13th Quarterly Progress Report

October 1, 2005 to December 31, 2005

Neural Prosthesis Program Contract N01-DC-02-1006

The Neurophysiological Effects of Simulated Auditory Prosthesis Stimulation

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This report describes our progress during the 13th quarter of contract NIH-NIDCD-DC-02-1006 (October 1, 2005 - December 31, 2005). During this quarter, we conducted five physiology experiments that continued and extended our investigations of interactions between cochlear implant channels. These experiments, as well as other work completed during the quarter, are described briefly in the next section. The final section of this report briefly describes the work we plan for the next quarter.

Summary description of work over the last quarter

During the previous quarter we completed five neurophysiology experiments investigating responses to stimulation of single and multiple auditory information channels. These studies used acoustic and electric stimulation of the cochlea, by pure-tone bursts delivered using a calibrated speaker and by modulated and unmodulated biphasic current pulse trains delivered using a cochlear implant. The extent of cochlear activation during stimulus presentation was determined by observation of neuronal activity along the tonotopic axis of the inferior colliculus (IC). The experiments completed during the previous quarter included initiation or continuation of:

- Studies investigating the cochlear activation by sinusoidally amplitude modulated (SAM) electrical current pulse trains delivered by a cochlear implant. In particular, we examined the relative effects of stimulus amplitude and envelope modulation depth on neuronal response profiles within the inferior colliculus during single-channel electrical stimulation of the cochlea. These studies were carried out using pulse train carriers with rates between 250 and 1000 pulses per second (pps) and envelope frequencies between 8 and 33 Hz. This range of envelope modulation frequencies was chosen because it lies with the range of phonemic modulation, and because previous experiments have demonstrated that nearly all single neurons within the central nucleus of the IC are able to follow envelope modulations at this rate. Analysis of data collected during these experiments is ongoing. Notification will be made in a future progress report when our manuscript describing the results of these studies has been submitted for publication.

- Studies investigating cochlear activation by tripolar current pulses with varying remote current fractions (RCFs). Quarterly progress report #8 describes our previous investigation of responses to these “partially tripolar” stimuli. The present experiments were conducted in order to compare theoretical predictions of a model of cochlear activation by these stimuli with experimental observations. At the termination of the recent experiments, the cochlear implant devices were fixed in place within the scala tympani and then amputated at the round window. These cochleas, with the implant electrodes in place, were subsequently fixed for histological examination. Further study of these cochleas will include characterization of the distance of each of the stimulating electrodes from cochlear structures and excitable neuronal elements, as well as characterization of the position of each stimulating electrode along the extents of the spiral ganglion and basilar membrane.

- Studies investigating the effects of changing the phase and frequency between sinusoidal modulation envelopes of pulse trains interleaved on two cochlear implant channels. Modulation of acoustic tones using a common envelope leads to perceptual grouping, while modulation using distinct envelope frequencies leads to separate percepts. In our recent studies we have begun to investigate physiological correlates of this perceptual phenomenon. We have also initiated investigation of the effects of changing the relative phase of pulse train

carriers of both modulated and unmodulated interleaved current pulse trains presented on two implant channels.

- Studies of acoustic forward masking in the inferior colliculus. These experiments have extended our previous work investigating acoustic two-channel interaction in a forward masking paradigm, which was initially described in QPR #6. In the present studies, we specifically examined responses of isolated single neurons within the IC during acoustic forward masking. This study was undertaken to acquire single-unit data for inclusion in a manuscript under preparation that describes acoustic forward masking. These acoustic forward masking studies comprise a basis for comparison of our studies investigating responses to electrical stimulation in a parallel forward masking paradigm.

Most of these experiments were conducted using bipolar stimulation, in which stimulation artifacts were absent or too small to be observed. Some experiments were also conducted using monopolar stimulation, in which stimulation artifacts were significantly larger.

