Seventh Quarterly Progress Report
N01-DC-9-2106

Effects of Remaining Hair Cells on Cochlear Implant Function

P.J. Abbas, C.A. Miller, J.T. Rubinstein, B.K. Robinson

Department of Otolaryngology - Head and Neck Surgery
Department of Speech Pathology and Audiology
Department of Physiology and Biophysics
University of Iowa
Iowa City, IA 52242

April 30, 2001

Contents

1 Introduction

In this contract, we are conducting physiological and computational model experiments to assess the effects that functional hair cells have on the auditory nerve's response to electrical stimulation. This work is relevant to the widening pool of cochlear implant candidates as audiological criteria (e.g., pure-tone thresholds) are becoming more relaxed and patients with residual hearing are being implanted. Intact hair-cells may interact with the electrically transduced signal in several ways. Acoustically evoked neural activity may interact or compete with electrically evoked activity. Also, the very presence of hair cells - without any exogenous acoustic stimuli - may also modify the electrically evoked neural response. It is possible that electrical stimuli may depolarize hair cells and initiate the release of neurotransmitter and nerve-fiber activation. It is also possible that quiescent release of neurotransmitter may modulate the response characteristics of nerve fibers, thereby changing their responsiveness to electrical stimuli. The experiments of this contract are designed to acquire evoked potential data from sets of experimental animals that have functional and nonfunctional hair cells. Comparisons will then be performed to assess the effect of functional hair cells on the transduction of electrical stimuli delivered by intracochlear electrodes.

2 Summary of activities in this quarter

In our seventh quarter (1 January through 31 March, 2001), the following activities related to this contract were completed:

1. We attended the ARO Midwinter meeting and reported on data collected relative to noise and tonal acoustic masking on responses to electrical stimulation in animals with functional hair cells (Miller et al., 2001

2. At that same meeting, Rubinstein (2001) reported on modeling work relating synaptic activity to morphological characteristics of the hair cell-neural junction.

3. We continue to refine procedures for using furosemide to compare responses to electrical stimulation with and without functional hair cells.

4. We have begun recordings of binaural ABR component in animals with acoustic stimulation in one ear and electrical stimulation of the opposite ear.

5. We welcomed Dr. Ning Hu to our research group as a postdoctoral associate in January of 2001. He brings to our expertise in physiological work, particularly with regard to planned experiments evaluating the effects of furosemide.

3 Introduction

The third quarterly progress report (Abbas et al., 2000) described comparisons between electrically evoked compound action potential (ECAP) before and after deafening. These experiments demonstrated in both the growth of response with stimulus level as well as in the temporal response pattern to pulse trains. In a subsequent report (Miller et al., 2000) we described experiments assessing the effects of simultaneous presentation of acoustic and electric stimuli on the ECAP. That report described changes in the ECAP growth function to a pulsatile stimulus in the presence of acoustic wide-band noise. Noise generally had the effect of decreasing the amplitude of the response. In subsequent experimental work, we have examined in more detail both the temporal properties of the masking effect as well the dependence on spectral characteristics of the acoustic noise. Initial findings in that work are described in this report.

Methodology is identical to that outlined in previous reports (Abbas et al., 2000; Miller et al., 2000). Sound was delivered to the ear canal with a Beyer DT-48 earphone coupled to a speculum. Electric stimuli were delivered to through monopolar intracochlear electrode in the same ear with a needle electrode as the return electrode. The stimulating electrode is positioned in the basal turn of the scala tympani via a cochleostomy.

4 Electrically evoked responses during and after stimulation with acoustic noise

In examining the interactions between acoustic and electric stimulation, we have used wide-band noise stimuli at levels up to 100 dB SPL (overall level) with durations on the order of a minute. Such stimuli can have a clear effect

on the subsequent responsiveness of auditory nerve fibers to sound stimuli (Young and Sachs, 1973). In collecting the data with acoustic noise we noted that changes in the amplitude of the response to electrical stimulation varied over the duration of the acoustic masker. In addition, the recovery to "unmasked" response amplitude was not immediate, i.e., the recovery took place over several seconds.

The time course of these changes are illustrated Figure 1. ECAP amplitude in response to 0.7 mA biphasic pulse is plotted as a function of time. Each point represents the response amplitude based the average of 20 recordings. This is a much lower number than is usual for our recordings and as a result the amplitude measures are somewhat noisy. We used this relatively low number of sweeps to ensure a finer time scale in order to better evaluate the changes in ECAP amplitude over time. During the data collection, a 96 dB SPL wide-band noise was introduced at the times indicated on the graph by the horizontal lines. For both presentations of the noise, there is a relatively fast (approximately 10 s) decrease in the response amplitude after which amplitude reaches an approximate steady state. After the noise is turned off, the recovery to pre-noise response amplitude is not immediate. In these cases, the recovery time is on the order of 1 minute.

