Limits of brain–computer interface

Case report

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✓ Most patients who are candidates for brain–computer interface studies have an injury to their central nervous system and therefore may not be ideal for rigorous testing of the full abilities and limits of the interface. This is a report on a quadriplegic patient who appeared to be a reasonable candidate for intracranial implantation of neurotrophic electrodes. He had significant cortical atrophy in both the motor and parietal cortical areas but was able to generate signal changes on functional magnetic resonance images by thinking about hand movements. Only a few low-amplitude action potentials were obtained, however, and he was unable to achieve single-unit control. Despite this failure, the use of field potentials offered an alternative method of control and allowed him some limited computer interactions. There are clearly limits to what can be achieved with brain–computer interfaces, and the presence of cortical atrophy should serve as a warning for future investigators that less invasive techniques may be a more prudent approach for this type of patient.

KEY WORDS • brain–computer interface • motor cortex • neuron firing pattern • neurotrophic electrode

SCIENCE fiction writing throughout the twentieth century is replete with multiple references to brain-controlled devices and machines with “brains.” Whether it’s *Forbidden Planet*, *Star Trek*, or *Star Wars*, artificial intelligence and the brain–machine interface have remained attractive illusions. Artificial intelligence proceeded to enter the culture much more quickly with the advent and rapid development of computers. The brute calculating power of artificial intelligence was demonstrated in such trivial pursuits as the defeat of chess World Champion Garry Kasparov by IBM’s *Deep Blue* in 1997. However, true intelligence and insight still is lacking.

Progress on the brain–machine interface was started by working backward. Throughout the last century, stimulation of the brain revealed interesting aspects of how machines could control brain activities. Classic demonstrations of this were developed by Dr. Jose Delgado, who was able to stop a charging bull with electric current generated at specific sites within the brain.¹² The stimulation would not harm the animal, yet gave at least the illusion of behavioral control. A more practical extension of this eventually developed into the deep brain stimulator, which is capable of controlling a variety of abnormal movements and is beginning to be applied to epilepsy, pain, psychiatric conditions and other diseases.²

The development of noninvasive techniques has opened the possibility of brain–computer interface by indirect

means. The direct brain–machine interface seemed doomed for the next century, but in 1998, it suddenly became a reality.¹⁴ These studies were an outgrowth of a great deal of work on primates over a long period of time, and demonstrated the ability of single neurons to change their firing pattern over time in a plastic manner.^{13,16,18} The ability to record signals from the same neuron over a long period of time led to speculation that the neuronal activity of an individual could be used to control machines. The obvious machine to control was a computer. The obvious first approach would be to restore communication to the patient who has lost that ability.

First Two Cases

Case 1

In the first patient in whom the interface was attempted, we proved the principle that electrodes could be implanted and receive signals, and that the patient could control those signals through an auditory feedback in response to commands.¹⁵ To succeed in that effort, it was believed essential to demonstrate that there was brain activity still present, even though motor function was absent. An fMR imaging study clearly demonstrated in this patient the ability to generate activity in the hand area that was no longer functional. Although she was quadriplegic, the patient was able to increase activity by thinking about moving her hand, and by relaxing her concentration she was able to decrease electrical activity in an electrode implanted in the hand area of her motor cortex, as demonstrated on fMR imaging.

Abbreviation used in this paper: fMR = functional magnetic resonance.

Case 2

In the next patient, the logical progression of taking those signals, identifying individual ones, and using those to control a computer through movement of a cursor was followed. This patient succeeded in an extraordinary way, leading to an incredible amount of interest within the field.^{8,20,22,25,31} In the initial paradigm, he was told to stop the cursor over large icons to generate a standardized computer-generated voice response. The quality and control of the signal improved with use, as has been confirmed in other studies.¹¹ Subsequently, a screen with a typewriter keyboard allowed him to produce short phrases and eventually short sentences. Although initially he was totally locked-in, he had partial recovery on the side ipsilateral to the electrode. Whether this was because of the increased activity within that area of the brain or in spite of the electrode introduced in that region is unknown. Nevertheless, very interesting data was obtained before his death, which occurred due to complications from his multiple metabolic and physical problems.^{6,15,17} Despite the successes, there has also been a notable failure. It is from this failure that we must learn, and that is the objective of this report.

