Feasibility Study of a Neural Interface System for Quadriplegic Patients

Jon A. Mukand, MD, PhD[1,2]; Steve Williams, MD[3]; Mijail Serruya, MD, PhD[5]; Abe Caplan[5], Maryam Saleh[5], Daniel Morris[4], John Donoghue, PhD[2,5]

[1]Sargent Rehabilitation Center, Providence, RI, [2]Brown University, [3]Boston Medical Center, [4]Stanford University, [5]Cyberkinetics, Inc., Foxboro, MA

Abstract

Objective: Develop an implantable neural interface system to provide quadriplegic patients with an output signal directly from the brain to a computer. **Design:** Preclinical studies, prototype testing, and clinical trial. **Setting:** Animal laboratory, outpatient clinics, patient homes **Participants**: Macaque monkeys and five quadriplegic patients. **Intervention:** Implantation of BrainGate™ microelectrode array sensor on the motor cortex surface. The array is connected to an amplifier, a signal processor, a decoder, and a patient-computer interface. The decoder correlates neural signals to desired actions using mathematical algorithms (linear regression). **Main Outcome Measures:** Safety assessment and ability to move a cursor to targets on the computer screen.

Results: 8 implants were placed in six macaques for an average of 10.2 months/implant. Side effects included 3 minor skin erosions (< 5 cm) and 1 treatable superficial skin infection around the connector. One implant recorded only one neuron and was explanted; another stopped recording at 12 months. For loosening, one connector required a strap. Three macaques were trained in a cursor control task. On the first decoding/testing day, all subjects achieved instant neural control of a cursor after a 15-minute calibration period. The FDA and local IRBs have approved a feasibility study, and the authors hope to present human data by 10/04.

Conclusions: Previous monkey studies established that neural activity can be decoded to generate useful output signals (Serruya et al., 2002 Nature 416:141). By deriving signals directly from the cerebral cortex, the BrainGate™ may allow human patients with severe motor impairments to control a cursor for the Internet, assistive software, and standard desktop activities.

Background

Needs for People with Impaired Motor Function

People with severe motor impairments have several common needs, regardless of the exact etiology of their paralysis. Activities of daily living that often are the most challenging to a person with quadriplegia include:

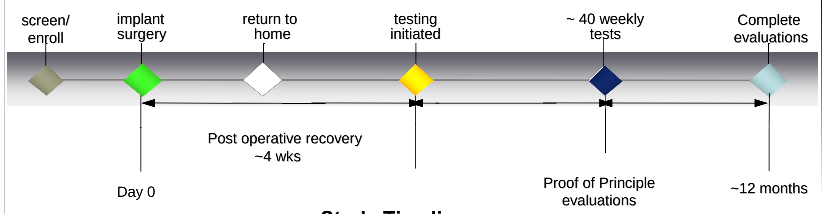
- feeding
- bathing
- grooming
- bladder and bowel
- transfers
- mobility

The device may someday increase independence in people with physical disabilities by linking thought directly to computers, environmental controls, wheelchairs, and nerve or muscle stimulators, e.g., functional electrical stimulation (FES).

Research and Product Development Goals

- By providing an easy-to-use neural cursor, enable someone to use e-mail and internet phone control to **communicate**.
- Improve independence via **environmental controls**, such as bed positioning, television, lights, and thermostats through a desktop application.
- Improve **mobility** by interfacing with powered wheelchairs.
- **Longer-term, cortical control could be interfaced with stimulators and other devices to provide closed-loop systems that improve respiratory, bladder and bowel control and move limbs via FES or robotics.**

Study Design



Study Timeline

Study Overview

An open-label, 12-month, longitudinal, feasibility clinical study of the BrainGate™ Neural Interface System (Cyberkinetics, Inc.) was initiated under Food and Drug Administration (FDA) Investigational Device Exemption (IDE) and Institutional Review Board (IRB) approvals in May 2004. The study is designed to gather preliminary safety and efficacy data on the System when used by people unable to use their arms or hands in a useful manner (quadriplegia or tetraplegia) to control a computer with thoughts.

As of September 2004, one person has been enrolled, implanted and is actively participating in the study at the Sargent Rehabilitation Center study site. Patient 001 is a 25 year-old ventilator-dependent male who is unable to move either upper extremity due to a C4 spinal cord injury suffered in July 2001.

