8th Quarterly Progress Report
July 1, 1996 to September 30, 1996

Fundamental Neurosciences Contract N01-DC-4-2143

Protective Effects of Patterned Electrical Stimulation on the Deafened Auditory System

Submitted by:

Maike Vollmer, M.D., Ph.D.
Patricia A. Leake, Ph.D.
Russell L. Snyder, Ph.D.
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

One of the most interesting and potentially important functional changes induced by chronic electrical stimulation is the marked alteration that has been demonstrated in the temporal response properties of central auditory neurons. We previously reported that the temporal resolution of neurons in the inferior colliculus, (i.e. their capacity to phase lock or follow pulse trains of increasing frequency) is significantly increased following chronic stimulation (Snyder et al., J. Neurophysiol. 1995 73: 447-467). Moreover, in a previous Quarterly Progress Report (QPR#5, September 30-December 31, 1995) we presented data indicating that the magnitude of the increase in temporal resolution of the central auditory neurons is dependent upon the specific temporal properties of the chronic stimulation. The higher frequency, temporally challenging protocols used in current studies induced marked increases in temporal resolution, whereas animals stimulated with simple pulse trains at 30 PPS were not significantly different from normal. This Quarterly Progress Report is an update on temporal resolution studies, presenting results from additional chronically stimulated animals, including preliminary data from 2 new experimental groups: long deafened/chronically stimulated cats, and adult deafened/chronically stimulated cats.

In addition, in order to better define the mechanisms underlying these increases in temporal resolution, further analyses of the data were performed, examining the *spatial distribution* of IC neurons with increased phase locking capacities following chronic stimulation. Results show that neurons in the external nucleus of the IC do not exhibit increased temporal resolution. But within the central nucleus, the effect appears to be broadly distributed across the tonotopic gradient and apparently is not selective either to the region of the IC normally encoding higher frequencies or to the location most sensitive to electrical stimulation with the chronically stimulated electrodes.

A. EFFECTS OF CHRONIC ELECTRICAL STIMULATION ON THE TEMPORAL RESOLUTION OF INFERIOR COLLICULUS NEURONS IN DEAFENED CATS.

Our previously published work (Snyder et al. J. Neurophysiol. 1995 73: 447-467) has demonstrated that in the deafened, developing auditory system, experience with chronic intracochlear electrical stimulation (ICES) profoundly alters the temporal resolution (i.e., maximum cut-off frequency to pulse trains) in the inferior colliculus (IC). Our hypothesis is that such changes in the temporal response patterns within the central auditory system may partly underlie individual differences and longitudinal changes in performance of cochlear implant subjects.

In addition, recent data presented in QPR#5 (September 30-December 31, 1995) showed that this induced increase in temporal resolution is dependent upon the temporal properties of the chronic electrical stimulation. Neonatally deafened cats that were chronically stimulated with a variety of higher frequency signals (>80 Hz) showed a marked and highly significant increase in temporal resolution of IC neurons with a mean maximum following frequency of 157 PPS, as compared to a mean of 98 PPS in normal cats. In contrast, neurons from similar cats stimulated with low frequency stimuli (<80 Hz) showed only a modest increase to a mean of 106 PPS.

1) Stimulation Histories

In this Report, we present data from additional chronically stimulated cats. Table 1 summarizes the deafening and stimulation histories for these recently studied animals.

Table 1

Cat Number	Age at Surgery	Age at Initial Stimulation	Stimulus Current (μAmps)	Stimulation Period	Stimulation Frequency	Age at Sacrifice
Stimulated Cats (High Frequency)						
K596	6 wks	7 wks	25-100	37 wks	SP Behavior	44 wks.
K598	7 wks	7 wks	25-100	32 wks	SP Behavior	39 wks.
K599	7 wks	8 wks	30-120	41 wks.	300/30Hz, Beh.	49 wks.
K600	8 wks	8 wks.	30-250	37 wks.	300/30Hz, Beh.	45 wks.
Long Deafened Stimulated Cats						
K553	6.5 yrs	6.7 yrs	36-112	17 wks.	Beh.(300/30Hz)	7.0 yrs.
K556	6.8 yrs	7.0 yrs	316-562	5.5 wks.	300/30Hz	7.2 yrs.
Normal Stimulated Cats						
CH158	1.5 yrs	1.5 yrs	100-200	21 wks	300/30Hz	1.9 yrs.
K401-3	32 wks	32 wks	141-200	19 wks	300/30Hz	1.0 yrs.

Neonatally deafened/chronically stimulated animals: The first group of 4 cats are additional neonatally deafened cats chronically stimulated with protocols designed to be temporally challenging to central auditory system. These animals were implanted with an intracochlear electrode at 6-8 weeks of age. Two cats (K96, K98) initially received passive chronic stimulation (4 hrs/d, 5 d/wk) with an analogue speech processor and subsequently they were behaviorally trained to determine thresholds to long phase duration pulses (5ms/phase) at low frequencies; the two other cats (K99, K00) initially received passive stimulation with an amplitude modulated signal (300 pps carrier, 100% sinusoidal amplitude modulated at 30 Hz). In addition, during the final phase of chronic stimulation, two of the cats (K98 and K99) were trained on an amplitude modulation discrimination task (300 pps carrier, sinusoidal amplitude modulated at 30 Hz vs. 8 Hz AM) and the other two animals were "yoked" to them, in order to examine directly the effect of behavioral training vs. passive stimulation in inducing central auditory system alterations.

