
First Quarterly Progress Report

August 1 to October 31, 2006

Contract No. HHS-N-260-2006-00005-C

Neurophysiological Studies of Electrical Stimulation for the Vestibular Nerve

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Reporting Period: August 1 – October 31, 2006

Approvals:

The contract was signed and implemented on August 1, 2006. We immediately submitted all of the just-in-time paperwork for project approval. This included Animal Care and Use Committee (IACUC) Project Review Forms, Request for Addition of New Personnel to Animal Use Protocol Forms, Environmental Health and Safety (EHS) Project Review Forms, Ocupational Health Questionnaires, Washington National Primate Research Center (WaNPRC) Research Project Approval Forms, and individual Animal Use Training (AUT) and Biosafety Level 2 (BSL2) training applications for all project staff. The project is currently approved by the UW IACUC, UW EHS, and Occupational Health, and has completed WaNPRC financial review in which the project was approved. All relevant project staff have completed and documented AUT, including BSL2 training where appropriate.

Funds:

A separate financial report will be submitted through the UW Office of Sponsored Projects. Funds for the project were released internally at the University of Washington subsequent to obtaining internal approval (effective 10/1/2006). This allowed most research staff members to join the project officially on 10/1/2006. Dr. Rubinstein had been pursuing development of the vestibular implant technology prior to this date, and his funding was retroactively adjusted to reflect this activity. In addition, Dr. Bierer represented the group at the Neural Prosthesis Workshop, August 21st -23rd, supported by project funds. At this meeting, Dr. Bierer met with representatives of NeuroNexus to discuss multiple single unit recording electrode design considerations.

Research Personnel:

The research personnel who were assembled in the first quarter include all of the original members of the research team stated in the project proposal. Dr. James Phillips is P.I. Dr. Jay T. Rubinstein is heading the Vestibular Implant Development Team and the Surgical Implantation Team. Dr. Albert F. Fuchs, Dr. Leo Ling, and Dr. Phillips jointly comprise the Behavioral and Neural Recording Team. Dr. Steven M. Bierer heads the Multiple Single Unit Electrode Development Team. Dr. Kaibao Nie heads the Software Development Team.

In addition, to overcome delays introduced by the internal approval process, we added several team members to help us progress. Robert Cent, who is a programmer with extensive 22 years experience in the development of real time software and hardware implementation in the primate laboratory, has been added to the project to assist in the rapid development of stimulus presentation, recording and analysis software for the project. Dr. Chris R.S. Kaneko, who is an oculomotor neuroscientist with experience in recording neural activity in the primate, and with electrical stimulation of the vestibular end organ, has been recruited to assist with the implantation of the prosthesis and

adaptation of the analog recording hardware to allow for multiple single unit recording. Ms. Monica Ibarreta, who is a laboratory technician, has joined the team to assist in training the rhesus monkeys used in the proposed experiments and to oversee the initial purchase and inventory of supplies used in the project.

In addition, two Otolaryngology residents have joined the research group as part of their resident research activity. Dr. Filipe Santos (R3) is working with Dr. Rubinstein in perfecting the surgical approach for the implantation of the stimulating electrodes and vestibular prosthesis. This development entails performing temporal bone dissections on rhesus monkey necropsy material and practicing the surgical approach in that material Dr. Valeria Potigailo (R1) will assist the behavioral and neural recording team in recording neural activity in the rhesus monkeys.

Structure of the Research Teams:

In the first quarter we organized into research teams to accomplish the specific tasks required for performance of the contract. It should be noted that the entire research group meets regularly to discuss our progress and share ideas. The research teams provide a focused approach to each major component of the research plan.

Vestibular Implant Development Team: This team is charged with development of the vestibular prosthesis. Members of this team will interact directly with the implant manufacturer to perfect the physical and electronic design of the implant. Members include Dr. Jay Rubinstein, Dr. James Phillips, Dr. Kaibao Nie, and Dr. Albert Fuchs.

Surgical Implantation Team: This team is responsible for the successful implantation of the vestibular prosthesis, including the development of new surgical approaches in the rhesus monkey. Members of the team include Dr. Filipe Santos, Dr. Jay Rubinstein, Dr. James Phillips, and Dr. Chris Kaneko.

