Mind over Matter

Brain-driven prostheses move from science fiction to science

By DAMARIS CHRISTENSEN

Blinking is neither the fastest nor the most accurate way to communicate. It was, however, the only way left for Jean-Dominique Bauby, editor-in-chief of France's Elle magazine. He suffered a stroke in 1995 that left him almost totally paralyzed, yet he was determined to write a book. Bauby dictated his story by having a colleague recite the alphabet to him and then blinking his left eyelid to select each letter of each sentence.

"Something like a giant invisible diving bell holds my whole body prisoner," he wrote in *The Diving Bell and the Butterfly* (Knopf), published just before he died in 1997. In the book, he recorded the difficulties of communicating with his friends, family, and doctors.

As many as a million people in the United States are locked inside their bodies the way Bauby was. They retain full control of their minds but can't breathe, eat, or move on their own because of injury or disease. Several researchers are looking for ways for these so-called locked-in patients to communicate.

The use of technology to overcome disabilities spans human history, ranging from simple crutches to modern prosthetic arms and hands that can move and grip with remarkable precision. However, these external devices only go so far. For years, science fiction writers and some scientists have dreamed of compensating for damage by connecting a person's brain directly to a prosthetic device or a computer running one. Bauby's task would have been easier if such a brain-to-computer link had been available to him.

Despite the appeal of such connections, hooking into the brain is no easy task. Even the simplest of everyday movements requires complex computations. The brain is constantly making calculations and sending out signals to hundreds of muscles in healthy arms, hands, legs, and feet.

Researchers have long thought that it should be possible to tap into the electric signals produced by nerve cells, or neurons, and use them to control the shifting path of a cursor on a computer screen, the movement of a wheelchair, or the grasp of a robotic arm. The problem is that no one yet fully understands the complex electrical signals the brain sends, says Eberhard E. Fetz of the University of Washington School of Medicine in Seattle. In addition, neural signals have turned out to be far from easy to intercept.

The advances in miniaturization that have made laptop computers commonplace, however, have also allowed scientists to eavesdrop more accurately on the brain. While complex brain-to-computer interfaces still lie many years in the future, a few recent studies have made direct neural control of computers or prosthetic devices appear more promising.

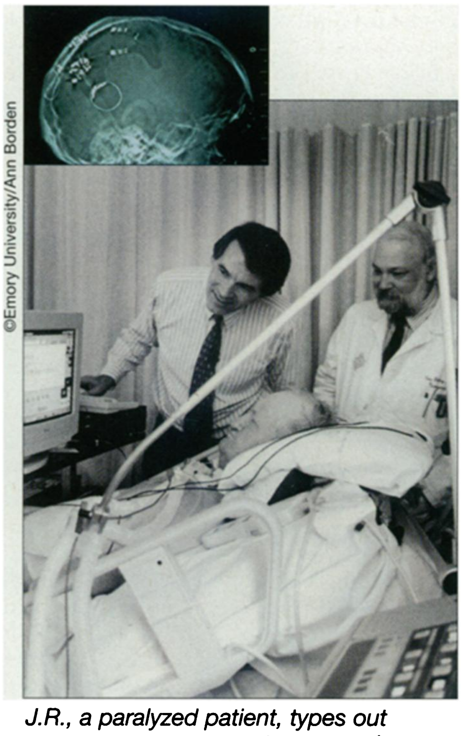
Two groups have worked with locked-in patients, helping a few to communicate with the world by moving a cursor on a computer screen. Another group has trained rats to move a lever not by using their muscles but by producing certain kinds of nerve signals in their brains.

"Extracting signals directly from the brain to directly control robotic devices has been a science fiction theme that seems destined to become fact," Fetz says.

