3rd Quarterly Progress Report

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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 newborn cats underwent neonatal deafening induced by our standard protocol of daily injections of neomycin sulfate. These animals are part of a new experimental series in which animals 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 will continue throughout the next quarter. DES treatment also will be continued throughout the chronic stimulation period.

2) Ongoing chronic electrical stimulation continued uneventfully in 2 other DES subjects. These subjects will complete their stimulation periods and will be scheduled for study during the next quarter in terminal acute electrophysiological experiments. One subject has undergone chronic stimulation with the CII research interface processor supplied by Advanced Bionics, Inc.

3) The main component of this Quarterly Report is a manuscript recently submitted to the journal Hearing Research, and entitled: "***A temporal bone study of insertion trauma and intracochlear position of cochlear implant electrodes. I: Comparison of Nucleus Banded and Nucleus Contour™ 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. Roland from NYU and Dr. 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 Nucleus banded electrode and the new "Contour™" electrode. A previous QPR (6th Quarterly Progress Report, Contract #N01-DC-02108, Jan. 1 to March 31, 2002) presented data from 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 26 specimens. Due to copyright issues, the completed manuscript submitted to the NIH Project Officer as an appendix will not be posted on the NIH website. The abstract is included below, and interested individuals may contact the investigators for a preprint.

Abstract: New designs of cochlear implant electrodes have been introduced in an attempt to improve their efficiency and performance by locating stimulation sites closer to spiral ganglion neurons and deeper into the scala tympani. The goal of this study was to document insertion depth, scala tympani position and insertion trauma with the Nucleus Contour™ electrode and to compare results to those observed with the earlier generation Nucleus banded electrode.

For this comparison 8 banded electrodes and 18 Contour™ electrodes were implanted in cadaver temporal bones using a realistic surgical exposure. Two experienced cochlear implant surgeons and two otology fellows with specialized training in cochlear implant surgery were selected for the study to represent a range of surgical experience similar to that of surgeons currently performing the procedure throughout the world. Following insertion of the electrodes, specimens were imaged using plain film x-ray, embedded in acrylic resin, cut in radial sections with the electrodes in place, and each cut surface was polished. Insertion depth was measured in digitized x-ray images, and trauma was assessed in each cross-section.

The *Contour*™ electrode inserted more deeply (mean depth = 17.9 mm or 417°) than the banded electrode (mean depth = 15.3 mm or 285°). The incidence and severity of trauma varied substantially among the temporal bones studied. However, differences in the injuries observed with the two devices were not remarkable. The *Contour*™ electrode clearly was positioned closer to the modiolus than the banded model, and also appeared easier to use. Based on this difference in position and data from previous studies we conclude that the *Contour*™ electrode will provide lower thresholds and improved channel selectivity, but the incidence of trauma remains a problem with the new design. The relative influences of electrode positioning and neural degeneration that may result from trauma are as yet unclear

4) Dr. Leake attended the *7th European Symposium on Paediatric Cochlear Implantation* in Geneva, Switzerland on May 2-5 to give an invited tutorial/review talk ("Effects of early deafness and electrical stimulation on the developing auditory system: Implications for Paediatriac cochlear implantation") in the opening plenary session. The presentation included a summary of several recent findings from our Contract research. In addition, Dr. Maike Vollmer attended a conference on *Molecular Mechanisms in Central Auditory Function, Plasticity and Disorders* on June 25-27 in Jackson Hole, Wyoming. Her invited presentation also reported research conducted on our Contract characterizing degraded temporal resolution in "long-deafened" animals and plasticity elicited by chronic stimulation, despite the very severe cochlear pathology seen in these subjects.

WORK PLANNED FOR THE NEXT QUARTER.

1) Ongoing daily chronic electrical stimulation chronic 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 scheduled for study during the next quarter in terminal acute electrophysiological experiments. Recording from the inferior colliculus will be carried out first using the 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 frequency series and AM data in isolated single units wherever possible. After completion of electrophysiological studies, if possible we will make restricted injections of neuroanatomical tracer into the spiral ganglion to examine neural projections to the cochlear nucleus. Brain and cochlear specimens will then be taken for histological studies.

2) Two additional subjects will be implanted and daily chronic electrical stimulation initiated using the Advanced Bionics BDCS processor in one subject, and passive amplitude modulated pulse trains in the second.

3) We expect a new litter of kittens to be born during the current quarter. As subjects become available depending on the size of the litter, we will obtain additional controls for a neomycin-only group, an new experimental group deafened by neomycin injections beginning at P30, and the DES treatment group, with controls studied at 6-8 weeks of age, at the time their littermates undergo cochlear implantation.

4) We are now finalizing design of a new feline intracochlear electrode. During the next quarter we will meet with engineers from Advance Bionics who have agreed to assist us in fabrication of foil contacts with larger surface areas (similar to those used in contemporary human devices) to be used in the new cat electrodes. Following completion of stimulating contact design the final mold specifications will be reviewed and the mold will be ordered.