Key Study Eligibility Criteria

- **Age 18 to 60 years**
- **Able to speak understandably**
- **Quadriplegia due to spinal cord injury, muscular dystrophy or stroke where quadriplegia is:**
  - **Complete quadriplegia (bilateral C2-C4)**
  - **Incomplete quadriplegia with muscle grade at specific cord levels as follows**
    - **≤ 3/5 at C5**
    - **≤ 2/5 at C6**
    - **< 2/5 at C7-T1 + lower extremities**
- **≥ 12 months post-injury**

Surgical Implantation

In June 2004, after obtaining informed consent, a surgical procedure consisting of an incision and 3 cm diameter craniotomy located above the right primary motor cortex was conducted under general anesthesia. A 4x4 mm, 100 channel sensor was implanted on the surface of the cortex, specifically in the precentral gyrus immediately posterior to the superior frontal sulcus,[1] as identified on presurgical MRI. This area of the motor cortex is primarily responsible for voluntary motor control of the contralateral hand and arm[2],[3],[4]. The surgery lasted approximately 3 hours and was uneventful. The patient was discharged to his primary residence 3 days post-surgery where he recovered for three weeks prior to initiation of device testing.

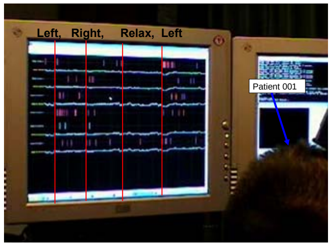
[1] Yousry TA, Schmid UD, et. al., *Localization of the motor hand area to a knob on the precentral gyrus*, Brain (1997) 120, 141-157.
[2] Seitz RJ et. al., *Plasticity of the Human Motor Cortex, Brain Plasticity*, Advances in Neurology, 73:321-333.
[3] Kleinschmidt A, et. al., *Somatotopy in the Human Motor Cortex Hand Area. A High-Resolution Functional MRI Study*., European Journal of Neuroscience, 1997, 9:2178-2186.
[4] Sanes JN and Donoghue JP, *Plasticity and Primary Motor Cortex*, Annu. Rev. Neurosci, 2000, 23:393-415.

Device Safety

Connector & Surrounding Skin 3 Months Post-Surgery

There were no post-surgical complications. No adverse events or other study-related complications have been reported. Safety assessments include daily checks of connector, weekly nurse visits, and monthly physician exams including neurological and mental status exams.

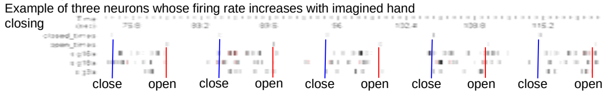
Preliminary Device Efficacy



Device testing began on July 12, 2004 and continues at present, with more than 20 sessions being completed.

Single-unit neuron recordings from motor cortex have been made over multiple sessions. The BrainGate System has been able to measure and record spike activity with a signal to noise >2.

Data Sample 7/26/04, 3:32:27 PM
Example of three neurons whose firing rate increases with imagined hand closing

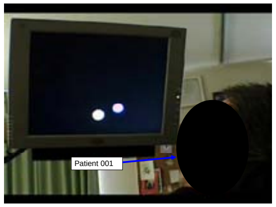


The patient is able to modulate or control neuronal activity. On multiple occasions, neuronal activity was increased when the patient was instructed to imagine moving his left hand and/or arm (see figures above).

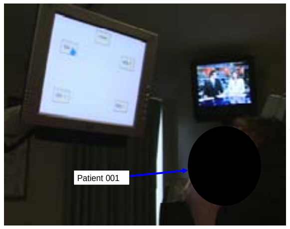
Neural Cursor Control Performance Over 4 Weeks

Center-Out Task	Pt. > Control	Pt. ≤ Control
Number Sessions	7	1
Percent Sessions	87%	13%

Significance Using Student's T Test at 0.01.
Light Blue: Neural Cursor controlled with thought
White: Target generated on computer screen



In 7 of 8 sessions conducted over 4 weeks, the patient reached 80 targets on the screen per session, significantly better than a control simulation. Instant control of the cursor was achieved without reported difficulty or significant level of concentration. The cursor was used in predefined tasks while the patient was speaking.



The patient used his neural cursor for environmental control. In combination with infrared technology, he turned his television on/off, change channels and adjust volume (see figure) - preliminary proof of principle that the technology may become a useful medical product.

Future Directions

The study will be expanded to additional sites and patients. A wireless version of the device is in early stages of development.

CAUTION: Investigational device. Limited by Federal (USA) law to investigational use – only being studied in USA.