Effects of Remaining Hair Cells on Cochlear Implant Function

10th Quarterly Progress Report

Neural Prosthesis Program
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1. Summary of Activities in This Quarter

During the tenth quarter of this contract (October 1 - December 31, 2004), we accomplished the following:

1. We attended the Neural Interfaces Workshop (November 15-17, 2004, Bethesda, MD) and presented a report on the progress of our contract work.

2. Two manuscripts that describe work directly supported by the Neural Prosthesis Program were published in Hearing Research. The first (Miller et al., 2004a) described a newly observed phenomenon of antidromic action potentials elicited by prosthetic (electric) stimulation of the cochlea. This study improves our understanding of the electrically-evoked compound action potential, which is used as a measure of the auditory nerve activity both in clinics and in animal research. The second report (Miller et al., 2004b) detailed our experimental efforts using the Michigan thin-film electrodes within the auditory nerve.

3. A manuscript accepted for publication now appears in the online version of Hearing Research (Nourski et al., in press).

4. We performed three acute guinea pig experiments that addressed binaural interactions in response to acoustic and electric stimulation using recordings from the central nucleus of the inferior colliculus.

5. We performed two acute cat experiments that addressed the auditory nerve single-unit and ECAP responses to combined acoustic and electric stimuli. One of the two preparations yielded little usable single fiber data due to unstable acoustic sensitivity, while the other one provided the largest yield, to date, of single-fiber acoustic-electric interaction data. Analysis of data obtained in that experiment is ongoing and will be reported later.

6. We performed four acute guinea pig experiments that examined masking and recovery of the ECAP in presence of acoustic and electric maskers. The present report summarizes preliminary results of that work.

7. We welcomed Jihwan Woo to our research group in November 2004. Mr. Woo is a PhD student in biomedical engineering from Hanyang University in Seoul, Korea. He will be spending approximately 6 months in the laboratory and will be contributing to our efforts on the contract.

2. Focus Topic: Simultaneous and forward masking of the ECAP by acoustic noise and high-rate electric pulse trains

2.1. Introduction

Our recent effort has focused on examining how auditory nerve responses evoked by acoustic and electric stimuli interact with each other. We use both gross-potential (i.e., the electrically-evoked compound action potential, or ECAP) and single-fiber measures in complementary ways to examine population and fiber-specific response properties, respectively. Work reported in QPRs 3, 5, and 7 examined how acoustic stimulation alters the ECAP response. As described in those reports, we observed both simultaneous and post-stimulatory effects on ECAPs evoked by 250 pulses/s electric pulse trains. Decreased ECAP amplitudes were observed both during and after presentation of a wideband acoustic noise stimulus. We hypothesized that this decrease was associated with desynchronizing and refractory effects induced by the noise. Post-stimulatory effects (i.e., recovery) were deemed to be due to processes associated with both adaptation to and recovery from the acoustic stimulus.

In the work first described in QPR 7, we employed a new method of evoking ECAP responses subject to acoustic masking. This paradigm employed very low-rate (5 pulses/s) electric probe pulses to avoid adaptation effects induced by the electric pulse train, as prior research has shown that higher-rate trains can alter the nerve's responsiveness (Haenggeli et al., 1998; Matsuoka et al., 2000; Hu et al., 2003). Our preliminary results obtained using this paradigm are generally consistent with our earlier data obtained with a faster, 250 pulses/s, train.

While our previous work has examined interactions caused by acoustic and electric stimuli, a basic issue that has not been addressed is the extent to which acoustic and electric adaptors have similar effects on auditory nerve responsiveness. Comparisons of the effects of acoustic and electric maskers on the ECAP are logical extensions of our prior work, as they will provide insight on differences and similarities in the physiologic mechanisms at play with each of these stimuli. Such work may be particularly valuable in modeling neural responses to arbitrary combinations of acoustic and electric stimuli.

Such comparisons are the focus of this report. As in prior work, we employed maskers in order to assess both simultaneous and forward masking. We also present a summary of masking effects of acoustic noise on ECAP across the group of subjects studied to date. In addition, we provide a preliminary within-subject comparison of the masking effects of acoustic and electric stimuli on the auditory nerve ECAP. The variable parameters used in this study were the levels of masker and probe stimuli.

2.2. Materials and methods

Adult guinea pigs with normal hearing were used in acute experimental sessions. Animal preparation and surgical methods are described elsewhere (Nourski et al., in press). Briefly, after inducing the surgical level of anesthesia, the cochlea and the auditory nerve trunk were exposed. A Pt/Ir wire electrode was inserted into the scala tympani via a cochleostomy for intracochlear monopolar electric stimulation. In the data sets reported here, this insertion typically resulted in a decrease in acoustic sensitivity of 10 dB or less.

Stimuli were digitally generated by a 16-bit digital-to-analog converter (100,000 samples/s), controlled by custom-written software. Acoustic clicks were produced by driving an earphone with 100 μs/phase biphasic electric pulses, presented using an interstimulus interval (ISI) of 30 ms. Broadband acoustic noise, presented in 400 ms bursts, was used as a masker in experiments that examined combined acoustic-electric stimulation. Sound pressure in the ear canal was monitored during each experiment using a probe-microphone system described in QPR #4. Overall sound levels of the noise stimulus were determined by accounting for the system frequency response.

Cathodic-first biphasic (40 μs/phase) electric pulses were used as probe stimuli. The pulses were presented with an interpulse interval (IPI) of 200 ms to avoid adaptation to the electric probe stimulus. In the experiments that examined masking of the ECAP by electric stimulation, we used high-rate electric pulse trains (IPI 0.2 ms, duration 400 ms). Both masker types (acoustic and electric) were presented with intervals of 1000-1600 ms to minimize auditory fatigue (the ISI increased with masker stimulus intensity).