Long-term neonatally deafened cats: The second group of chronically stimulated cats shown in Table 1 consists of 2 neonatally deafened animals that were maintained for extended periods prior to study -- the group we call "long term deafened" cats that have very severe degeneration of the spiral ganglion and auditory nerve due to the duration of deafness. In order to explore the possible factors underlying stimulation-induced increases in temporal resolution of central auditory neurons, we have initiated a study to determine a) whether these long deafened animals can be behaviorally trained to perform the amplitude modulation discrimination task described above and b) whether chronic electrical stimulation induces increases in central temporal resolution like those seen in younger animals with less severe pathology. Unfortunately, unprecedented problems compromised protocols in both of these animals. The first cat, K55, damaged the electrode almost immediately after implantation, and reimplantation was extremely difficult due to the presence of a polypoid-like connective tissue surrounding the electrode in the scala tympani. After extensive dissection of this tissue, a new device was implanted. This animal then received stimulation exclusively in a behavioral task to determine detection thresholds for amplitude modulated signals, (300 pps/30 Hz, 500/30 and 300/8 Hz). The daily training period was approximately 30-40 minutes. Although detection thresholds were obtained for amplitude modulated signals, this cat was never able to perform the AM discrimination task (see QPR#6 of this contract), and after 17 weeks of training the final electrophysiology experiment was conducted. Subsequent dissection of the cochlea in this cat revealed that at the time of reimplantation, the electrode array had perforated the bony wall of the scala tympani at a point about 5-6 mm from the round window and electrode pair 1-2 was actually positioned within the modiolus, adjacent to the auditory nerve. The possible effect, if any, of this misplacement upon measurements of the temporal resolution of central auditory neurons in this cat is unknown.

The second long term deafened cat, K56, exhibited extremely aggressive behavior, and it was not possible to train this animal nor to extend the passive stimulation (300pps/30 Hz) for more than 26 days.

Adult deafened/chronically stimulated cats: The final group of chronically stimulated cats consists of 2 animals that were deafened and implanted as adults, after growing up with intact auditory systems and normal auditory experience during development. This group is intended to model cochlear implant subjects with adult-onset deafness, and the purpose of this study is to examine the extent of plasticity that can be induced with chronic electrical stimulation in the adult central auditory system.

2) Methods of measuring temporal resolution.

The temporal resolution of neurons in the IC was determined in all these animals during the final electrophysiological experiment by recording responses of isolated single neurons to pulse trains (0.2 msec / phase) of increasing frequencies. As described previously (Snyder et al. J. Neurophysiol. 1995, 73: 447-467) these pulse series are typically recorded beginning at 10 pps and proceeding with frequency increments of 5-10 pps until the neuron no longer responds to the sustained stimulus (although it may still exhibit an onset response). The responses are recorded in peristimulus time histograms (PSTH) and the resulting modulation transfer functions correlate the number of spikes elicited with the frequency of the stimulus. For each isolated neuron, the 6 dB cut-off frequency and the maximum cut-off frequencies were determined. The 6 dB cut-off frequency is defined as the frequency at which the number of spikes per stimulus is reduced to 50%; the maximum cut-off frequency (MAX) is the maximum frequency the neuron can follow in a synchronized manner (significance < 0.01).

3) Results in experimental groups.

Table 2 summarizes the average 6 dB and maximum cut-off frequencies for the single units of these recently studied cats. The results are shown for both the total IC including external and central nucleus and for the central nucleus (ICC) alone.

Neonatally deafened/chronically stimulated cats: It should be noted that in the final electrophysiological experiment in cat K96, the cortical recording experiment was conducted prior to the IC experiment. When the surgical exposure of the IC was performed in this animal, there was severe bleeding which resulted in a deep infarct that significantly limited the IC region in which responses were recorded. Thus, the quite low temporal resolution recorded in this cat (MAX=64 pps) may be a result of the limited sample of single units recorded in the animal.

In a second neonatally deafened / stimulated cat, K00, the subsequent histological analysis of the ears revealed the presence of intact hair cells throughout the cochlear spiral. Further inquiry revealed that this cat was a normal hearing cat that was somehow switched with a deafened littermate in the UCSF Animal Care Facility. Although no conclusion can be drawn from a single animal, it is interesting to note that the 6 dB and MAX temporal resolution values in this animal are identical to the mean for normal unstimulated cats (total IC-MAX: 100 pps; see also Fig. 3f). This finding suggests that normal auditory input from an intact ear may prevent the chronic electrical stimulation effects on temporal resolution, and maintain more normal temporal response patterns in the IC. (Because of these problems, the data from both K96 and K00 will be excluded from further analyses of group data for the neonatally deafened / chronically stimulated cats.)