Research Methods

As part of an ongoing research project that was approved by the Food and Drug Administration, a series of patients were evaluated as potential candidates for implantation of the neurotrophic electrode (Neural Signals, Inc., Atlanta, GA). Surgeries were performed at Emory University after receiving Internal Review Board approval and informed patient consent.

Case Report

History. This 38-year-old man had a 10-year history of progressive, spastic quadriplegia from a factor-Q deficiency. At evaluation, he was able to communicate only through eye blinks and head nods under specific circumstances with a communication board. Although able to breathe on his own, he was unable to speak and frequently had pulmonary problems. A percutaneous gastrostomy tube had been inserted for his nutrition and medications. He required 24-hour nursing care and resided in a convalescent home. Both a living will and power of attorney had been established. He had heard about investigational procedures that attempt to improve communication in patients who lack the ability to communicate by normal means. He had a great deal of familiarity with computers and was quite interested to participate in this program.

Examination. After initial evaluation, it was decided not to proceed with surgery because of marked atrophy in the primary motor and parietal areas (Fig. 1) and an apparent inability to communicate adequately with the patient. On appeal, it was emphasized that communication during the initial evaluation had been suboptimal due to technical problems, and that on the fMR image he did demonstrate increased signal in what was presumably the arm area during imagined arm movements. On further review, it was clear that the patient's communication skills were better than previously assessed. On this basis, surgery was performed.

FIG. 1. Axial fMR image obtained in a patient with spastic quadriplegia, demonstrating significant sensorimotor cortical atrophy.

Operation. A right frontal craniectomy was performed over the hand area of the motor cortex as identified on fMR imaging by using Stealth imaging guidance. Two neurotrophic electrodes and transmitters were implanted. It was noted that the cortex was very gliotic. To provide adequate space for the transmitters, one device was placed on the left, and the outer cortical bone and dipole were removed bilaterally beneath the transmitters with a high-speed drill. Cranioplasty was used to secure the connectors and electronics as well as to provide a layer of protection over the top of them. There were no intraoperative complications and the patient was taken to the intensive care unit after surgery.

Postoperative Course. There was some difficulty with the extubation due to the patient's long-standing respiratory insufficiency, but he was successfully extubated on postoperative Day 1. Postoperative x-ray films demonstrated bibasilar atelectasis, which was managed with aggressive pulmonary toilet. Physical therapy, nutritional consultation, and speech therapy were performed during the postoperative recovery period. On postoperative Day 4, the patient was discharged in stable condition. Prophylactic antibiotic drugs were used for 10 days and the remainder of the postoperative course was uneventful.

Brain-Computer Interface. Although signals could be obtained from the neurotrophic electrodes, the number and characteristics were abnormal compared with previous patients. The ability of this patient to control the signals was minimal. Because he was not able to interface with the computer successfully, intracranial local field potentials were obtained that allowed computer interactions.¹⁷ The patient's local field potential signals were transmitted wire-

lessly to a receiver and translated by computer software into computer cursor movement for a virtual keyboard. This was useful but very limited in its capabilities.

Discussion

Brain–computer interfaces have a great potential for allowing patients with severe neurological disabilities to return to interaction with society through communication and prosthetic devices that control the environment as well as the ability to move within that environment. Interest in this area has dramatically increased, but a great deal remains to be discovered and a great number of problems need to be solved. What exactly is the limit on which types of neural signals can be obtained and controlled by the patient? In the present case, the patient was highly motivated and was very familiar with the paradigms, but still was unable to have a successful interface.

Many types of wires have been inserted into the brain to record neural activity,^{1,5,24,26,28–30} but there is only one biomechanical electrode that is integrated into the neuropil. The neurotrophic electrode was invented by Philip Kennedy, M.D., Ph.D., and is described in detail elsewhere.^{12,14} Briefly, it consists of a permanently implanted conical glass electrode through which neuronal processes can grow. The cone contains gold contact recording wires inserted through its wide end. These wires differentially record the electrical activity of the ingrown neuronal processes (axonal and dendritic).¹⁸ Before implantation, neurotrophic substances or peripheral nerve fascicles are placed inside the cone. Autologous sciatic nerve was initially used as the attractant for axonal growth, based on the work of Benfey and Aguayo,³ who showed that Schwann cells from the sciatic nerve would induce axonal sprouting from the underlying neurons when placed in rat cortex.

