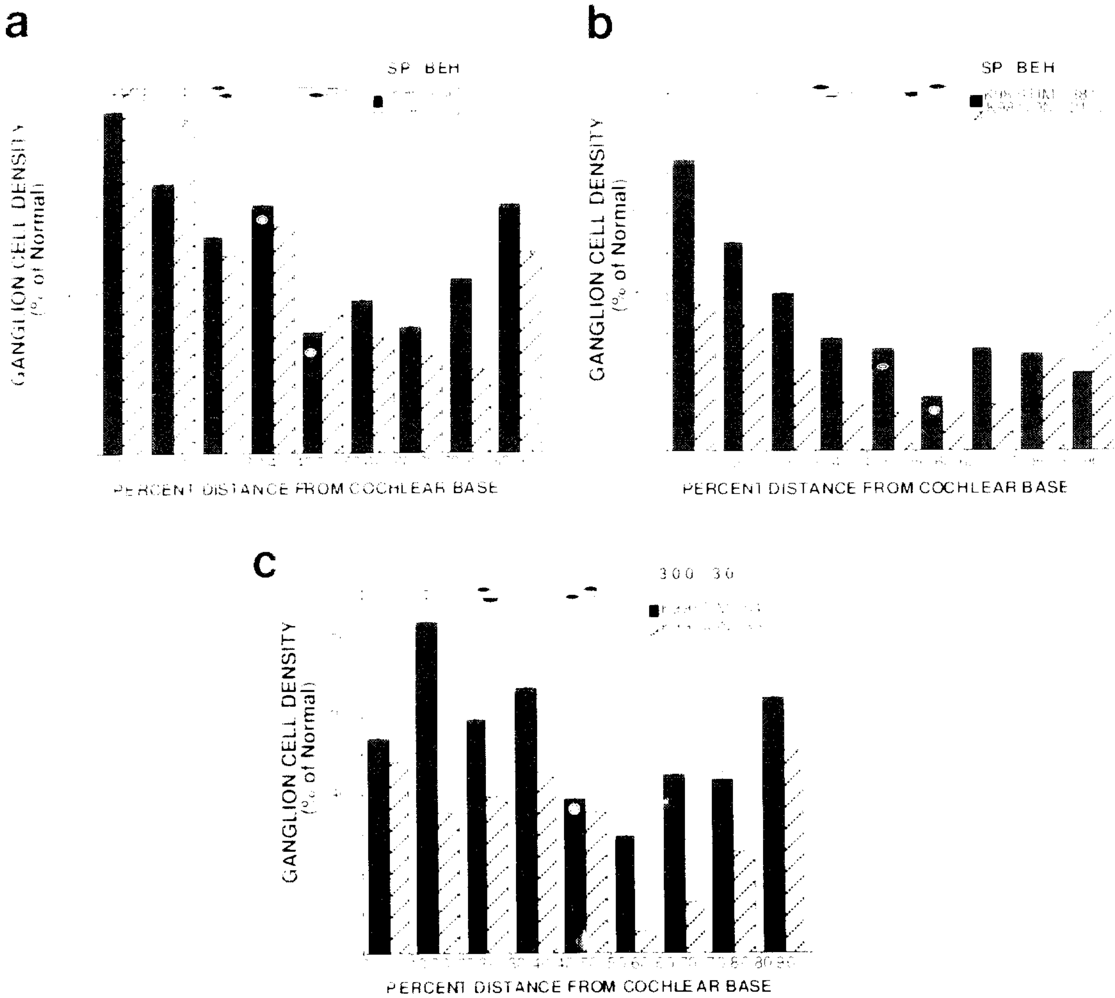

Figure 3 Morphometric data documenting increased spiral ganglion survival in chronically stimulated ears. Small drawings indicate position of scala tympani electrode contacts. Black data bars indicate density of spiral ganglion cells in the implanted stimulated cochleas; striped bars are data from control deafened cochleas. White markers indicate regions in which mechanical damage from the electrode array was observed.