Table 2

Cat Number	Stimulation History	Mean Cut-off Frequency (pps)			
		Total IC (external and central)		Central Nucleus Only	
		6 dB	Maximum	6 dB	Maximum
Neonatally Deafened / Stimulated Animals					
K96*	SP Behavior	43	64	45	57
K98	SP Behavior	41	75	42	76
K99	300/30Hz Beh	69	172	72	180
K104**	300/30Hz Beh	50	100	53	106
Average (K98,K99)		**55**	**124**	**57**	**130**
Young Deafened / Stimulated Animals					
K55	Beh (300/30Hz)	30	54	33	58
K56	300/30Hz	53	124	57	132
Average		**42**	**89**	**45**	**95**
Adult Deafened / Stimulated Animals					
[illegible]	300/30Hz	65	132	72	156
[illegible]	300/30Hz	42	115	46	130
Average		**53**	**124**	**59**	**143**

Table 2. Summary of temporal resolution data from recently studied cats. *An infarct in the IC limited the sample of single units isolated in this cat. **Normal hearing cat that was implanted and chronically stimulated without being deafened by ototoxic drugs.

The results from the third cat in this group, K98, show an average MAX in the total IC that is markedly lower (75 pps) than the previously reported (QPR#5,1995) mean for the neonatally deafened/chronically stimulated cats (157 pps); in fact, this value is even lower than the mean previously reported for normal unstimulated animals (MAX: 99 pps; see also Fig. 3c). It is unclear what accounts for this low temporal resolution. One possibility is that it is attributable to the long period (121 days) of psychophysical testing during which this animal was trained to respond to long phase duration (5 msec/phase) signals at low frequencies (2-80 Hz). This would suggest that the effect of initial training was not reversed by the short (23 days) final training period during which the animal was trained on the 300 pps/30 Hz AM discrimination task.

The final cat in the neonatally deafened/chronically stimulated group exhibited a marked increase in temporal resolution similar to the animals previously studied after chronic stimulation with these AM signals. The mean 6 dB cut-off was 69 pps and the MAX value was 172 pps.

Long term neonatally deafened/chronically stimulated cats The two long term deafened cats show opposite results. In K55 the 6 dB cut-off frequency was 30 pps and the MAX value was 54 pps. This degradation in temporal resolution is typical of long deafened cats studied in previous experiments *without* chronic stimulation. The mean values for this group (as reported previously (QPR #5) were 48 pps for the 6 dB cut-off and 80 pps for the MAX. Recall that this cat had to be reimplanted and underwent almost all of the behavioral training with an electrode pair (2,3) one element of which was subsequently found to be mispositioned and located in the internal auditory meatus. In retrospect, the position of the electrode and the abnormal EABR waveforms obtained in this animal after reimplantation suggest that the cat may have been responding to non-auditory stimulation in the behavioral training and effectively did not receive any chronic stimulation of the auditory nerve. Alternatively, the very limited extent of auditory stimulation delivered in the behavioral training (e.g., an average of 30 suprathreshold trials/session) might have been insufficient to induce the changes in temporal resolution seen in other chronically stimulated cats. If so, then the poor temporal resolution in this cat support the findings in the long term deafened/unstimulated group. However, as mentioned previously, the effect of this misplacement upon measurements of the temporal resolution of central auditory neurons is unknown.

The second long deafened cat, K56, received less than 6 weeks of chronic stimulation because it was so aggressive and difficult to handle. Yet the IC experiment in this animal revealed a 6 dB cut-off of 57 pps and a MAX value of 132 pps. This is a markedly better temporal resolution than seen in any other long deafened animal. Previous results demonstrated a mean 6 dB cut-off of 48 and MAX value of 80 in a group of 4 animals deafened for periods of 2-4 years. Thus, the temporal resolution in K56, which is not only higher than other long term deafened cats, but also higher than *normal* cats is extremely interesting. It suggests the possibility that even relatively limited experience with chronic electrical stimulation may drive striking alterations in temporal response properties of central auditory neurons. Clearly, no conclusion can be drawn based upon the initial, diametrically opposed results in these first 2 chronically stimulated long term deafened cats. But the results in K56 suggest that further studies of long term deafened animals may be extremely interesting.

Adult deafened/chronically stimulated cats: The first two cats in the new group of prior-normal adult deafened/chronically stimulated cats (CH158, K401.3) both showed an increase in temporal resolution. As indicated in Table 2, the mean MAX values were 132 and 115 in these 2 cats, and the average for all IC units was 124 pps. This is a statistically significant increase of about 25% above the normal/unstimulated value of 98 pps (see QPR#5). Although data are quite limited with an *n* of just 2 cats studied, results so far appear to be consistent and indicate that the adult auditory system is capable of significant plasticity in temporal response properties, at least to the level of the inferior colliculus. Again, definite conclusions must await additional data.

