4th Quarterly Progress Report

July 1 to September 30, 2004

Neural Prosthesis Program Contract N01-DC-3-1006

Protective and Plastic Effects of Patterned Electrical Stimulation on the Deafened Auditory System

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SUMMARY OF WORK COMPLETED DURING THE PAST QUARTER.

1) During the past quarter, two cats were deafened with neomycin injections beginning at 30 days of age, rather than immediately after birth (our usual protocol for neonatally deafened animals). These animals are part of a new experimental series in animals in which the effects of a short but potentially significant period of normal hearing early in life will be evaluated (i.e., by comparing effects of deafness and chronic stimulation in neonatally deafened vs 30-day deafened animals). One subject underwent cochlear implantation at 7 weeks of age, and chronic electrical stimulation was initiated immediately and will continue throughout the next quarter. The other subject was euthanized as a control at 7 weeks of age.

2) Ongoing chronic electrical stimulation continued in two neonatally deafened, implanted subjects. These animals are part of a new experimental series in which subjects are receiving daily injections of a new selegeline drug (-)desmethyldeprenyl (DES), reported to be effective in reducing neuronal apoptosis. Both subjects underwent cochlear implantation at 6 weeks of age, and chronic electrical stimulation was initiated immediately and continued for periods of 6 months duration. One of these subjects has undergone chronic stimulation with the Advanced Bionics CII speech processor *via* a research interface supplied by the device manufacturer. These subjects will completed their stimulation periods and are scheduled for study in terminal acute electrophysiological experiments during the next quarter.

3) The main component of this Quarterly Report is a manuscript that has been submitted to the journal Hearing Research, and entitled: "***A temporal bone study of insertion trauma and intracochlear position of cochlear implant electrodes. II:*** **Comparison of *Spiral Clarion*™ and *HiFocus II*™ Electrodes."** This research was done in collaboration with two otolaryngology fellows, Drs. Wardrop and Whinney, from the United Kingdom who recently worked in the Epstein Laboratory on 6-month fellowships from the TWJ Foundation and also in collaboration with Dr. William Luxford from the House Ear Institute. The manuscript provides full details of findings in their human temporal bone studies examining the incidence and nature of surgical insertion trauma and the intracochlear positioning of the original Clarion spiral-shaped electrode and the newer "HiFocus II™" electrode with

attached positioner. A previous QPR submitted for our prior contract (8th Quarterly Progress Report, Contract #N01-DC-02108, July 1 to September 30, 2002) presented data on the initial 16 insertion trials conducted for this study. This final report includes complete histological analysis of insertion trauma and electrode position data for a total of 28 specimens, and additional data and analysis of electrode dimensions compared to scala tympani dimensions. Due to copyright issues, the completed manuscript is being submitted to the NIH Project Officer as an appendix and will not be posted on the NIH website. The abstract is included below, and interested individuals may contact the investigators for a preprint.

Abstract:

In recent years, several new designs of cochlear implant electrodes have been introduced clinically with the goal of optimizing perimodiolar placement of stimulation sites. Previous studies suggest that perimodiolar stimulation sites may increase both the efficiency and performance of a cochlear implant. This is the second of two studies designed to examine the positioning of electrodes and the occurrence of insertion-related injury with these newer designs and to directly compare two perimodiolar electrodes to their predecessors. In our previous report we compared the Nucleus™ banded electrode with the Nucleus *Contour*™ perimodiolar electrode. In the present study, using the same protocol, we examine the *Spiral Clarion*™ electrode and its successor, the *HiFocus II*™ electrode with attached positioner.

Eight Clarion Spiral™ arrays and twenty HiFocus II™electrodes with positioners were inserted into human cadaver temporal bones. Following insertion, the specimens were embedded in acrylic resin, cut in quarters with a diamond saw and polished. Insertion depth, proximity to the modiolus and trauma were evaluated in x-ray images and light microscopy. The newer electrode was consistently positioned closer to the modiolus than the previous device whereas the angular depth of insertion measured for the two electrodes was similar. The incidence of trauma was minimal when either electrode was inserted to a depth of less than 400°. However, severe trauma was observed in every case in which the HiFocus II™ with positioner was inserted beyond 400° and in some cases in which the Spiral Clarion™ was inserted beyond 400°. To evaluate the possible role of electrode size in the trauma observed we modeled both devices relative to the dimensions of the scala tympani. We found that the fully inserted *HiFocus II*™ electrode with positioner was larger than the scala tympani in approximately 70% of temporal bones measured. The results suggest that both the *Clarion*™ spiral and *HiFocus II*™with positioner can be inserted with minimal trauma, but in many cases not to the maximum depth allowed by the design.

4) Three abstracts were submitted for presentations of research findings from this Contract at the Midwinter Meeting of the Association for Research in Otolaryngology in February 2005.

WORK PLANNED FOR THE NEXT QUARTER.

1) Ongoing daily chronic electrical stimulation and DES treatment will continue in 2 subjects in our new experimental series in which the anti-apoptotic drug desmethyldeprenyl (DES) has been administered in deafened neonates both prior to implantation and continuing throughout the chronic stimulation period. These subjects will complete their stimulation periods and will be studied during the next quarter in terminal acute electrophysiological experiments. Recording from the inferior colliculus will be carried out first using 16-channel silicon probes to construct threshold -vs.- depth functions (spatial tuning curves). Following completion of several (5-6) probe penetrations, 1-2 additional recording penetrations will be made with conventional tungsten electrodes, recording unit and multiunit responses to pulses presented at increasing frequency and AM pulse trains in which both the carrier frequency and modulation frequency are varied. After completion of electrophysiological studies, if the condition of the animals permits, we will attempt to make restricted injections of the neuroanatomical tracer Neurobiotin™ into the spiral ganglion in order to examine neural projections to the cochlear nucleus.

2) Daily 2-channel intracochlear electrical stimulation will also continue in an animal deafened at 30 days, rather than neonatally. This animal is part of a new experiment evaluating the potential critical period effects of a short period of normal hearing early in life.

3) One additional normal-hearing control subject will be implanted and daily chronic electrical stimulation initiated using the Advanced Bionics CII BDCS processor.

4) We have recently finalized the design of a new feline intracochlear electrode with stimulating contacts positioned along the inner radius of the electrode, reflecting the design of contemporary human electrodes. During the next quarter the mold will be ordered from an outside vendor and initial electrodes will be fabricated and tested in trial insertions in cat cochleae.