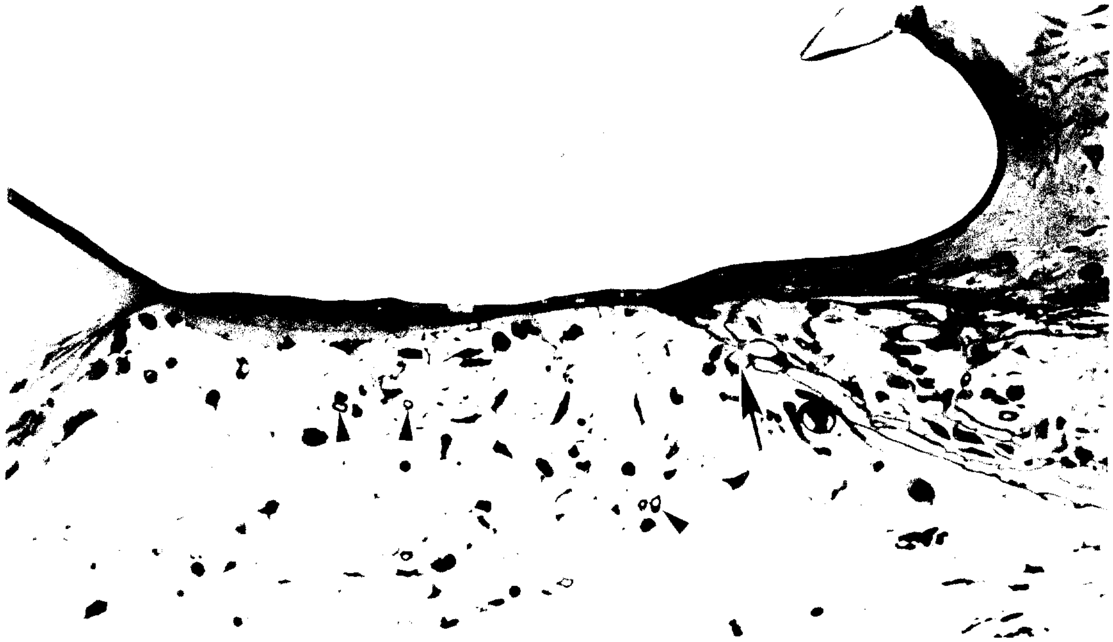

Figure 4 Light microscopic section from K99 showing the organ of Corti in the region 3.5 mm from the base. Small arrowheads indicate small myelinated axons which have sprouted into the scala tympani under the basilar membrane and into the connective tissue over the implanted electrode array. Large arrow points out small capillary passing through the habenula perforata, suggesting the probable course taken by the sprouting fibers to enter the scala tympani.