4) Comparisons among experimental groups.

Because of the experimental problems in K96 (infarct in the IC) and K100 (not deafened) the data from both these animals will be excluded from all subsequent analyses of group data for the neonatally deafened/stimulated cats (see figs. 1 and 2). The number of animals in this group of higher frequency (>80 Hz) stimulated cats now includes a total of 10 cats, excluding data from K98 and K99.

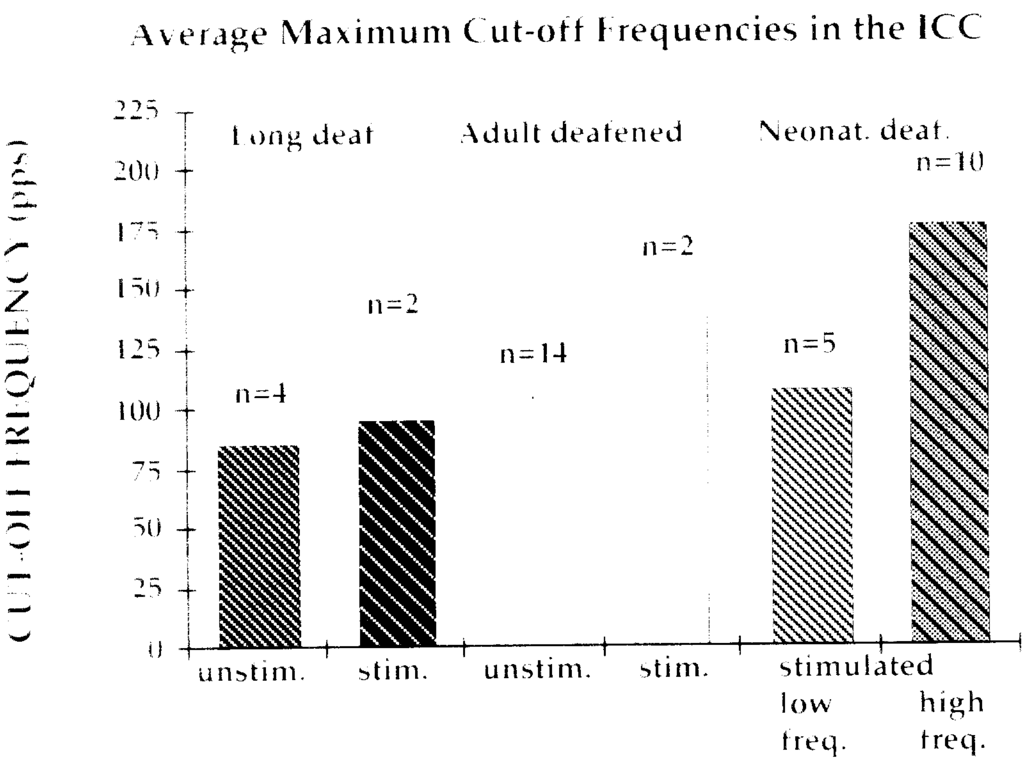

Figure 1. Summary of temporal resolution data averaged for ICC units in all animals in the experimental groups.

Figure 1 compares the mean MAX cut-off frequencies for all the experimental groups including the two new groups of adult deafened/chronically stimulated and long term deafened/chronically stimulated animals. Note that in this summary of temporal resolution data the values shown are for units in the central nucleus of the IC. Data for neurons in the external nucleus were excluded, based upon the observation that temporal resolution remains unchanged after stimulation for units in this region (see section B, below).

The long term neonatally deafened/unstimulated cats exhibit the poorest temporal resolution. The preliminary data from 2 long term deafened/stimulated cats shows a large variance reflecting the opposite results observed in these 2 animals. Our preliminary interpretation is that the cat with the mispositioned electrode, K55, did not receive effective or sufficient electrical stimulation of the central auditory system and hence exhibited the poor temporal resolution characteristic of the unstimulated long deafened group; results from the other cat suggest that stimulation can induce a relative increase in temporal resolution even in these long deafened cats, but data from additional long term deafened cats must be obtained before any firm conclusion can be drawn.

Normal unstimulated animals show an average MAX in the ICC of 112 pps, and the preliminary data from the 2 adult deafened and chronically stimulated cats show a significant increase in temporal resolution (MAX 143pps).

Finally, the group of neonatally deafened, stimulated animals is subdivided into those animals which received low frequency stimulation (≤80 Hz) and those with high frequency stimulation (>80 Hz). Following low frequency stimulation animals show a slight increase in temporal resolution compared to the normal unstimulated group, but this difference is not statistically significant. In contrast, a marked and highly significant increase in temporal resolution is demonstrated in the group of animals stimulated with higher frequency, more temporally challenging protocols (MAX 176 pps). From these preliminary data it is unclear whether the difference in temporal resolution between adult deafened (normal) stimulated and neonatally deafened / high frequency cats is related to the differences in stimulation period (average for normal: 20 weeks vs. average for stimulated: 31 weeks) or whether it indicates that ICES has a more pronounced effect upon the deafened, developing auditory system that on the adult deafened system. Again, further studies are required to resolve this issue.

