SECTION C -- DESCRIPTION/SPECIFICATION/WORK STATEMENT

ARTICLE C.1. BACKGROUND

The Neural Prosthesis Program of the National Institute of Neurological Disorders and Stroke is committed to research and development on functional neuromuscular stimulation (FNS) to restore hand and arm function in quadriplegic individuals at the highest functional level possible. These FNS systems operate in a manner that paralyzed muscles are functionally activated by direct electrical stimulation under the voluntary control of the individual. Generating voluntary control signals from patient's uninjured motor cortical areas is a crucial part of a potentially effective FNS system. For example, movement of a paralyzed hand might be controlled with signals from the contralateral motor cortical areas in spinal cord injured quadriplegic individuals. The goal of this research is to establish the feasibility of generating control signals from cortical neurons involved in the voluntary control of limb movement.

To demonstrate that cortical neural signals can be used to control a prosthesis, we need to first demonstrate that activities of selected populations of cortical neurons can be reliably recorded for an extended period of time. It then must be shown that the volitionally controlled neuronal signals can be reliably converted to electrical signals that can control a device such as an electromechanical "arm/hand". During the current contract period, considerable progress has been made on both of these research areas in studies of cells in the primary motor cortex. Using either microwire arrays or silicon microelectrode electrode arrays (Utah arrays) it has been demonstrated that cortical neuronal activities can be recorded for a period of several months from the same microelectrode. In addition, the signals recorded from these microelectrodes have been successfully used to control a three-dimensional positioning task in a virtual reality environment. Promising results from these studies support the proposition that the recorded neuronal activities can potentially be used as control signals for a prosthesis. In addition, results from recent fMRI studies of motor cortical activity in spinal cord injured individuals are consistent with the hypothesis that these individuals retain the ability to volitionally activate cortical sensorimotor representations when attempting hand movements following years of injury (Nature 413:793, 2001).

The focus of this research will be on the development of chronic microelectrode recording techniques in primates with a gyrencephalic brain, which can realistically be adapted to human implantation. There will also be research on extracting control signals from the recorded neural activities. Based on the results of these studies the contractors will make recommendations about the feasibility of future human studies. Experiments on human subjects, however, are not included in the current supported research program, but may be considered in future trial studies.

Results from this area of research are needed by the Neural Prosthesis Program for providing information on the design of microelectrode recording array, the selection of recording sites, the number of cells required for providing stable and functional control signals, and the plasticity in recorded cell populations when the neural activity is co-opted to control an artificial device. These factors are all critical to establishing reliable control signals from recorded neural activity. Further decisions to initiate feasibility studies in spinal cord injured individuals will be made based on this information.

ARTICLE C.2. STATEMENT OF WORK

Independently and not as an agent of the Government, the contractor shall undertake performance of a research study in an attempt to demonstrate, in a suitable animal model, the feasibility of obtaining control signals recorded directly from CNS neural activity and determine the factors that are essential for generating a robust, reliable neural-electronic interface.

I. Specifically the contractor shall:

A. Select appropriate animal model(s) (excluding chimpanzees) and CNS areas where chronic control signals for an FNS system can be obtained, taking into consideration of factors that shall include:

    1. the relationship of the brain area to limb movements,
    2. the accessibility of the brain area for microelectrode implantation,
    3. the survival and the viability of the brain area after spinal cord lesions,
    4. the presence of a gyrencephalic brain, and
    5. the ability to train the animal to do a 3-dimensional reaching task.

B. Obtain or develop the necessary recording microelectrodes and instrumentation capable of chronically recording populations of single unit neuron activities in the CNS. In selecting this system strong consideration shall be given to developing a recording system that permits stable recording from the same neurons for the full duration of the experiment once the implant has stabilized. If it is not feasible at present to record from the same neurons over a period of several months, then a plan for tracking the change in neurons over time shall be developed.

C. Obtain or develop an electromechanical arm that can be controlled in at least one degree-of-freedom by neuronal activity from the selected brain areas. The proposed arm shall be capable of delivering rewards to the animal. Under neural control, it shall be capable of being switched on and off, and shall have a graded response.

D. Obtain or develop a real-time interface between the recorded neural data and the electromechanical arm such that a variety of neural control methods may be evaluated. This interface shall be capable of transforming the neural activity into a control signal with a time delay of less than 200 milliseconds.

E. Using the animal model(s) and resources in A through D, chronically implant arrays of recording microelectrodes into the selected CNS area and evaluate:

    1. The stability of the neural recordings and the control signals derived from them over a period of at least 6 months giving consideration to:
        a. the number of neurons required to provide stable control signals,
        b. the effects of naturally occurring movement of electrodes on the stability of control signals, and the ability of the real-time interface, the coding scheme, and the animal's adaptability to compensate for the electrode movement, and

c. the nature of any plasticity demonstrated by the neurons under study, the extent to which it is adaptive or maladaptive, and the time and/or training needed to demonstrate plastic changes.

2. The ability of the animal to control the mechanical arm giving consideration to:
   a. the accuracy and rate of information transfer,
   b. the ability to use the arm in retrieving rewards,
   c. the adaptability of the animal to generate new patterns of neural activity to optimize control of the arm, and
   d. the ability of the animal to control the electromechanical arm after functional loss of its real arm by lesion or reversible block of the spinal cord or peripheral nerves.

F. At the conclusion of the above experiments, sacrifice the animals and determine histopathologically the extent of damage produced by the chronic microelectrodes, paying particular attention to the condition of neurons near the recording sites.

G. Based on the results of the studies in E and F, modify the microelectrode arrays and signal processing system as appropriate to improve the performance of the system.

H. Before the end of the contract period deliver to the project officer an assessment of the feasibility of utilizing the techniques developed to initiate pilot studies in human volunteers.

I. Coordinate your efforts, through the Project Officer, with other investigators in the Neural Prosthesis Program.

J. Upon completion of the tasks specified above, prepare and deliver to the government a comprehensive final report that shall summarize what was achieved, what was not achieved and shall include recommendations for future research and development in this research area.