The stimuli evoking the response are biphasic electrical pulses and we are measuring the response amplitude at a latency 0.2-0.3 microseconds. Based the short latency, the responses are clearly not electrophonic in nature and we assume that they represent direct stimulation of the spiral ganglion cells. They are nevertheless affected by the presence of acoustic noise, possibly due to increases in synaptic activity. After the noise is turned off, even though synaptic activity in response to the noise has ceased, the effect of that stimulus persists for time. The relatively slow time course of recovery suggests a metabolic process but the specific site and mechanism are not clear at the present time.

Based on observation such as those illustrated in Figure 1, we have modified our procedure to in collecting noise-masking data. We first measure the response to a signal in quiet. We then turn on the noise and measure the response to the same stimulus in the presence of a particular noise stimulus. After turning off the noise we then measure the response to the same stimulus sequentially until the response amplitude reaches pre-noise response amplitudes. In this way, we attempt to minimize the effect of previous stimulation on the response to each noise band.

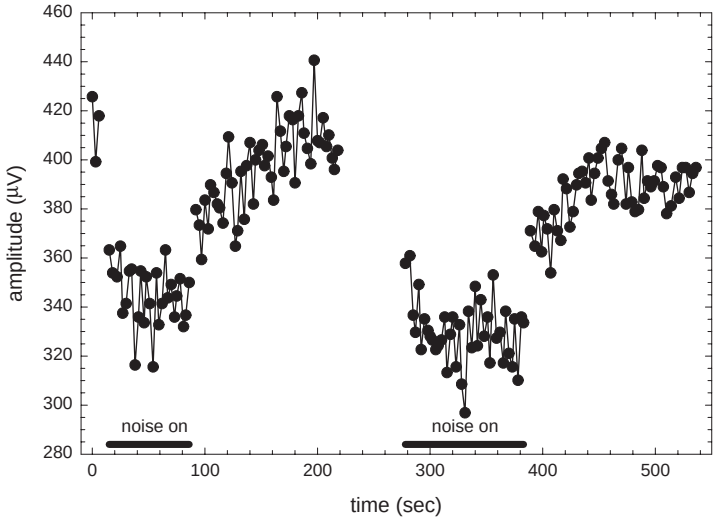

Figure 1: ECAP amplitude in response to a 0.7 mA biphasic pulse is plotted as a function of time. Each point represents the response calculated on the basis of 20 stimulus presentations. Wide-band noise masking at 96 dB SPL is turned on at times indicated by the bars along the abscissa.

5 Electrically evoked responses with high-pass acoustic noise

Figure 2 illustrates the stimulus paradigm used in these experiments. We basically have collected response data with various high-pass noise stimuli as the acoustic masker, always using biphasic current pulses delivered through a monopolar electrode in the base of the cochlea as the electrical stimulus. In all cases, the spectrum level of the noise is held constant as the high-pass cut-off frequency is varied across stimulus conditions. The two high-pass conditions represented in panels A and B of that Figure illustrate the theoretical basis for this manipulation. With a low-frequency cut-off frequency (part A), the mechanical response in the cochlea will be broad and presumably all fibers across place will be affected. For a higher frequency cutoff as illustrated in part B, the effect of the noise is limited to those fibers in the base of the cochlea and presumably the effects of the noise will be limited to those fibers innervating hair cells in the base. By manipulating the cut-off frequency, we can then assess the fiber population that is affected by the noise.