B SPATIAL DISTRIBUTION OF MAXIMUM CUT-OFF FREQUENCIES WITHIN THE INFERIOR COLLICULUS

In our IC experiments, the surgical exposure allows visualization of the entire dorsolateral surface of the IC. The trajectory of the recording electrode is in the coronal plane, tilted off the sagittal plane by 45°, so that the electrode is introduced at the dorsolateral surface of the IC and advances toward its ventromedial boundary. This standard trajectory ensures that penetrations are perpendicular to the IC isofrequency laminae, so that penetration depth corresponds to relative characteristic frequency, with low frequencies represented most superficially within the central nucleus of the IC and progressively higher frequencies at progressively deeper sites.

One question that arose about the temporal resolution data was whether chronic stimulation altered responses of the whole population of IC neurons, or alternatively, for example, does stimulation alter phase locking of neurons only in the high frequency regions of the IC — neurons which normally encode higher frequency auditory information. Another hypothesis would be that the neurons most sensitive (lowest threshold) to the chronic ICES might be *selectively* effected by the stimulation, whereas the remainder of the neuronal population would remain unaltered in temporal resolution.

To address this question, additional analyses of the temporal data were performed to examine the MAX frequencies of single units as a function of the IC penetration depth (distance along the CF gradient). Figure 2 shows this analysis for the following groups of animals: long deafened unstimulated cats, normal unstimulated, and both low- and the high-frequency stimulated cats. Because of the limited number of animals and therefore insufficient sample of single units, the groups of the normal stimulated and long deafened stimulated cats are not included in this graph.

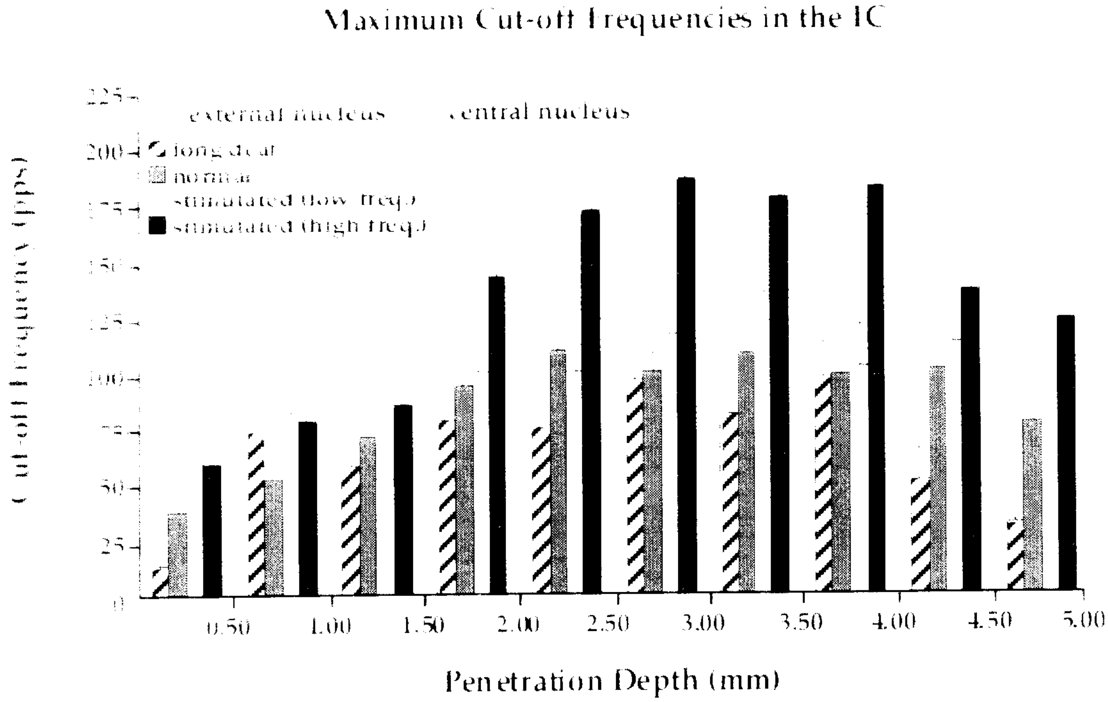

Figure 2. Summary of distribution of MAX frequencies as a function of IC depth (relative to [illegible] CF) in the 4 experimental groups for which sufficient data are in hand.

The dashed line in Figure 2 indicates the border between the external and central nucleus of the IC. The data reveal that there are no significant differences among any of the groups in temporal resolution of neurons within the external nucleus. Even high frequency chronic electrical stimulation has no significant effect on the temporal resolution of this population. In contrast, in the central nucleus we see an increase of temporal resolution for all groups, which is more pronounced for the stimulated and especially for the high frequency stimulated cats. Furthermore, the cut-off frequencies for the groups of the long deafened unstimulated, the normal unstimulated and the low frequency stimulated cats exhibit a relatively smooth and flat distribution across the central nucleus, whereas the temporal resolution of the high frequency stimulated animals shows a broad peak in the area between 2.5 and 4 mm. Thus, the gradient of temporal resolution apparently does not correlate with the tonotopic gradient: that is, the high frequency region, the deepest sector of the IC, does not have the highest temporal resolution. Instead, chronic electrical stimulation results in increased temporal resolution throughout the ICC, with a maximum effect seen in an area near the center of the ICC.