Auditory nerve evoked potentials were recorded using a ball electrode positioned on the auditory nerve trunk. The responses were amplified (gain=10x), low-pass filtered at 30 kHz, and digitized by a 16-bit converter (sampling rate 50 kHz) for subsequent analysis. Acoustic sensitivity was assessed by measuring acoustically evoked compound action potentials (ACAP) in response to click stimuli and determining a threshold response level using visual criterion. ECAP response growth functions were obtained by presenting alternating-polarity biphasic electric pulses (duration 40 μs per phase, IPI 30 ms) at different levels. ACAP thresholds and ECAP growth functions were obtained repeatedly during each experiment to monitor the stability of the animal preparation.

The experimental paradigms used in the present study are summarized in Figure 1. The stimulus paradigm used to examine masking effects of acoustic noise on ECAP (Figure 1A) was similar to that introduced in QPR #7. A series of 15 *masker + probe* stimuli was presented with the electric probe onset being delayed relative to the masker. This delay, Δt, increased from 0 to 150 ms in approximately logarithmic steps (Δt = 0, 1, 2, 3, 4, 5, 7, 10, 15, 20, 35, 50, 70, 100, 150 ms) across the 15 stimuli. The 15 masker + probe conditions were presented under computer control to obtain 15 sets of time-averaged responses. In addition, a 16th *probe-alone* condition was presented to provide a comparison and monitor the stability of the animal preparation.

In the experiments that examined the effects of masking by high-rate electric stimulation on the ECAP, a similar approach was used (Figure 1B). Electric pulse train maskers differed from acoustic in that there could be significant stimulus artifact as well as ECAP response to individual masker pulses. For this reason, we chose to subtract the measured response to the masker pulse train alone from that to the masker plus probe in order to extract the response. Consequently, the sequence of probe delays was the same as in the case of acoustic masker, except for the first stimulus, where Δt was set at 400 ms. This provided us a condition in which there was no overlap between the masker and the probe pulses. It was used as a template to obtain responses to the probes in stimuli 2 through 15.

We note further that the probe stimulus presented during the masker train was synchronous with a masker pulse timing, such that a probe pulse simply replaced a masker pulse rather than adding to it. Thus the probe pulse presented during the masker had the same amplitude as the probe pulse presented after masker offset as illustrated in Figure 1. However, in cases when the intensity of the masker stimulus was equal to or exceeded that of the probe stimulus, subtraction technique to eliminate stimulus artifact was ineffective. As a result, the response to probe could not be determined with simultaneous masking for those stimulus conditions.

The amplitudes of ECAP responses were analyzed by measuring their amplitudes using custom-designed software. As we have previously done, the ECAP amplitudes of the *masker + probe* condition were subtracted from those of the *probe-only* condition to evaluate the absolute change in response amplitude and thus demonstrate the net effect of the masker. Decreases in ECAP amplitudes in response to the probe were plotted as functions of time after the masker stimulus onset.

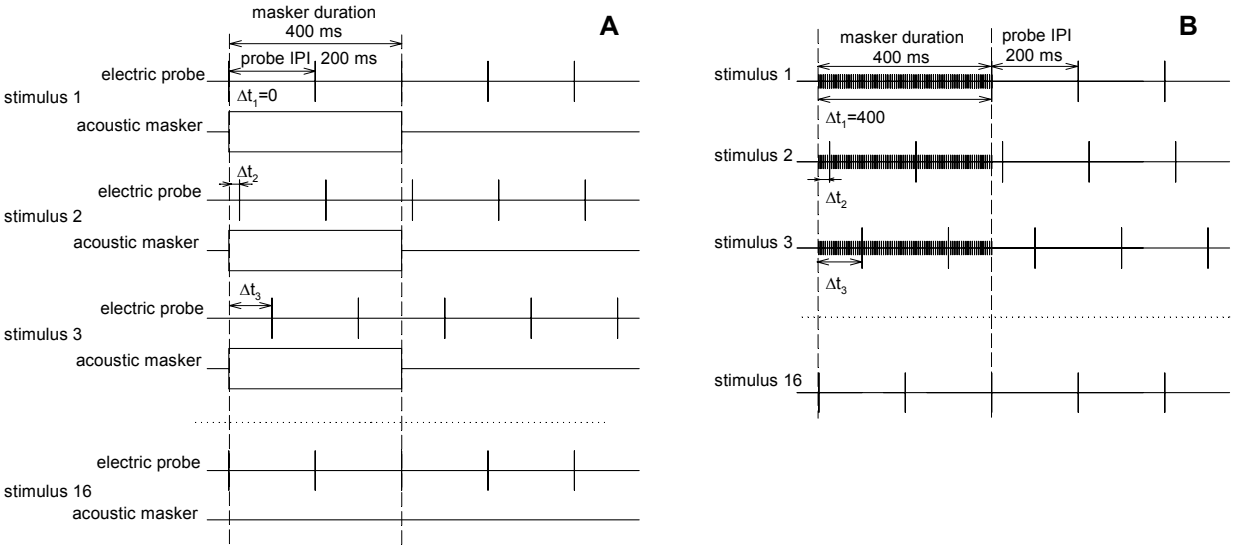

Figure 1. Schematic of stimulus presentation paradigms. A: Electric probe and acoustic masker. B: Electric probe and electric masker. Rectangles indicate bursts of noise; vertical bars indicate electric pulses, dashed lines indicate onset and offset of the masker stimulus. IPI, interpulse interval; Δt, pulse onset delay time. See text for additional details.

2.3. Results

Figure 2 demonstrates an example of simultaneous and post-stimulatory effects of a high-rate (5000 pps) electric pulse-train masker on the ECAP amplitude in response to probe stimuli of four different intensities. The amount of masking is evaluated as the difference between the ECAP amplitude in response to the probe stimulus only (i.e., unmasked control) and the ECAP recorded in the presence of the electric pulse train masker. The decrease in ECAP amplitude is plotted as a function of time after the masker stimulus onset.