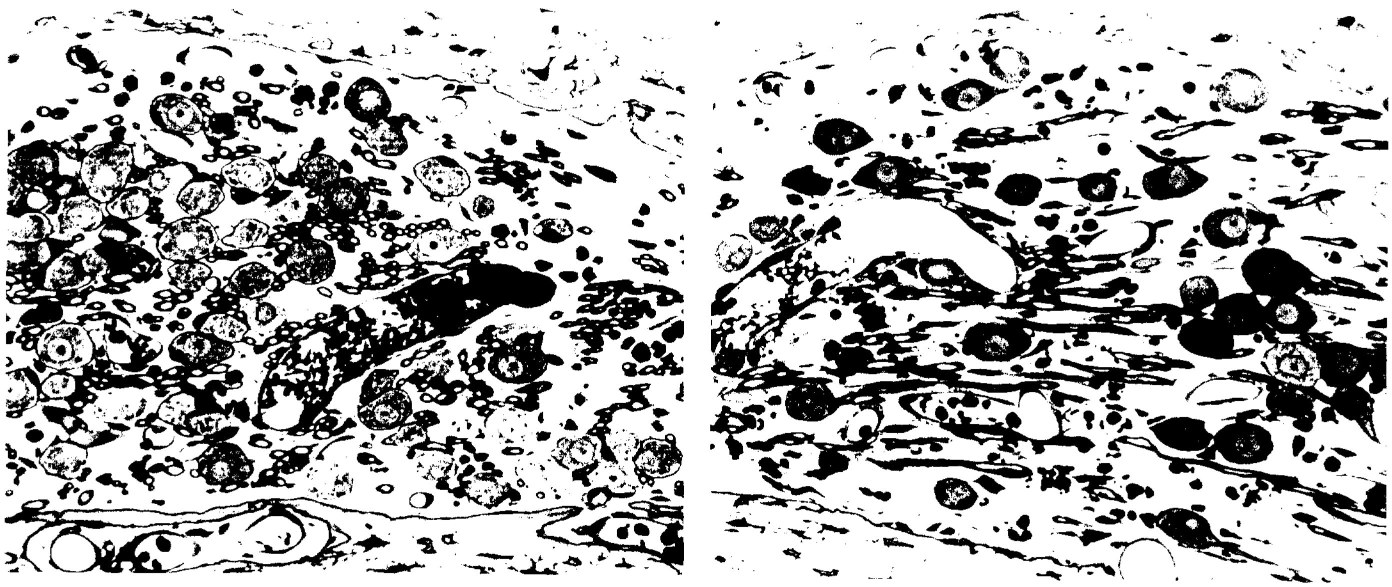

Figure 5 Sections through Rosenthal's canal showing spiral ganglion cell density in the stimulated cochlea (left) and in the control deafened cochlea (right) in the region 3.5 mm from the base in K99. Survival is about 83% of normal in this region of the stimulated cochlea as compared to 35% in the deafened, unimplanted ear.

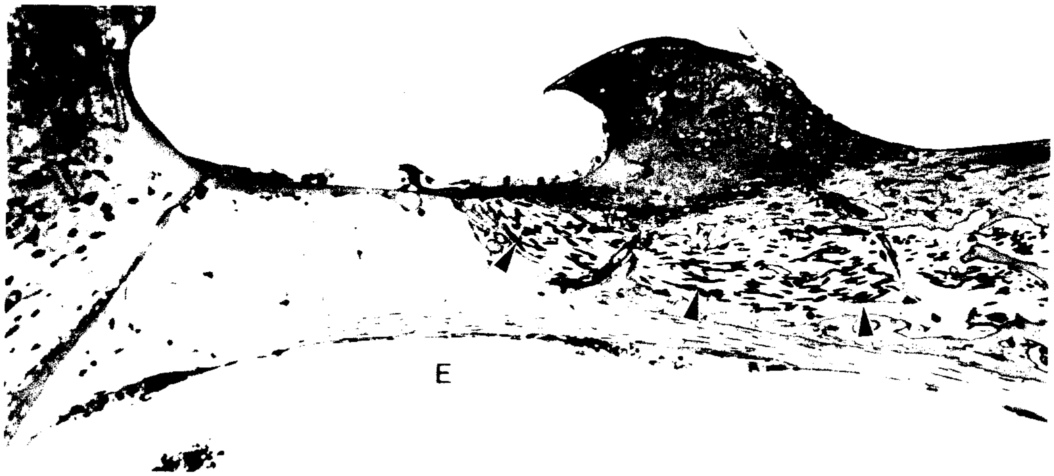

Figure 6. Another section from the stimulated cochlea in K99, showing the organ of Corti at a more apical location, in the region 6.5 mm from the base. Small arrowheads indicate myelinated axons which have remained intact within the osseous spiral lamina. The position of the electrode (E) in the scala tympani under the basilar membrane is apparent from the configuration of the connective tissue encapsulating the array.