This area of highest temporal resolution can be even more distinct when these MAX distribution data are plotted for individual cats from the high frequency stimulation group. Figures 3a-d (following page) show the MAX-distribution for 4 high frequency stimulated animals compared to the average of normal unstimulated animals. While the normal cats again show a flat distribution of MAX along the IC, each of the high frequency stimulated animals shows a specific area of highest temporal resolution. The arrow in each graph shows the average position of the spatial tuning curve tip for that individual

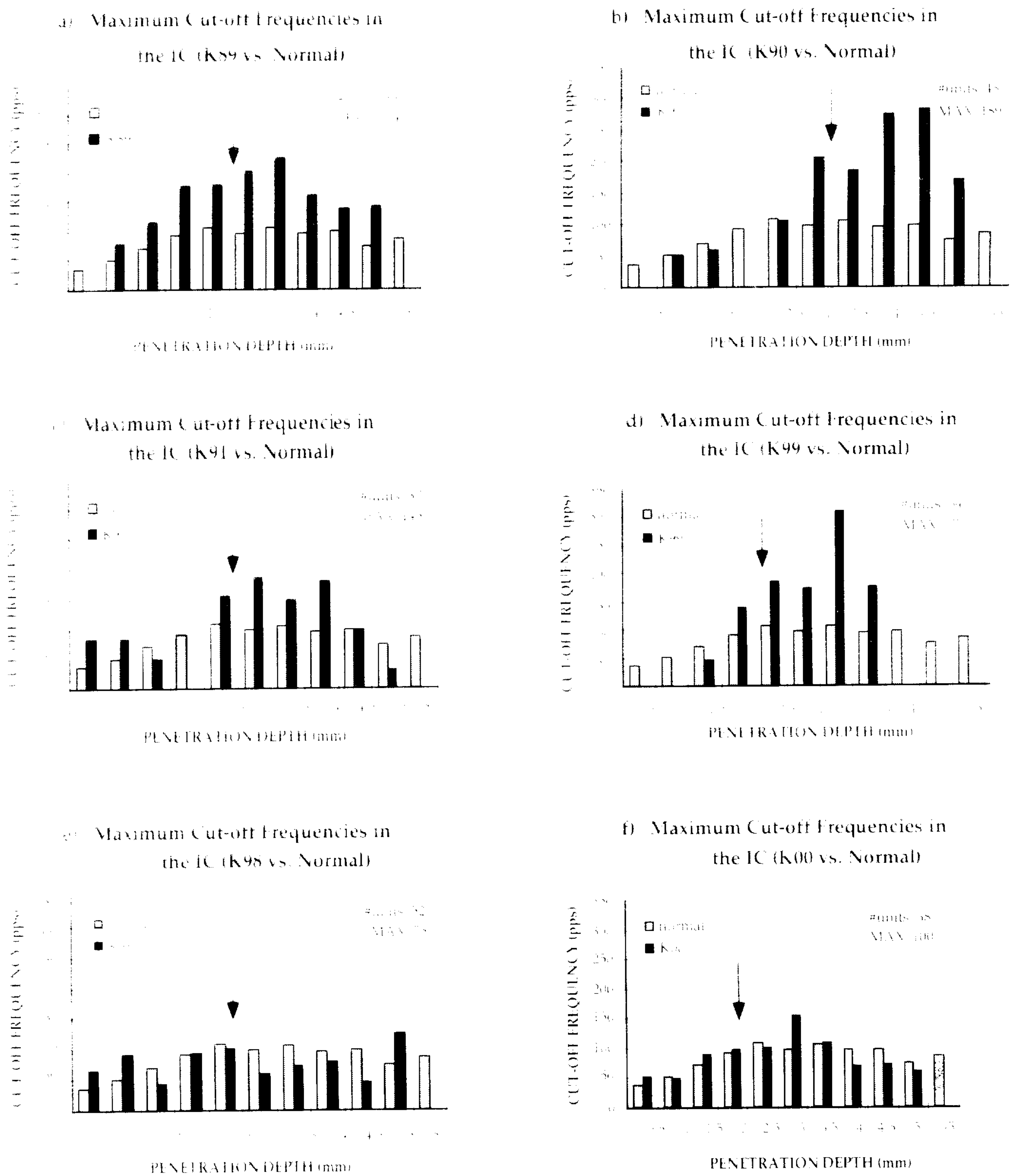

Figure 3. Spatial distribution of the maximum cut-off frequencies of single units in the IC of indiviual cats in the high frequency stimulation group, compared to the average of normal unstimulated animals. The total number of neurons isolated and the average MAX value for the animal are shown in each graph. Arrows indicate the ideal position of the lowest threshold for ICES with the chronically stimulated electrodes.

cat. This represents the location of maximum sensitivity to the chronic ICES delivered by electrode pair 1 2. Apparently there is no clear relationship between this location and the region of *maximum* temporal resolution, although in all cases it lies within the area of *increased* temporal resolution.