In the top panel of Figure 2, the intensities of the probe and the masker stimuli are equal. Note that we did not evaluate simultaneous masking for that condition, as the response waveform subtraction method did not allow the extraction of the response to the probe. In general, the time course of changes in ECAP amplitude illustrated in Figure 2 exhibits the same features as the effects of an acoustic masker on ECAP (see QPR #7). Specifically, simultaneous masking features an onset effect and a partial recovery of the ECAP to a steady state. Post-stimulatory recovery is not instantaneous and can exhibit a non-monotonic time course, as is particularly evident for I_p=0.73 mA. We also note that a fixed masker level has a greater post-stimulatory effect on the ECAP in response to a lower-level probe stimulus. The recovery of the ECAP amplitude following the masker offset occurs faster for relatively high probe levels.

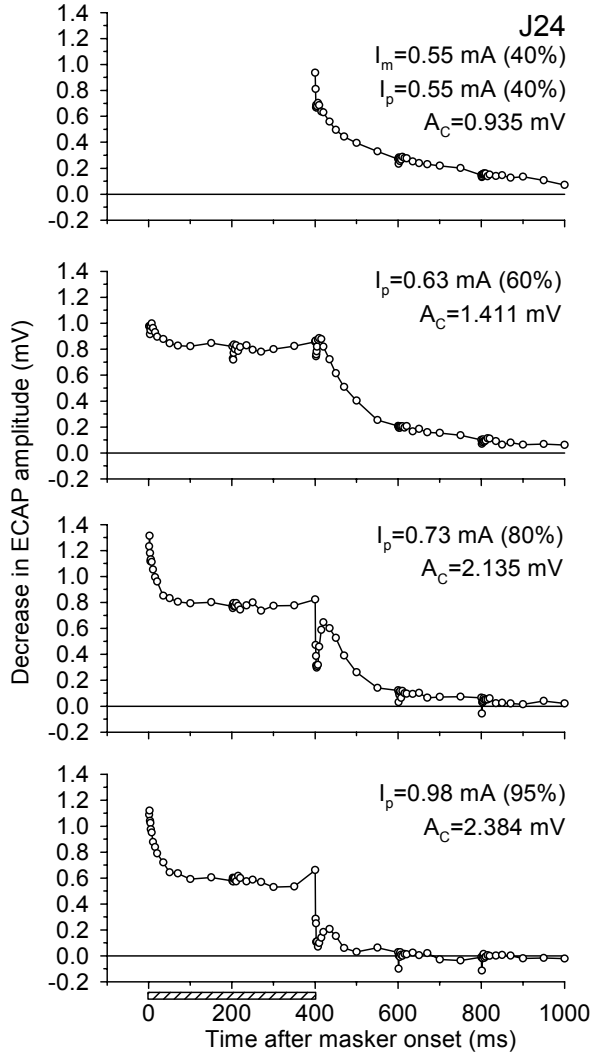

Figure 2. Simultaneous and post-stimulatory effects of an electric pulse-train masker (stimulation rate 5000 pps) on the ECAP response to electric probes of different intensities. Decreases in ECAP amplitude (ECAP amplitude measured in the presence of the masker stimulus subtracted from ECAP amplitude in response to the probe alone) are plotted as functions of time after masker onset. I_m, electric masker stimulus current (0.55 mA); I_p, electric probe stimulus current; A_c, ECAP amplitude to the probe alone (control). Horizontal bars indicate presentation time of the masker. Percentage numbers in parentheses indicate normalized ECAP amplitude in response to a particular stimulus current (relative to saturation of the ECAP growth function).

Figure 3 shows an example of the effects of a high-rate electric masker presented at different intensities on the ECAP evoked by a fixed-level probe pulse. The amount of masking (both following the masker onset and the steady-state effect) increases with masker intensity. When the pulse train was presented at the lowest intensity (see Figure 3, top panel), it produced a negative simultaneous masking effect on ECAP. This corresponds to an enhancement in ECAP amplitude compared to the control. It is a novel finding, and it has not been observed in cases of acoustic masking. When presented at higher levels (Figure 3; I_m=0.35, 0.45, 0.55 mA), the masker produced a transient post-stimulatory enhancement of the ECAP. In this example, the probe stimulus was presented at a high level, which resulted in little post-stimulatory masking compared with other data.