In addition to the physiology experiments described above, we have also made progress in other areas:

- Electrode fabrication: Three new UCSF-type multichannel scala tympani cochlear implants were fabricated for use in our physiology experiments.
- Data analysis: We have begun analysis of data from the experiments described above, and continued our analyses of data obtained during experiments reported in previous QPRs.
- Software upgrades: We have modified our experiment control software to facilitate generation of stimuli, acquisition of responses, and and analysis of results of stimulation with modulated pulse trains on multiple cochlear implant channels.

Abstracts (Text included in Appendix below)

Bonham, B., Snyder, R.L., Middlebrooks, J.C., Rebscher, S.J, and Hetherington, A. (2006). Physiological measures of cochlear prosthesis channel interaction. Assoc. Res. Otolaryngol. Midwinter Meeting, Baltimore.

Work planned for next quarter

We will continue our studies of responses to SAM pulse trains. These studies, described above, include investigating effects of modulation depth on a single channel, as well as between channel differences in envelope phase, carrier phase, and envelope frequency.

We will continue our experiments investigating two-channel current steering using bipolar stimulation. These experiments have been designed to examine physiologically responses to stimulating “virtual channels” created by dividing stimulus current between two or more stimulating electrodes within the cochlea.

We will proceed with histological processing and examination of cochleas with embedded implants (described above).

We plan to begin a series of experiments in collaboration with with Dr. Donal Sinex of Utah State University. In this series of experiments, we will investigate and compare responses to acoustic speech, presented via a loudspeaker, with responses to electrically processed speech presented via a cochlear implant.

Dr. Snyder will travel to the University of Michigan to complete ongoing studies of electrical forward masking work with Dr. John Middlebrooks. The previous experiments were conducted in the Epstein laboratory, but Dr. Middlebrooks' schedule would not allow him to travel to UCSF. Therefore, these experiments will be completed in his laboratory in Ann Arbor.

We plan to complete and submit several manuscripts that are currently in various stages of preparation. Topics of these manuscripts, and primary authors, include: Acoustic forward masking (B. Bonham), Effects of changing the remote current fraction (B. Bonham), Effects of electrode placement within cochlea (R. Snyder), and Development and fabrication of the UCSF-type cochlear implant for the guinea pig (S. Rebscher).

Appendix

Bonham, B., Snyder, R.L., Middlebrooks, J.C., Rebscher, S.J, and Hetherington, A. (2006). Physiological measures of cochlear prosthesis channel interaction. Assoc. Res. Otolaryngol. Midwinter Meeting, Baltimore.

Contemporary human cochlear implants (CIs) are multichannel devices. Each of these channels is thought to excite a unique restricted and tonotopically appropriate population of auditory nerve fibers, similar to populations excited by spectrally limited acoustic stimuli. This is the basis for current processing strategies used in CIs. Psychophysical and clinical studies indicate that these devices provide many users with open-set speech reception. Our animal studies seek to understand the physiological mechanisms that underlie this performance.

Using deaf animal models and intracochlear electrodes that approximate commercial CI electrodes, we have shown that many factors influence the spatial (spectral) and temporal distribution of neural activity evoked in the central auditory system by CI stimulation. Among these factors are: the amplitude of stimulus pulses, the pulse waveform (symmetric biphasic or pseudomonophasic), the orientation and separation of the electrode contacts, the mode of stimulation (monopolar, bipolar, or tripolar), the relative location and timing of concurrently activated channels (auditory nerve populations), and the relative location and timing of previously activated channels. This poster describes the effects of cochlear electrode position and stimulating mode on the distribution of neural activity in the inferior colliculus. In some cases, the patterns of activation approximate those that are evoked by tonal acoustic stimuli, while in other cases they are significantly different. As an example, stimulation of widely spaced longitudinal bipolar electrode pairs using symmetric biphasic current pulses results in patterns of activation with two clearly resolvable peaks, one peak corresponding to each electrode site. As bipolar spacing is decreased the distance between these peaks decreases and the peaks eventually coalesce.