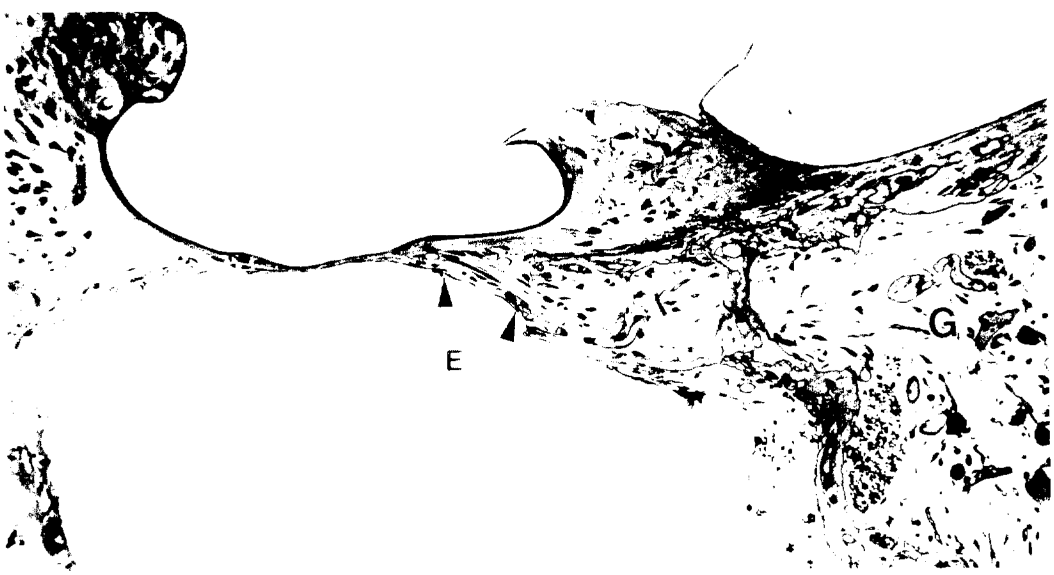

Figure 7. Section illustrating the mechanical trauma induced by insertion of the electrode array (E) in K99. The osseous spiral lamina has been fractured (arrowheads) and is slightly displaced upward toward the scala media in this region near the tip of the electrode (about 50% basilar membrane distance from the base). Spiral ganglion (G) degeneration is severe in this region.

In contrast to the striking difference in spiral ganglion survival induced by chronic stimulation in K98 and K99, the third cat (K96) demonstrated no difference in survival between the stimulated (53%) and unstimulated (50%) cochleas (Figure 3a). There is, however, a highly unusual finding in the data from K96, in that the neuronal survival was remarkably high in the control ear. The data from the first 2 groups shown in Figures 1 and 2, as well as the data from K98 and K99, indicate that animals that are deafened for this length of time usually have spiral ganglion survival in the contralateral cochlea that averages about 30% of normal. In the first group of 5 cats (K83-K89), the overall survival was 29.9% in the control cochleas; in the second group (K91-K94) this value was 34.2%, and the average for K98 and K99 was 27%. In addition to the unusually high overall ganglion cell density, it should be noted that the control cochlea of K96 showed *no significant loss* of spiral ganglion neurons in the basal 20% of the cochlea. This finding suggests that there may have been a significant population of residual hair cells surviving in the basal sectors of this cochlea after ototoxic drug treatment. Although no hair cells could be identified in this cochlea at the time of histological examination, this does not rule out the possibility that they were present earlier. Another highly unusual finding was that supporting cells and the tunnel of Corti were recognizable in the extreme base of this cochlea. As shown in Figure 4, the organ of Corti in the basal cochlea is usually replaced by a layer of squamous epithelial cells after the extended survival periods in these neonatally deafened cats. Thus this finding of intact supporting cells in the base of the control cochlea in K96 suggests that the ototoxic drug was not initially effective in destroying all the hair cells in this region, although the severe damage did ultimately progress to total hair cell loss over time. For this reason, the data from this animal will be excluded from the group analysis summarizing the effects of higher frequency, temporally challenging stimulation.