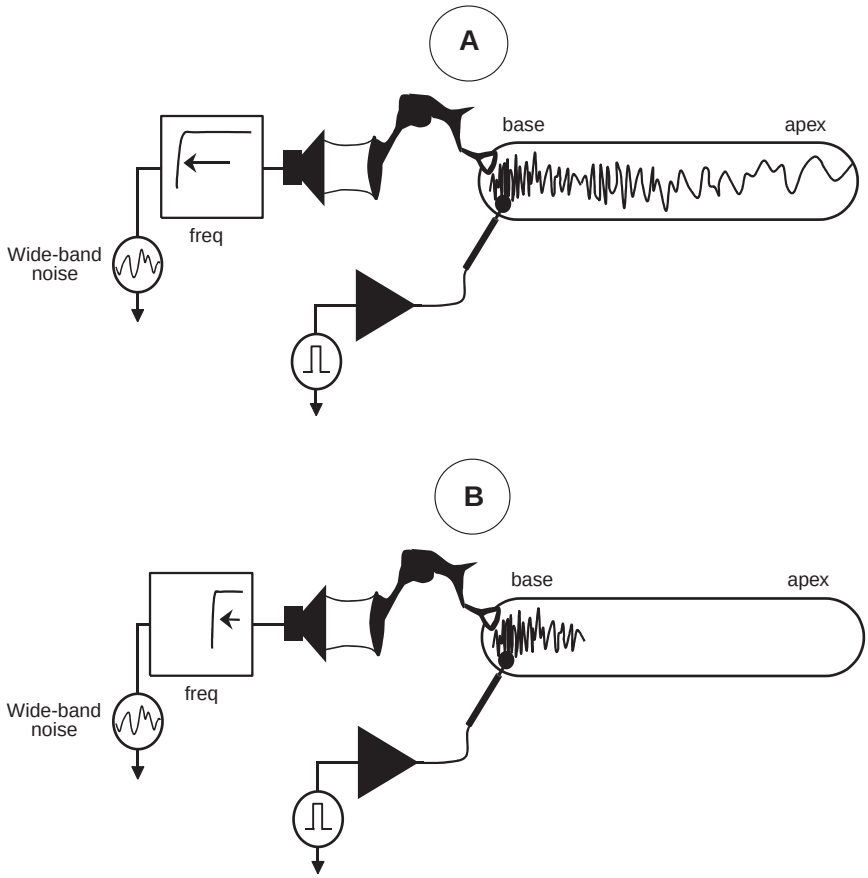

Figure 2: Schematic illustrating the paradigm used to investigate the effects of spectral content of the acoustic stimulus on the response to electrical stimulation.

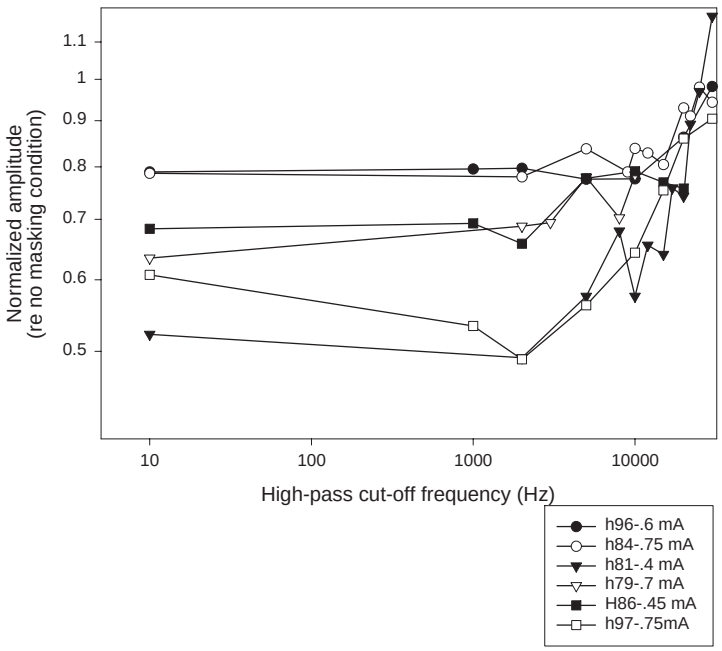

Figure 3: Amplitude of the response to a biphasic electrical pulse is normalized to the response to the same pulse without acoustic masking. Each value is plotted as function of cut-off frequency of the high-pass acoustic noise. Data are plotted for 6 subjects, the electric stimulus level is indicated in the legend for each. Masking noise for all subjects is 96 dB SPL for the wide-band stimulus. Spectrum level is held constant for across all filtering conditions.

Results from six guinea pig ears are plotted in Figure 3. In each case, the wide-band masking noise was set at 96 dB SPL. Level of the electric biphasic pulses was set near the middle of the dynamic range for that ear. Response amplitude is measured in each masking condition and referenced to the response in the unmasked condition. These normalized values are then plotted as function of high-pass cutoff frequency. The degree of masking for the wide-band condition varies somewhat across subjects. Nevertheless, for all six subjects, the degree of masking changes little for cut-off frequencies up to 3-4 kHz. A steep increase in amplitude is seen only for cut-off frequencies above 10 kHz. These data are consistent with a hypothesis that masking is effective only for basal nerve fibers, suggesting that those spiral ganglion cells are primarily contributing to the response to electrical stimulation.