In Fig. 3e results for the stimulated cat K98 are plotted. The distribution of MAX is relatively flat and the temporal resolution is below the average of normal unstimulated cats suggesting that the results from this cat are not representative of stimulated animals, as discussed previously.

In Fig. 3f the MAX distribution of the normal hearing but chronically stimulated cat K60 is plotted. This distribution is very similar to the average of normal unstimulated animals, indicating, as mentioned above that intracochlear electrical stimulation does not significantly alter the temporal resolution capacity of animals with normal hearing. This suggests a dominance of the unilateral normal acoustic stimulation over the electrical stimulation.

Fig. 4 demonstrates the large individual differences in the distribution of the temporal resolution of K55 and K56. While the distribution of K55 is flat and below the average of normal unstimulated animals, the temporal resolution of K56 is significantly increased above normal with a peak area around 2.5-4 mm. As discussed above, further studies are necessary to provide a basis for final interpretation of these interesting but disparate results.

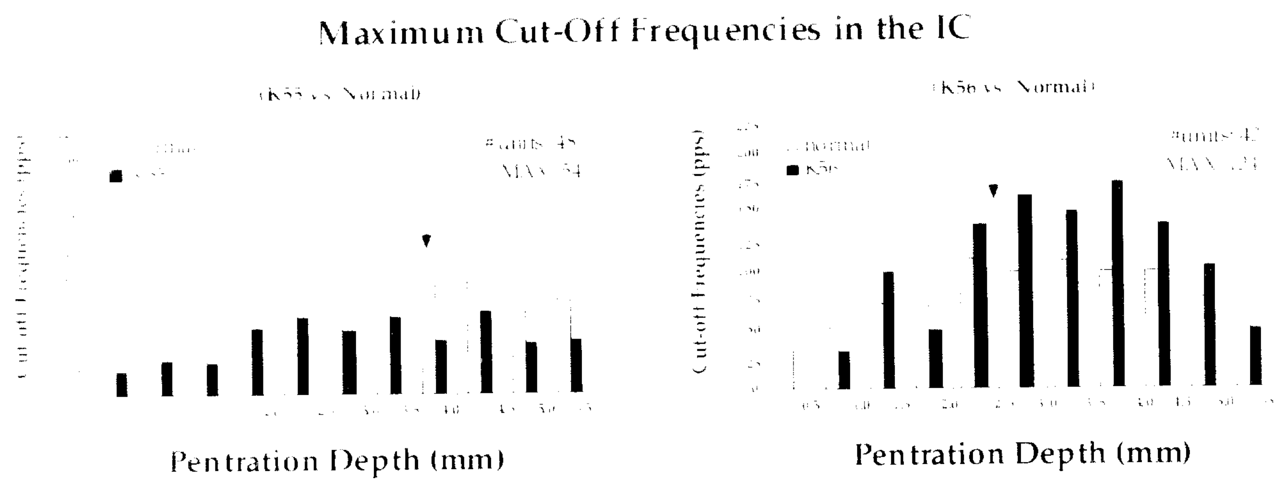

Figure 4. Distribution of MAX frequencies in the IC for the two long deafened/chronically stimulated cats as compared to the average values for the adult deafened, unstimulated group. The total number of neurons isolated and the average MAX value for each animal are shown. Arrows indicate the mean position of the lowest threshold for ICES with the chronically stimulated electrodes. Note that scale bars are different from Fig. 3.

Finally, fig. 5 shows the MAX distribution of CH158 and K401.3, the adult deafened/chronically stimulated cats. The data from both these animals again show the effect of high frequency stimulation with a significant increase in temporal resolution in the ICC and a peak area in the central ICC. It should be noted that the marked peak in CH158 is an artifact of sampling -- only a single neuron was isolated in the 2-2.5 mm region of this cat. Obviously the number of single units per bin is often limited in data from individual cats.