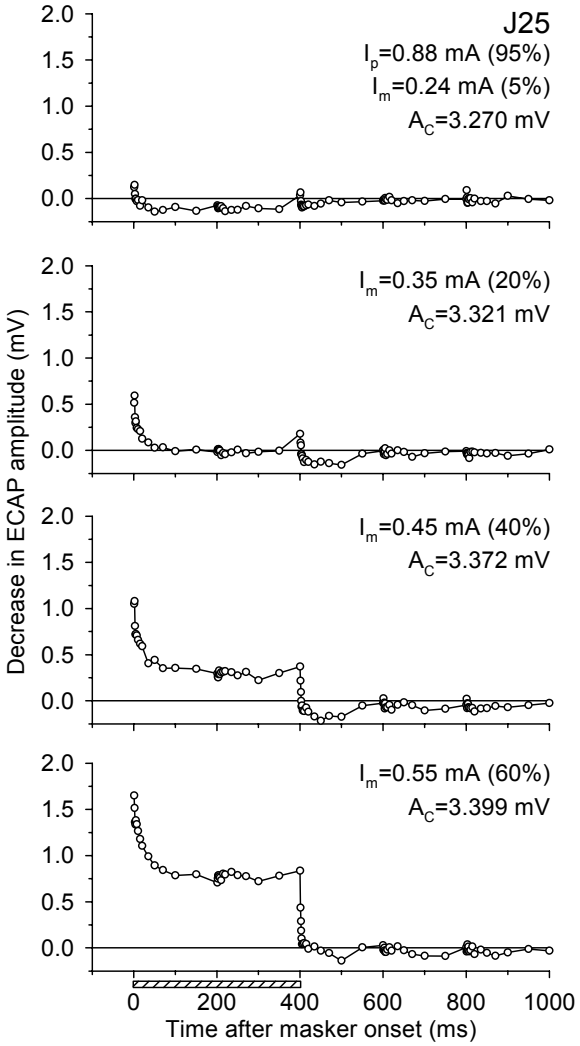

Figure 3. Simultaneous and post-stimulatory effects of electric pulse-train maskers of different intensities (stimulation rate 5000 pps) on the ECAP response to a high-intensity electric probe. Decreases in ECAP amplitude (ECAP amplitude measured in the presence of the masker stimulus subtracted from ECAP amplitude in response to the probe alone) are plotted as functions of time after masker onset. I_m, electric masker stimulus current; I_p, electric probe stimulus current (0.88 mA); A_c, ECAP amplitude to the probe alone (control). Horizontal bars indicate presentation time of the masker. Percentage numbers in parentheses indicate normalized ECAP amplitude in response to a particular stimulus current (relative to saturation of the ECAP growth function).

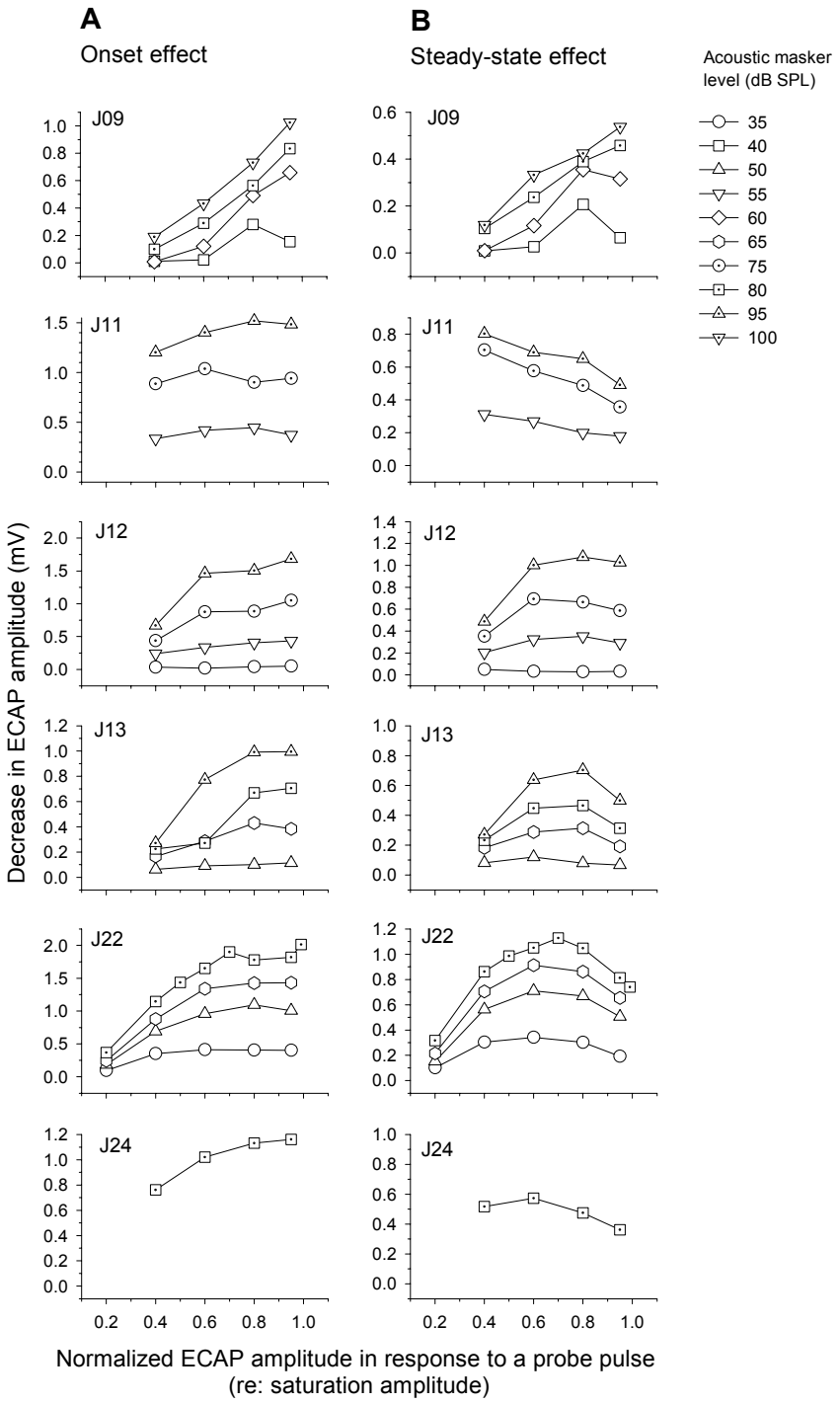

Figure 4. Summary of data from six subjects demonstrating onset (A) and steady-state (B) effects of a broadband acoustic noise masker on the auditory nerve response to an electric probe. A: Maximum decreases in ECAP amplitude following masker onset (relative to the probe-only control) are plotted as functions of normalized ECAP amplitude (relative to saturation of the ECAP growth function). B: Average decreases in ECAP amplitude within a time window of 200 to 350 ms following masker onset (relative to the probe-only control) are plotted as functions of normalized ECAP amplitude (relative to saturation of the ECAP growth function).