One approach to robotic control is to tap into electrical noise generated by the brain's normal activity. Electrodes on the scalp can measure the tiny amounts of current generated by nerve cells in the brain as they fire. People can use biofeedback techniques to learn to control the patterns of these electroencephalograms, or EEGs. Because it does not require surgery, this approach is considered safe. Learning to control the patterns is time-consuming, however. Moreover, some researchers say that EEGs may not contain enough information to enable patients to quickly and gracefully manipulate an object in several dimensions.

A German team reported in the March 25 Nature that two locked-in patients have learned to operate a spelling device by controlling their EEG brain responses. Both patients suffer from advanced amyotrophic lateral sclerosis, or ALS, and can't breathe or eat on their own.

The German device flashes half of the alphabet up on each side of a computer screen. The ALS sufferer selects one half or the other by controlling his or her EEG signals. The patient thus repeatedly divides the alphabet until a single letter is chosen.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J.R., a paralyzed patient, types out messages on a computer screen by activating nerve cells near electrodes implanted in his brain. Inset shows the electrodes in J.R.'s head.

Writing in this way is not much faster than Bauby's painstaking technique—a person can select about two letters each minute—but the system is accurate and allows these people to communicate on their own, says research leader Niels Birbaumer of the University of Tüebingen in Germany. "Even a slow spelling device is helpful," he says.

In similar work, Jonathan R. Wolpaw at the State University of New York at Albany has shown that normal and paralyzed volunteers can use other types of EEGs to control a cursor on a computer.

In another approach, scientists implant electrodes directly into a person's brain to detect signals from neurons in the area that once controlled an arm. A research team based at Emory University in Atlanta has inserted tiny electrodes, each surrounded by a glass cone, into the brains of three locked-in patients. The cones contain proteins that encourage nerve cells to grow near the electrode. Bursts of activity detected by the electrodes can drive a cursor across a computer screen. Each electrode may measure the activity of a few nerve cells. So far, the researchers have implanted just one or two electrodes into each patient.

One patient learned to control a cursor but died of ALS just 2 months after Bakay implanted the electrodes.

Another patient, named J.R., uses the cursor to select different icons on a screen. Each conveys a different message—for example, that he's thirsty. The researchers have also copied a computer keyboard onto the screen so can slowly type out messages.

The technology has its limits. Currently, J.R. can control the cursor for just under an hour each day. It's hard for him to maintain the focus required to move the cursor, and he is very sick and tires easily, says Roy A.E. Bakay of Emory.

"This is a lot of work for him, but this is one of the few ways he can get messages out," he says.

A small but promising study in rats uses tiny electrode arrays—each electrode in contact with a different neuron. The results suggest that animals can directly control a robotic device with their brain activity. Researchers in Philadelphia and Durham, N.C., implanted the arrays in the motor cortexes of half a dozen rats. This is the area of the brain involved in movement.

The researchers measured the brain activity of the normal, healthy rats as they learned to push a lever attached to a robotic arm. If the animals pushed the lever hard enough, the robotic arm carried water to a place where the animal could drink.

The researchers then fed the rats' brain signals to a computer, which identified a burst of electrical activity released just before an animal pushed the lever. Each rat produced similar but not identical signals. The researchers then devised a program to move the robotic arm as soon as a rat's brain made these electrical signals. Some rats learned over time that they didn't actually have to push the lever to get the robotic arm to move, says research leader John K. Chapin of the MCP Hahnemann School of Medicine in Philadelphia.

"Previously, researchers have focused on single neurons in the motor systems. We took a broader look," he says. They found that a larger sample of the many neurons involved in movement eased the task of finding reliable, detectable signals to trigger a prosthetic device.

Although many technical hurdles remain, Chapin says, "we believe we have all the key elements to be able to make this technology one that could, in the not-so-distant future, make a substantial difference in the lives of people who are limited in their physical abilities but not their neurologic capabilities."

This is the first study showing that simultaneous recordings from a number of neurons can immediately trigger movement of an external device, Fetz says. "It's surprising that [in rats] neural activity could be dissociated from movement," he says.