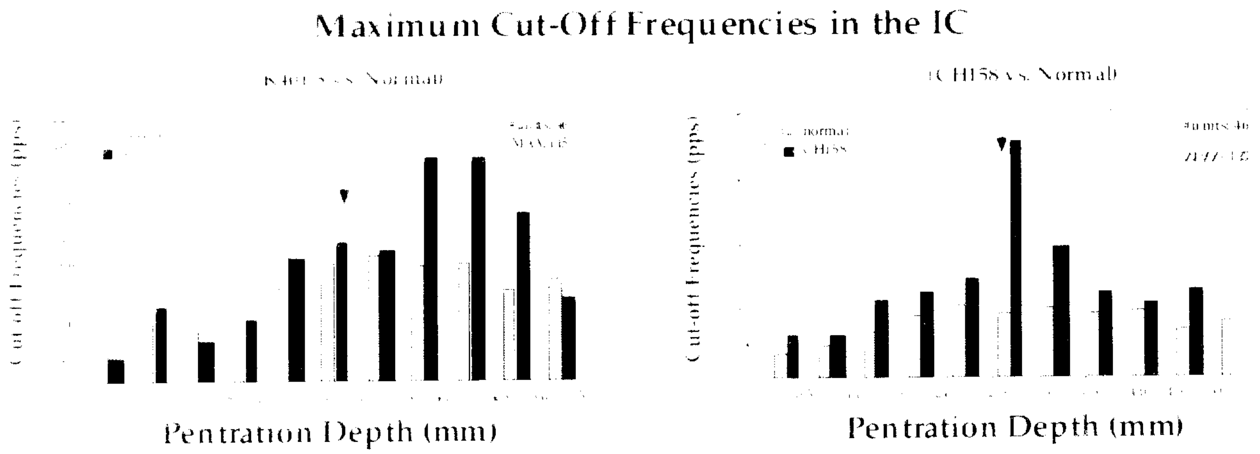

Figure 5. Distribution of MAX frequencies in the IC for the two adult deafened/chronically stimulated cats as compared to the average values for the adult deafened, unstimulated group. The total number of neurons isolated and the average MAX value are shown for each animal. Arrows indicate the mean position of the lowest threshold for ICES with the chronically stimulated electrodes. Note that the scale bars are different for the 2 cats.

Summary:

Chronic electrical stimulation profoundly alters the temporal resolution capacities of ICC neurons also in the adult auditory system.

Chronic stimulation has no significant effect on the temporal resolution of neurons in the external nucleus of the IC.

The gradient of temporal resolution in the ICC after chronic high frequency stimulation does not correlate with the tonotopic gradient.

Work Planned for the Next Quarter

1. One more adult deafened cats has been implanted and a second will be implanted during the next quarter using the new model UCSF cat electrode. These animals will undergo chronic stimulation using a temporally challenging (but passive and invariant) electrical stimulus (300 pps amplitude modulated with a 30 Hz sinusoid). Studies of spiral ganglion cell survival and cochlear nucleus morphology in the previously studied adult deafened cats will be completed during the next quarter. These data should indicate 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) Three neonatally deafened kittens have been implanted and are currently undergoing chronic electrical stimulation. Chronic stimulation these animals was initiated on two independent bipolar channels. Behavioral training now has been initiated to determine the behavioral thresholds to the chronic amplitude modulation signal. At least 2 of these animals will be studied during the next quarter, and two additional kittens will be implanted in the coming quarter.

3) Analyses of EABR and CAP data will continue during the next quarter. An update on progress in these noninvasive studies of temporal resolution is planned for the next Quarterly Progress Report.

Note: The work reported in the following two abtracts was supported by this contract. Both abstracts have been accepted for presentation at the ARO conference in February, 1997.

[illegible]

[illegible] temporal and spatial [illegible] in the inferior colliculus [illegible] deafened [illegible]

[illegible] nyder, P.A. Leake, [illegible]

[illegible] ...ences in the temporal and spatial resolution of neural [illegible] intracochlear electrical stimulation were [illegible] in deafened cats. Modulation transfer functions of [illegible] neurons in the inferior colliculus (IC) were quantitatively [illegible] in three animal models of cochlear implant use: 1) prior [illegible] deafened adults, 2) neonatally deafened, [illegible] adults, and 3) neonatally deafened chronically [illegible] adults.

[illegible] average temporal resolution (mean maximum cut-off frequency [illegible]) of neurons in the external nucleus of the IC was [illegible] different in any of these groups. In contrast, [illegible] temporal resolution in the central nucleus (ICC) was [illegible] increased in the chronically stimulated group. This [illegible] was related to the temporal characteristics of the chronic [illegible] from cats stimulated with high frequency (>80 [illegible]) showed a marked increase in temporal resolution (54% [illegible]), whereas cats stimulated with low frequency signals [illegible] were not significantly different from normal. Moreover, in [illegible] cats the gradient of temporal resolution in the ICC did [illegible] with the tonotopic gradient. Rather, the region of [illegible] temporal resolution corresponded to the region of highest [illegible] the chronically activated electrode pair.

[illegible] of the spatial distribution of response thresholds [illegible] significant changes in the tonotopic organization of [illegible] neonatal deafening and complete auditory deprivation [illegible] as compared to normal animals. In contrast, both [illegible] stimulation (up to 1 yr.) and long term (2-6 yrs.) [illegible] deprivation resulted in a significant decrease in the [illegible] of the electrical signal.

[illegible] results suggest that individual differences and gradual [illegible] in speech performance in implant subjects may be partly [illegible] to similar chronic and plastic changes in the temporal and spatial representations of signals in the IC.

[illegible] NIH contract N01-DC-4-2143 and DFG Vo 640/1-1