One of the goals of the present report was to compare the masking effects of acoustic and electric stimuli on the auditory nerve ECAP. To address this, we sought quantitative descriptions of these effects across stimulus parameters for both acoustic and electric maskers. Figure 4 summarizes the onset (panel A) and steady-state (panel B) effects for six subjects over a range of acoustic masker and electric probe stimulus levels. Here, the onset effect was measured as the maximum decrease in ECAP amplitude that occurred following the onset of the masker. The steady-state effect of noise was computed as an average decrease in ECAP amplitude over a time window of 200 through 350 ms following noise onset. Masker duration was 400 ms in all experiments. Note that in this figure, the probe stimulus level is presented as "normalized ECAP response amplitude", i.e., the response to an electric stimulus of a particular level relative to saturated (maximum) ECAP amplitude. This was done to facilitate comparisons across subjects, as they exhibited variations in absolute sensitivity that are of secondary concern.

It can be observed that the maximum amount of masking (Figure 4A) generally increases with masker and probe stimulus levels. This is consistent with our earlier results obtained using 250 pps electric pulse trains as probe stimuli (QPR #5; Nourski et al., in press). The steady-state masking effect (Figure 4B), however, tends to decrease at higher probe stimulus intensities or even across the entire range of probe levels (subject J11).

Figure 5 presents a summary of data on simultaneous effects of an electric pulse-train masker on the response evoked by an electric probe. As in Figure 4, the electric stimulus intensities are expressed here in terms of normalized response amplitude. Note that although the amount of masking clearly increases with the masker level, the effect of probe intensity is less obvious across the range of stimulus levels tested. The increase in the maximum masking effect with probe level (Figure 5A) is moderate, whereas the steady-state effect exhibits a decrease across the entire range of probe levels for a particular masker intensity (Figure 5B).

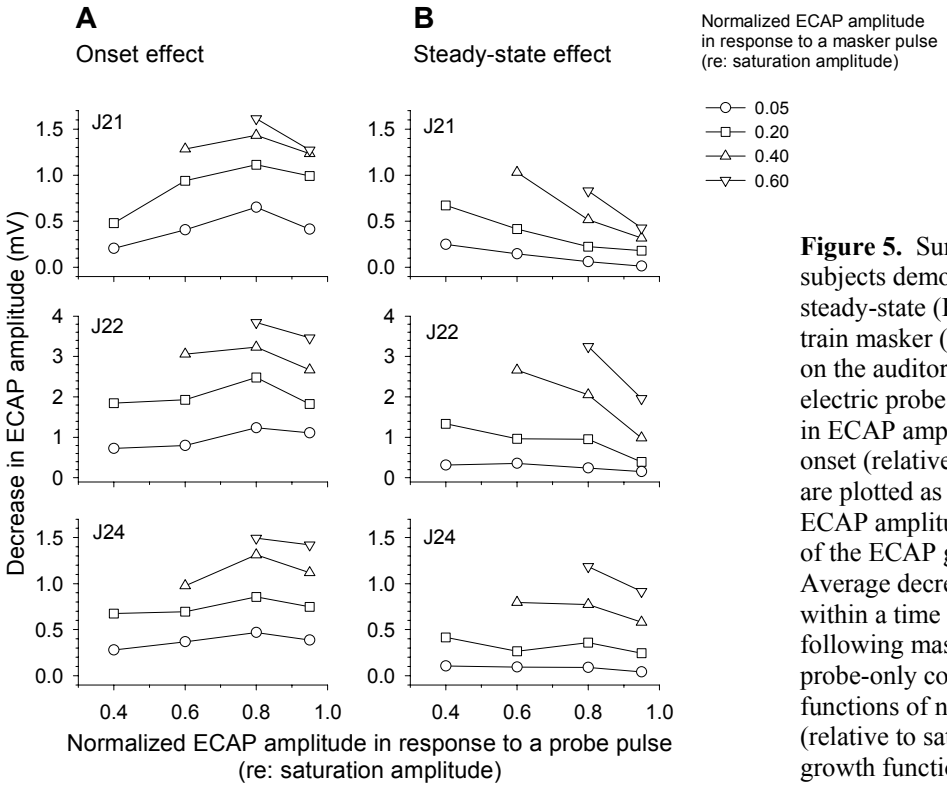

Figure 5. Summary of data from three subjects demonstrating onset (A) and steady-state (B) effects of electric pulse train masker (stimulation rate 5000 pps) on the auditory nerve response to an electric probe. A: Maximum decreases in ECAP amplitude following masker onset (relative to the probe-only control) are plotted as functions of normalized ECAP amplitude (relative to saturation of the ECAP growth function). B: Average decreases in ECAP amplitude within a time window of 200 to 350 ms following masker onset (relative to the probe-only control) are plotted as functions of normalized ECAP amplitude (relative to saturation of the ECAP growth function).

As noted earlier, both acoustic noise and high-rate electric pulse trains produced effects on the ECAP that followed a similar time course. We therefore sought to determine whether the time course of simultaneous and post-stimulatory effects could be described by the same mathematical models for both types of maskers. Based on our earlier acoustic-electric interaction data (QPR #5), we described post-onset partial recovery of the ECAP (simultaneous effects) by an exponential function with two decaying components:

$$A_{s(t)} = A_{s1}e^{(-(t-t_{s0})/\tau_{s1})} + A_{s2}e^{(-(t-t_{s0})/\tau_{s2})} + A_{ss}$$

where
A_s - decrease in ECAP amplitude;
t - time after masker onset;
A_{s1}, A_{s2} – magnitude coefficients; ($A_{s1}>0$, $A_{s2}>0$);
t_{s0} – peri-stimulatory recovery onset time;
τ_{s1}, τ_{s2} – rapid and short-term recovery time constant, respectively (*i.e.*, $\tau_1<\tau_2$);
A_{ss} - steady-state decrease in ECAP amplitude.