Because of their safety, devices that externally measure EEGs may initially be more widely used than electrodes implanted in the brain, says William J. Heetderks of the National Institute of Neurological Disorders and Stroke in Bethesda, Md. Despite Bakay's success, widespread use of implanted electrodes in humans is probably at least a decade away, Heetderks says.

There is a large leap from showing that rats can move a robotic arm back and forth to demonstrating that humans can continuously operate a prosthetic device to mimic a human arm, or even can move a wheelchair, Fetz says.

The tiny electrodes used by Bakay and Chapin stem from a quiet revolution in miniaturization of bioelectronic components. "We don't yet know what the limitations of this new, emergent technology are" says Richard A. Normann of the University of Utah in Salt Lake City.

"Chapin's work is not enough to prove that arrays of electrodes implanted in the brain can control a robotic arm in a graded, proportional fashion," he says. "One of the remarkable things about humans and animals is that they can move so gracefully, and we should strive for that."

Bakay and his colleagues say that their lab's electrodes are sensitive enough to measure subtle differences in the rate at which nerve cells fire. If so, the devices might work as dimmers rather than simple on-off switches. Such proportioned control is critical if paralyzed patients are to accurately tilt a hospital bed, run a wheelchair, or move a prosthetic arm, he says.

"Right now, you can walk your way through the world without thinking consciously about what you are doing," says Normann. "It would be nice for a completely paralyzed person to likewise have multiple degrees of control over their movement—for example, to be able to make a wheelchair go faster and turn left all at the same time."

Many challenges lie ahead. For humans to be able to produce complex external movements, researchers will have to establish links with many more neurons than they have in the experiments so far. That task will require smaller, longer-lasting electrodes, and surgeons will have to place the devices more precisely. To register brain signals over a long period, electrodes must not move, cause scarring, or repel growing nerve cells, says Heetderks.

Researchers may have to look beyond the primary motor cortex to measure enough neurons to control complex movement, notes Chapin.

One possible problem with using signals from the primary motor cortex emerges from some studies showing that the brain reconfigures itself once sensory input has changed, says Miguel A.L. Nicolelis of Duke University Medical Center in Durham, who worked with Chapin. After an injury, areas of the brain that used to control the limb that became paralyzed may degenerate or rewire themselves to control other parts of the body. Such rewiring might mean that the implanted electrodes are not measuring electrical activity from neurons that would be involved with movement of the limb. The changes may make it less likely that patients can operate a prosthetic device by simply thinking about moving a missing or paralyzed limb.

Nicolelis hopes to address the possible rewiring of the brain as part of his current study of owl monkeys. Because monkeys have bigger brains than rats, however, it may be harder to identify neurons involved in a particular kind of movement, he says.

Richard A. Andersen of the California Institute of Technology in Pasadena has a possible solution to the motor cortex's degeneration or rewiring. In new experiments, he plans to target a different area of the brain called the posterior parietal cortex. This part of the brain seems to be responsible for taking in sensory information and for planning movements, he says.

Andersen and his colleagues have implanted in monkeys electrodes similar to those used by Chapin's group. They hope to train the monkeys to move images of prosthetic arms on a computer screen. From there, it's just a small step to actual movement of a robotic prosthetic device, says Andersen.

"The eventual hope is to use these technologies to assist patients who are paralyzed, but the long-term safety and reliability of the devices must be proven first," Heetderks says. "When you get up in the morning, you expect your arm to work the same way it did yesterday."

Another issue for researchers is portability of any EEG or neuron-monitoring devices. All strategies for monitoring brain activity, so far, require tethering patients to equipment.

Despite the challenges that remain, researchers hope that the phrase *mind over matter* will eventually become more than a cliché. "Right now, we're just taking a few baby steps," says Bakay. "I don't think anybody yet knows the best way to do this, and maybe we will eventually use aspects of all this work."

Even imperfect steps offer great benefit to severely paralyzed patients, the researchers point out. Birbaumer's first patient spent 16 hours writing a thank-you note to him, one letter at a time. □