The key feature of this electrode compared with any other is that instead of placing the electrode's metal recording tip in the neurons, the neuronal processes grow against the electrode tip and are held there as a bridge of tissue isolated within the glass cone. After a few weeks, processes grow in from surrounding neurons and become myelinated. Because the tissue grows through the cone and anchors it in the cortex, the recording wires in the device move with the tissue being recorded during normal movements of the brain, thus providing signal stability. The actual duration for which recordings can be made has not yet been determined, but we have recorded individual units for long periods of time; up to 19 months in monkeys and 4 years in humans.^{6,13–16,17,18} Although they were few and of low amplitude, this patient did have continuous neuronal signals so that the electrode did what was expected.

Single-unit conditioning is the key to implementing real-time brain–computer interfaces in this paradigm. In 1973, Fetz and Baker⁹ demonstrated in monkeys that one neuron could be conditioned to fire and another to suppress firing. This finding supports the suggestion that not only can the desired neurons be conditioned to fire at specific rates, but also that undesirable neurons can be suppressed if they are contributing to unwanted background activity, thus physiologically improving the signal-to-noise ratio. Burnod, et al.,⁴ confirmed that conditioning of motor neuronal firings in monkeys is possible during task-specific conditioning.

Multiple, precise control functions can be achieved by the isolation of independent single units.

Wyler, et al.,³⁵ confirmed that monkeys could control firing rates within predetermined firing ranges or levels (expressed as the modal interspike intervals of unit firings). Wyler³² also demonstrated that when pairs of units were recorded and a reward was contingent on the firing rate of one of the pair, the other unit's firing rate did not covary with the firing rate of the conditioned unit. This result, in addition to those of Fetz, et al.,¹⁰ suggests that two units can be conditioned separately, especially if they are related to different movements or separate aspects of one movement (for example, agonist/antagonist pairs). The monkey experiments conducted by Kennedy and colleagues^{13,16} provide evidence that recordings can now be made of units that fire reciprocally. In addition, longer recording times are available to us than were available to earlier workers, and this persistence should provide the time needed for thorough testing of all recorded units.

The work of Wyler and colleagues also showed that closed-loop control was required for operant conditioning to occur. That is, if the spinal cord dorsal columns were transected at the C1–2 level, operant conditioning was diminished but not lost.³³ If the monkey's contralateral ventral roots were sectioned, however, operant control was totally lost.³⁴ This provides evidence against open-loop control. However, the role of the visual and auditory senses as compensatory means of closing the loop was not investigated systematically. These results have important implications for all patients, because their lesion would leave an open feedback loop. Nevertheless, it has been shown that a well-motivated paralyzed human can condition units by using auditory and visual feedback^{14,15} via internal hemispheric, cerebellar, and/or brainstem loops.

Why then did the patient in this case fail to control his firing patterns enough for them to be useful for brain–computer interfacing? We may never know for sure. The degree of brain atrophy in this patient was unusually high; he clearly had more atrophy than was seen in previous patients. Although he did have areas of signal on fMR imaging, these were not nearly as robust as those in previous patients. Also, at the time of surgery, the degree of gliosis certainly suggested that very few neurons were left. Nevertheless, signals were obtained. The primary problem may be that in addition to motor cortex atrophy there was parietal cortical atrophy, leading to concerns about sensory feedback and plasticity changes. There was a 4-month period before signals could be obtained, and in that time there may have been changes in the ability to control those units.

We put a lot of faith in the fact that intended thought could be translated into action as long as we had a confirmation on the fMR imaging studies. If we had used other techniques or different sites, we might have been more successful. There was brain atrophy in the first patient in whom this electrode was used,¹⁴ as could be expected,^{7,19,23,27} but it was mild and more restricted to the motor cortex. Whatever the cause of failure in the patient in the present case, it should serve as a warning that marked sensorimotor atrophy should be considered a contraindication for attempts at direct motor cortical–computer interfacing.

Local field potentials or electrocorticographic signals are another alternative signal source that do not penetrate

the cortex and have higher spatial resolution than electroencephalographic signals.²¹ The local field potential signals from the most successful patient, the one in Case 2, were able to be used in a crude manner to control the finger movements of a cyber hand.¹⁷ Thus, although there are many advantages to be had by using the neurotrophic electrode, its utility remains to be determined, as does the identification of other sites that may be useful. A great deal of improvement in the technology is needed, but the key to successful brain-machine interface will always be patient selection.

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