Recovery from masking (post-stimulatory effects), which often had a non-monotonic time-course, was described by a three-component exponential function with two decaying and one rising component:

$$A_{p(t)} = A_{p1}e^{(-(t-t_{p0})/\tau_{p1})} + A_{p_2}e^{(-(t-t_{p0})/\tau_{p2})} - A_{p_3}e^{(-(t-t_{p0})/\tau_{p3})}$$

where
A_p - post-offset decrease in ECAP amplitude;
t - time after masker onset;
A_{p1}, A_{p2}, A_{p3}- magnitude coefficients ($A_{p1}>0$, $A_{p2}>0$, $A_{p3}>0$);
t_{p0} - post-stimulatory recovery onset time;
τ_{p1}, τ_{p2} - rapid and short-term recovery time constant, respectively (*i.e.*, $\tau_{p1}<\tau_{p2}$);
τ_{p3} - exponential rise time constant.

Examples of fits to the recovery functions are shown in Figure 6. We used the coefficient of determination, r^2, to evaluate the goodness of fit. It can be observed that, in the cases shown, the proposed models provide good fits for the time course of effects of both acoustic (Figure 6, top panel) and electric (Figure 6, bottom panel) maskers on the ECAP. In general, we note that the two-component exponential function provided adequate descriptions of simultaneous effects of acoustic and electric maskers in most of our observations. The three-component exponential function provided a good fit to the post-stimulatory data for both types of maskers in cases when the recovery followed a nonlinear time course.

Within-subject comparisons of the time constants failed to reveal any dependence on either masker or probe stimulus intensity. Analysis of data on acoustic and electric masking yielded the following time constants (in milliseconds):

Type of masker	Number of subjects	Simultaneous effect		Post-stimulatory effect		
		τ_{s1} (S.D.)	τ_{s2} (S.D.)	τ_{p1} (S.D.)	τ_{p2} (S.D.)	(S.D.)
Acoustic	6	4.47 (1.93)	98.5 (53.5)	4.59 (1.54)	112 (57.4)	5.63 (2.78)
Electric	4	1.89 (2.00)	28.8 (12.2)	2.73 (1.01)	67.1 (38.0)	13.2 (10.5)

In order to compare the mean values of time constants between acoustic and electric masking, we performed a series of t-tests. The comparisons revealed that peri- and post-stimulatory recovery time constants were significantly smaller in the case of electric stimulus-induced masking. The post-stimulatory exponential rise time constant, τ_{p3}, was significantly smaller for recovery following an acoustic masker stimulus.

Finally, we attempted to perform a direct within-subject comparison between the temporal properties of acoustic and electric masking of the electrically-evoked auditory nerve response. This was addressed by adjusting the levels of the acoustic and electric masker stimuli so they would produce approximately the same amount of initial masking. An example of a such matched-effect approach is presented in Figure 7. Here, the acoustic masker (Figure 7A) has a greater steady-state effect on the ECAP compared to the electric masker (Figure 7B). This phenomenon is associated with a faster peri-stimulatory recovery in the latter case. Also, post-stimulatory recovery occurs almost instantaneously following the offset of the electric pulse train, whereas recovery from acoustic masking features a noticeable residual effect. The amount of "matched-effect" data collected to date makes it impossible to generalize any differences at this point. However, we observe that while acoustic and electric masking of the ECAP share common temporal features, the time course of adaptation and recovery may differ quantitatively for the two types of masker stimuli.

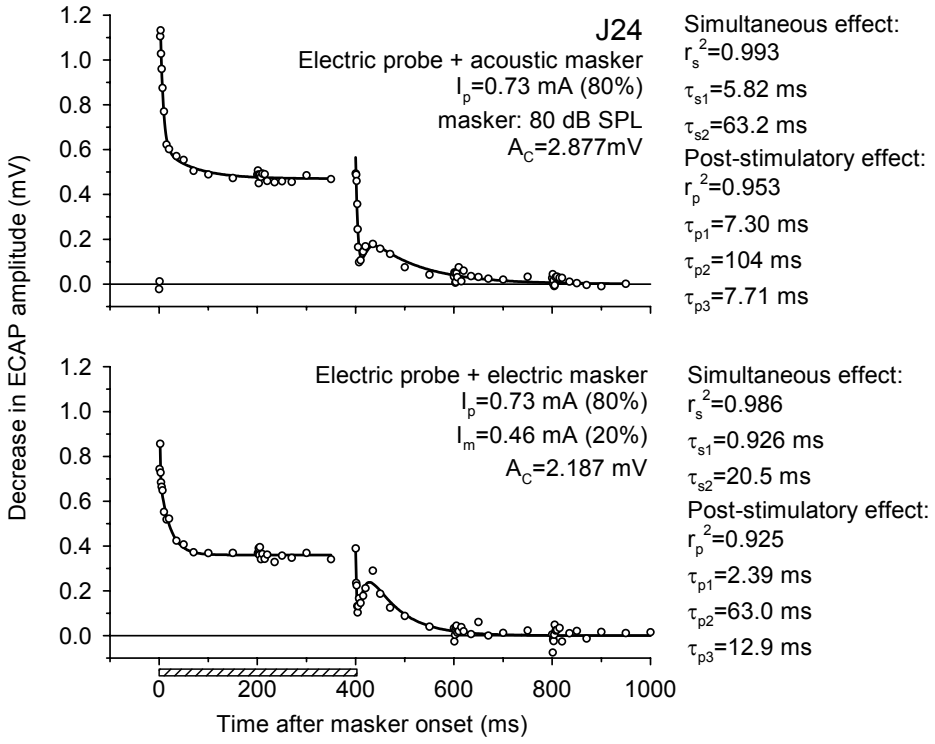

Figure 6. Exponential curve fitting of peri-stimulatory (simultaneous) and post-stimulatory ECAP recovery from masking by broadband acoustic noise (upper panel) and electric pulse train (stimulation rate 5000 pps) (lower panel). Decreases in ECAP amplitude (ECAP amplitude measured in the presence of the masker stimulus subtracted from ECAP amplitude in response to the probe alone) are plotted as functions of time after masker onset. I_p, electric probe stimulus current (0.78 mA in both cases); I_m, electric masker stimulus current; A_c, ECAP amplitude to the probe alone (control). Horizontal bars indicate presentation time of the masker. See text for the description of the models. Percentage numbers in parentheses indicate normalized ECAP amplitude in response to a particular stimulus current (relative to saturation of the ECAP growth function).