Figure 8 shows a summary figure, incorporating the morphometric data from from the two new "wing" electrode cases (K98 and K99) with the data from the earlier group of cats (K83-K89). For this group of 7 chronically stimulated cats, the mean overall spiral ganglion survival was increased by about 20%, from 29.1% of normal in the deafened control cochleas to a mean of 49.4% in the stimulated cochleas. Regional increases of 30-35% were seen over the basal one third of the cochlea, but marked maintenance was observed throughout the cochlea. The pooled data support the preliminary conclusion based upon findings in the earlier higher frequency stimulation series (K83-K89): a notably greater difference is observed when chronic stimulation is effected with higher frequency, temporally challenging stimuli, as compared to effects demonstrated in previous experiments using 30 Hz pulsatile stimuli with either intracochlear stimulation (13% difference in ganglion cell survival) or extracochlear stimulation (6% difference). These results suggest that the specific parameters of stimulation (e.g., frequency of stimulus, intra- vs. extracochlear mode) are critically important in maximizing the protective effect of electrical stimulation on the auditory nerve.

INCREASED SPIRAL GANGLION SURVIVAL WITH TEMPORALLY CHALLENGING STIMULATION (K83-89, K98,99)

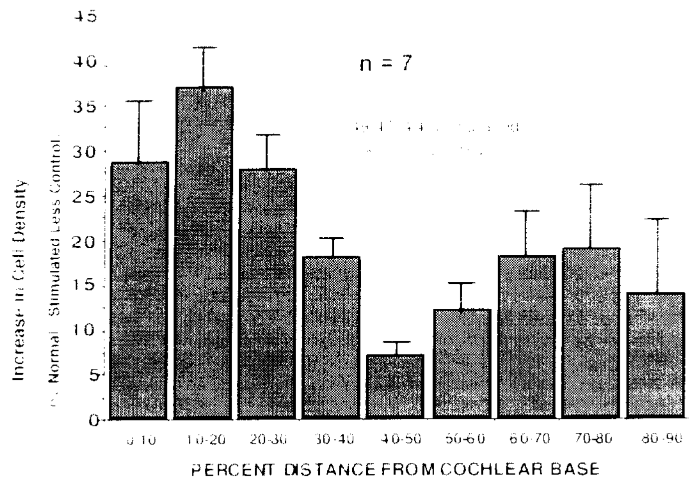

Figure 8. Pooled data from all valid cases in the higher frequency temporally challenging stimulation series. The data include 5 animals from the previous series (K83-K89, shown in Figure 1 and 2) of the cats (K98 and K99) from the new "wing" electrode series. Data are shown as difference (stimulated less control) values for spiral ganglion cell density, expressed as percent of normal values for each cochlear sector. The increased survival was offset by insertion damage which occurred near the tip of the electrode in the 40-50% sector in all 7 cases. Overall spiral ganglion cell density was increased by about 20% and this difference was highly significant (P<0.001, Student's paired t-test).

Work Planned for the Next Quarter

1. Two adult-deafened cats have been implanted with the new model UCSF cat electrode and EABR thresholds are stabilized at acceptable levels. These animals have been undergoing chronic stimulation using a temporally challenging (but passive and invariant) electrical stimulus (300 pps amplitude modulated with a 30 Hz sinusoid). During the next quarter these animals will be studied in acute electrophysiological experiments to evaluate spatial selectivity (STC widths) in the inferior colliculus and AI and thus to determine if functional alterations observed in neonatally deafened cats after chronic stimulation 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. Two neonatally deafened kittens have been implanted and are currently undergoing chronic electrical stimulation. Chronic stimulation in the one kitten has been initiated on two independent bipolar channels. Behavioral training has been initiated in the other kitten to confirm and extend initial results with the behavioral amplitude modulation discrimination task described in the last QPR. One additional kitten will be implanted in the coming quarter.

3. Histological processing of the cochlear nucleus specimens will be completed for 5 additional chronically stimulated cats in the 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.