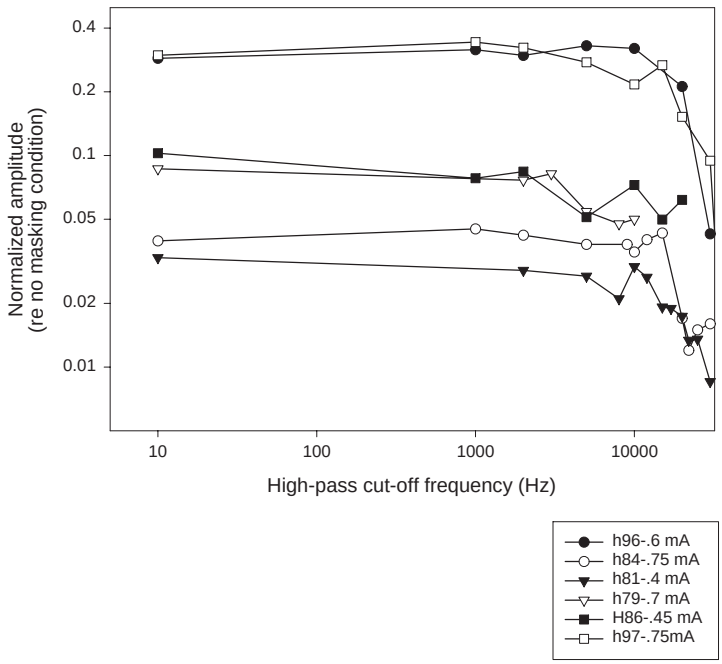

Figure 4: Derived amplitude of response (see text) is normalized to the response to the same pulse without acoustic masking and plotted as a function of high-pass noise cut-off frequency. Data are for the same conditions and subjects as in Figure 3.

An alternate method of analyzing the data from these masking experiments involves a variation of the derived response technique described by Teas et al., (1962). In this case, we subtracted the waveform recorded in the high-pass masking condition from that recorded in quiet. The resulting waveform represents the response of those neurons that were masked by the noise. We then measure an amplitude of the "masked" response and normalize that to the amplitude in the no masking condition for that subject. This derived response method provides an estimate of the response waveform that is masked, rather than simply a difference between two amplitudes as in Figure 3. Differences in response latency and waveform morphology between the masked and unmasked responses are consequently accounted for in the derived response.

The resulting functions showing normalized amplitude as a function of high-pass cut-off frequency for the same 6 ears are plotted in Figure 4. Consistent with the data in Figure 3, the wide-band response amplitudes vary

across subjects. High-pass cut-off frequencies above 10 kHz result in small response amplitude, consistent with a relatively small number of neurons being effectively masked. High-pass cut-off frequencies 3-4 kHz and below show relatively constant amplitude, consistent with a hypothesis that fibers below that frequency are not contributing significantly to the ECAP amplitude.

While these data are consistent with a limited area of effective masking of electrical stimulation, we plan to examine this question in more detail in future experiments under this contract. Our current plans include examining level effects of both noise masker and electric probe, as well placing the stimulating electrode at different longitudinal locations within the cochlea. Such data should lead to a more complete understanding of the interactions between electrical and acoustic stimulation. Further details of the time course of masking and the recovery process will also be examined.

6 Plans for the next quarter

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

- We will conduct additional experiments and analyses examining the effects of high-pass noise as described above.
- We will continue to develop techniques and collect data using furosemide to examine the effects of functional hair cells.
- We will continue experiment examining the interaction between acoustic and electrical stimulation in the binaural system.

References

[1] Abbas, P.J., Miller, C.A., Rubinstein, J.T., Robinson, B.K. (2000) Effects of remaining hair cells on cochlear implant function. Third Quarterly Progress Report N01-DC-9-2106.

[2] Miller, C.A., Abbas, P.J., Rubinstein, J.T., C. Runge-Samuelson, Robinson, B.K. (2000) Effects of remaining hair cells on cochlear implant function. Fifth Quarterly Progress Report N01-DC-9-2106.

[3] Miller, C.A., Abbas, P.A., Robinson, B.K., Runge-Samuelson, C. (2001) Electrically evoked auditory nerve responses from ears with intact hair cells. Abstracts ARO Midwinter Meeting.

[4] Rubinstein, J.T. (2001) Application of cochlear implant models to a vestibular prosthesis, Abstracts ARO Midwinter Meeting.

[5] Teas, D.C., Eldredge, D.H., Davis, H. (1962). Journal of the Acoustical Society of America. 34, 1438-1550.

[6] Young, E.D, and Sachs, M.B. (1973) Recovery from sound exposure in auditory-nerve fibers. Journal of the Acoustical Society of America. 54, 1535-1543.