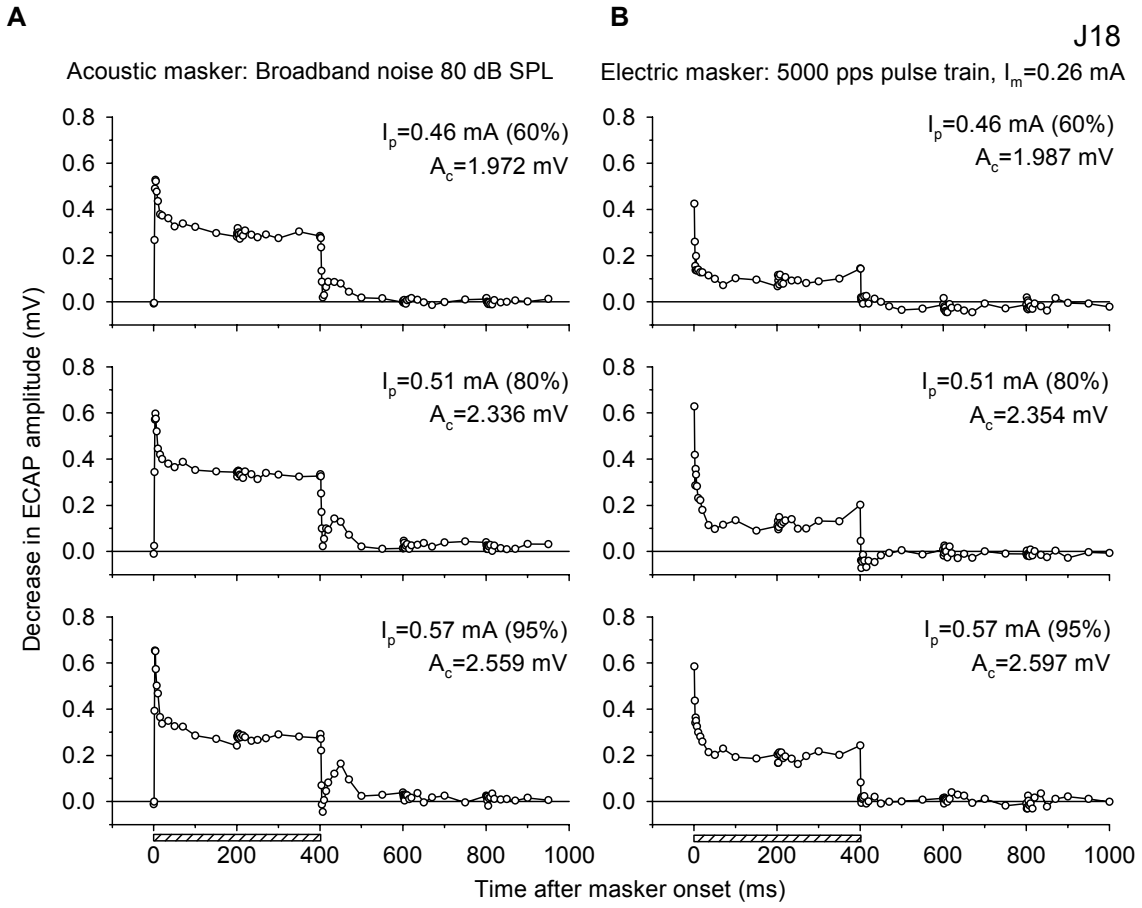

Figure 7. Within-subject comparison of masking effects of broadband acoustic noise (A) and electric pulse train (stimulation rate 5000 pps) (B) on the ECAP response to an electric probe. Decreases in ECAP amplitude (ECAP amplitude measured in the presence of the masker stimulus subtracted from ECAP amplitude in response to the probe alone) are plotted as functions of time after masker onset. I_m, electric masker stimulus current; I_p, electric probe stimulus current; A_c, ECAP amplitude to the probe alone (control). Horizontal bars indicate presentation time of the masker. Percentage numbers in parentheses indicate normalized ECAP amplitude in response to a particular stimulus current (relative to saturation of the ECAP growth function).

2.4. Discussion

The major goal of the present report was a comparison of the masking effects of acoustic and electric stimuli on the auditory nerve ECAP. To address this, we first examined effects of high-rate electric stimulation on the ECAP in a simultaneous and forward masking paradigm. We also provided an initial comparison of these effects with acoustic-electric interactions observed on the level of the auditory nerve under comparable stimulation conditions. The results indicate that the temporal pattern of ECAP masking and recovery due to acoustic stimulation can to some extent be emulated by using an electric masker stimulus instead. However, the differences in the time constants that describe ECAP recovery during and after presentation of acoustic and electric maskers may be the result of different mechanisms of excitation due to the two types of masker stimuli.

In previous reports on this contract, we have attributed the changes in ECAP amplitude during and after stimulation with acoustic noise to a combination of refractory and adaptation effects. While the refractory mechanism is associated with intrinsic properties of the neuronal membrane, adaptation in the auditory periphery can be attributed to several loci. These are: (1) hair cell-auditory neuron synapse, (2) neurotransmitter receptors at the postsynaptic membrane of the auditory neuron, and (3) voltage-gated ion channels in the membrane of the auditory nerve fiber (Eggermont, 1985; Chimento & Schreiner, 1991).