Software Development Team: This team is focused on software development 1) to program the vestibular implant, 2) to interface the implant with the coil (eye position) signals in the recording booth, 3) to coordinate electrical, visual, and rotational stimuli during experiments, and 4) to record and analyze single and multiple single unit activity. Members of the team include Mr. Robert Cent, Dr Steven Bierer, Dr. Leo Ling, Dr. Kaibao Nie, Dr. James Phillips, and Dr. Jay Rubinstein.

Behavioral and Neural Recording Team: This group is responsible for performing all of the neural recording experiments, and recording overt behavior in response to vestibular stimulation. This group is also responsible for training and maintaining the rhesus monkeys. Member of the team include Dr. Steven Bierer, Dr. Albert Fuchs, Ms. Monica Ibarreta, Dr. Leo Ling, Dr. James Phillips, and Dr. Valeria Potigailo.

Multiple Single Unit Electrode Development Team: This group is responsible for the design, development and testing of the multiple single unit recording electrodes and post

amplifiers. Member of this team include Dr. Steven Bierer, Dr. Albert Fuchs, Dr. Leo Ling, and Dr. James Phillips.

Performance Benchmarks:

The performance benchmarks included in the contract timeline for the first quarter include 1) creation of a project web page and 2) purchase of laboratory equipment and hardware for the study. 3) In addition, included in the body of the proposal, there is a criterion of a local communication of the project objectives and accomplishments to an outside audience. 4) Implicit in these benchmarks is that we will obtain the internal approvals required to begin our work. All of these performance benchmarks have been met, and we have also made substantial progress toward our overall objectives.

First, our project web page has been implemented and is online. It includes introductory information about our research objectives, biographical and contact information for project personnel, technical information about our approach, a download area allowing users to obtain software as it is developed for the project, and a site for announcements of technical advancements, presentations and meetings related to the project.

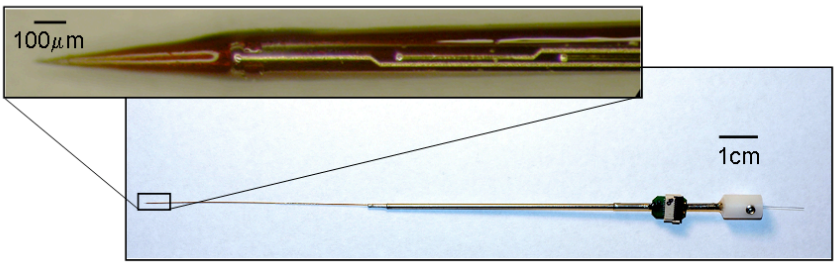

Figure 1: Design of a prototype electrode developed for multiple single unit recording. Multiple recording sites are pictured in the inset (above) with the full electrode displayed below. This electrode differs from our specific design requirements in its length and headstage connector, but should be useful for refining the design of our recording apparatus.

Second, we have purchased the multiple single unit recording electrodes, amplifiers, equipment modifications to our digitizing hardware, required analysis and data collection computers and computer upgrades. In addition, Dr. Bierer and Dr. Phillips have obtained a commitment from NeuroNexus and FHC Corporation to provide prototype multiple single unit recording electrodes for development purposes during the period of fabrication of electrodes meeting our specific design requirements. The prototype electrodes are pictured above in figure 1.

In addition, we have made considerable progress in the development of the vestibular stimulation prosthesis. Dr. Rubinstein has had multiple meetings with representatives of both Cochlear Corporation and Advanced Bionics Corporation to discuss the requirements for our prosthesis. Both companies are independently pursuing the development of this technology for our project. Dr. Rubinstein has met personally with the design engineers to discuss electrode configuration and the required rigidity of the implant. Currently, engineers from Cochlear Corporation have proposed a rigid curved implant with a bipolar electrode design, using circumferential electrodes of 200-250 um diameter.

Third, we have presented our project design and objectives at two meetings. The first meeting, at which we will present monthly, is a local research meeting for affiliates of the Neuroscience Division of the WaNPRC. In attendance were core staff, faculty affiliates, research scientists, post-doctoral, predoctoral and undergraduate students interested in basic primate neurophysiology. In addition, Dr. Phillips introduced the project at the October meeting of the Clinical Vestibular Disorders Group. In attendance were clinicians and clinician researchers from University of Washington Medical Center, Harborview Medical Center, Swedish Medical Center and Children's Hospital and Regional Medical Center, as well as clinicians in private practice. These local presentation and discussion sessions will occur quarterly.