Specific mechanisms of adaptation may be difficult to distinguish on the basis of the ECAP recovery function analysis, especially as they all have comparable time courses (Eggermont, 1985; Killian et al., 1994; Moser & Beutner, 2000). However, in the case of masking of the ECAP with an electric stimulus, adaptation and recovery from adaptation are likely to be associated mainly with the neuronal membrane (Killian et al., 1994). A more specific approach to address this issue would entail a comparison of masking effects of high-rate electric stimuli on the ECAP in hearing and deafened preparations. We are currently conducting experiments using this approach.

The results presented in this report suggest that neural adaptation in response to an acoustic stimulus is a major contributing factor to the acoustic-electric interactions. The two lines of evidence that support this hypothesis are the residual effects of acoustic noise on the ECAP and the notion that similar effects can be achieved by an electric masker stimulus, as in both cases the absence of ongoing acoustic stimulation makes the contribution of synapse-associated mechanisms rather unlikely.

Adaptation to the ongoing stimulus may have two opposite effects on the ECAP response. First, it can cause a decrease in response to the masker stimulus, thus making simultaneous masking less effective over time. This, in turn, may account for a partial recovery of the probe-evoked ECAP during presentation of the masker stimulus. On the other hand, a decrease in neuronal responsiveness due to masker-induced adaptation can affect responses to the probe stimuli as well. Recovery from this adaptation following masker offset may account for its residual effects.

An unusual finding of the present study was an apparent “anti-masking” effect of a high-rate electric pulse train on the ECAP (see Figure 3, top panel). We note that such an effect (which has been observed in three subjects to date) could be achieved at masker intensities comparable to the ECAP electric sensitivity threshold levels. It has been demonstrated that subthreshold electric stimulation could produce a transient (<1 ms) decrease in response thresholds to a following suprathreshold stimulus (Dynes, 1995). The anti-masking phenomenon observed in our experiments may be related to the sensitization effect reported by Dynes (1995). A low-level electric masker stimulus might produce a subthreshold depolarization of a subpopulation of auditory nerve fibers, thus increasing their responsiveness to a higher-level probe stimulus. Consequently, an increase in neural activity evoked by

the probe might produce an enhancement in the population response (ECAP). However, at this point we cannot exclude the possibility that such an enhancement was an artifact of the methodology, as responses to the probe pulses had to be measured following subtraction of the "masker-only" waveform from the "masker + probe" recordings. We are planning to investigate this phenomenon in greater detail in the future.

3. Plans for the Next Quarter

In the next quarter, we plan to do the following:

1. Attend the Association for Research in Otolaryngology Midwinter Meeting (February 19-24, 2005, New Orleans, LA, USA) and present results related to the contract work.

2. Perform additional within-subject comparisons of acoustic and electric masking of the ECAP in acute guinea pig experiments.

3. Investigate apparent differences between acoustic and electric maskers for single-fiber measures in cats.

4. Conduct additional acute guinea pig experiments to compare masking effects of high-rate electric stimuli on the ECAP in hearing and deafened preparations.

5. Report on bilateral acoustic-electric interactions for measures in the inferior colliculus in guinea pigs.

4. References

1. **Chimento, T.C., Schreiner, C.E. (1991).** Adaptation and recovery from adaptation in single fiber responses of the cat auditory nerve. *J. Acoust. Soc. Am.,* 90(1):263-273.

2. **Dynes, S.B.C. (1995).** Discharge characteristics of auditory nerve fibers for pulsatile electrical stimuli. Ph.D. thesis, MIT, Cambridge, MA.

3. **Eggermont, J.J. (1985).** Peripheral auditory adaptation and fatigue: A model oriented review. *Hear. Res.,* 18:57-71.

4. **Haenggeli, A., Zhang, J.S., Vischer, M.W., Pelizzone, M., Rouiller, E.M. (1998).** Electrically evoked compound action potential (ECAP) of the cochlear nerve in response to pulsatile electrical stimulation of the cochlea in the rat: effects of stimulation at high rates. *Audiology,* 37:353-371.

5. **Hu, N., Abbas, P.J., Miller, C.A., Robinson, B.K., Nourski, K.V., Jeng, F.C., Abkes, B.A., Nichols, J.M. (2003).** Auditory response to intracochlear electric stimuli following furosemide treatment. *Hear. Res.,* 185:77-89.

6. **Killian, M.J.P., Klis, S.F.L., Smoorenburg, G.F. (1994).** Adaptation in the compound action potential response of the guinea pig VIIIth nerve to electric stimulation. *Hear. Res.,* 81:66-82.

7. **Matsuoka, A.J., Abbas, P.J., Rubinstein, J.T., Miller, C.A. (2000).** The neuronal response to electrical constant-amplitude pulse train stimulation: Evoked compound action potential recordings. *Hear. Res.*, 149:115-128.

8. **Miller C.A., Abbas, P.J., Hay-McCutcheon M.J., Robinson B.K., Nourski K.V., Jeng F.C. (2004a).** Intracochlear and extracochlear ECAPs suggest antidromic action potentials. *Hear. Res.,* 198:75-86.

9. **Miller C.A., Robinson B.K., Hetke J.F., Abbas P.J., Nourski K.V. (2004b).** Feasibility of using silicon-substrate recording electrodes within the auditory nerve. *Hear. Res.,* 198:48-58.

10. **Moser, T., Beutner, D. (2000).** Kinetics of exocytosis and endocytosis at the cochlear inner hair cell afferent synapse of the mouse. *Proc. Natl. Acad. Sci. U.S.A.,* 97(1): 883-888.

11. **Nourski K.V., Abbas P.J., Miller C.A., Robinson B.K., Jeng F.C.** Effects of acoustic noise on the auditory nerve compound action potentials evoked by electric pulse trains. *Hear. Res.* [In press].