Fourth, as implied in the activities above, we have obtained the necessary approvals for continuation of the project into quarter two.

Additional activities and accomplishments:

In addition to the benchmarks achieved above, we have made other strides in the first quarter toward achieving the overall objectives of the study.

Members of our group, Dr. Bierer and Dr. Nie, have attended programming workshops sponsored by Cochlear Corporation to acquire the skills necessary to implement our programming objectives in a programmable device from that corporation.

We have organized regular project meetings to discuss the progress of the project, and to better define the design objectives of the vestibular prosthesis. Dr. Francis A. Spelman, Professor and former Chairman of Bioengineering at the University of Washington, participated in one of these meetings and is reviewing our design specifications to determine if locally developed implant technology could be adapted to resolve some of the outstanding design issues that we have encountered.

In our project timeline, we indicated that we would initiate software development in the first quarter. Robert Cent, working with Dr. Ling and Dr. Phillips, modified the existing unit and sinusoidal behavioral analysis software which was developed for the Macintosh computer so that it can be integrated into an multiple single unit recording environment based in Spike 2 (Version 5) for CED. A screen shot of the new software, which is

currently being evaluated by Dr. Phillips on single unit data digitized using Spike 2 recording software, is pictured in Figure 2.

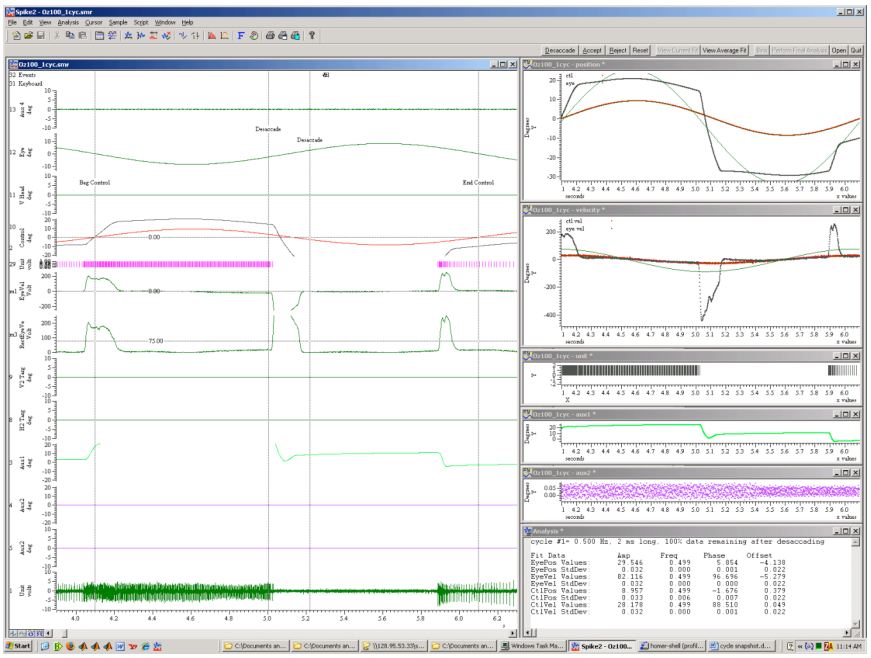

Figure 2: Screen shot of the newly developed Spike 2 cycle analysis program created for offline analysis of single unit discharge during sinusoidal rotation or smooth pursuit of sinusoidally moving targets. The program is constructed to automatically desaccade individual cycles of behavior and unit discharge, and then fit the resulting traces and unit discharge with sine functions. Data from successive cycles are accumulated and then a final fit is performed. Unit data can be binned or subjected to an interspike interval analysis comparable to the behavioral fits. This program is functionally similar to existing Macintosh based analysis software, but has been rewritten as a fist step toward implementing simultaneous multiple unit analysis in Spike 2.

Drs. Bierer, Fuchs, Ling, Kaneko and Phillips have made considerable progress in the design of the new interface, microdrive, cannula and micropositioner for the multiple single unit recording electrodes. The modifications, which are currently being drafted for machining, will allow for quick conversion from the standard single unit microelectrodes and cannula, in which the tungsten microelectrodes are backloaded into the prepositioned cannula, to a front loading system required by the premanufactured multiunit headstage connector on the back of the NeuroNexus multiunit probe.