Mind Over **Muscles**

When two emerging technologies meet, paralyzed people can move their limbs—just by thinking about it.

BY VICTOR D. CHASE

ON A COLD DAY IN LATE 1998, JIM JATICH, 51, SAT AT A table in Cleveland, Ohio's MetroHealth Medical Center and donned a cloth beanie with dozens of wires protruding from its surface. He had been practicing twice a week over several months for this moment, and he was so intent on the task at hand that the magnitude of it didn't sink in until he emerged from the hospital later in the day.

"That's when it hit me," he recalls. "I got tears in my eyes, turned to my sister, and said, 'Damn, I actually moved my hand by thinking about it.'"

Jatich is a quadriplegic who lost the use of his hands and legs in a swimming accident 21 years earlier. But in a series of first-of-a-kind experiments that hold out the promise of a more normal life for the handicapped, researchers led by biomedical engineer P. Hunter Peckham of Case Western Reserve University have succeeded in reestablishing the damaged connection between Jatich's brain and body. Their strategy: combine two cutting-edge technologies into a system that uses brain waves to move paralyzed limbs.

The more advanced of the two technologies is functional electrical stimulation (FES), in which electrodes implanted under the skin are used to choreograph movement in the muscles of paralysis victims. For several years, Jatich has used a commercially available FES system known as Freehand; this "neuroprosthetic" allows him to open and close his hand and manipulate everyday objects like pencils and telephones. Normally, Jatich triggers his Freehand's mechanism with a shrug of his shoulder. Now, by combining FES with a second, much earlier-stage technology known as brain-computer interface (BCI), the Cleveland team has given Jatich rudimentary control over the Freehand using his brain waves alone.

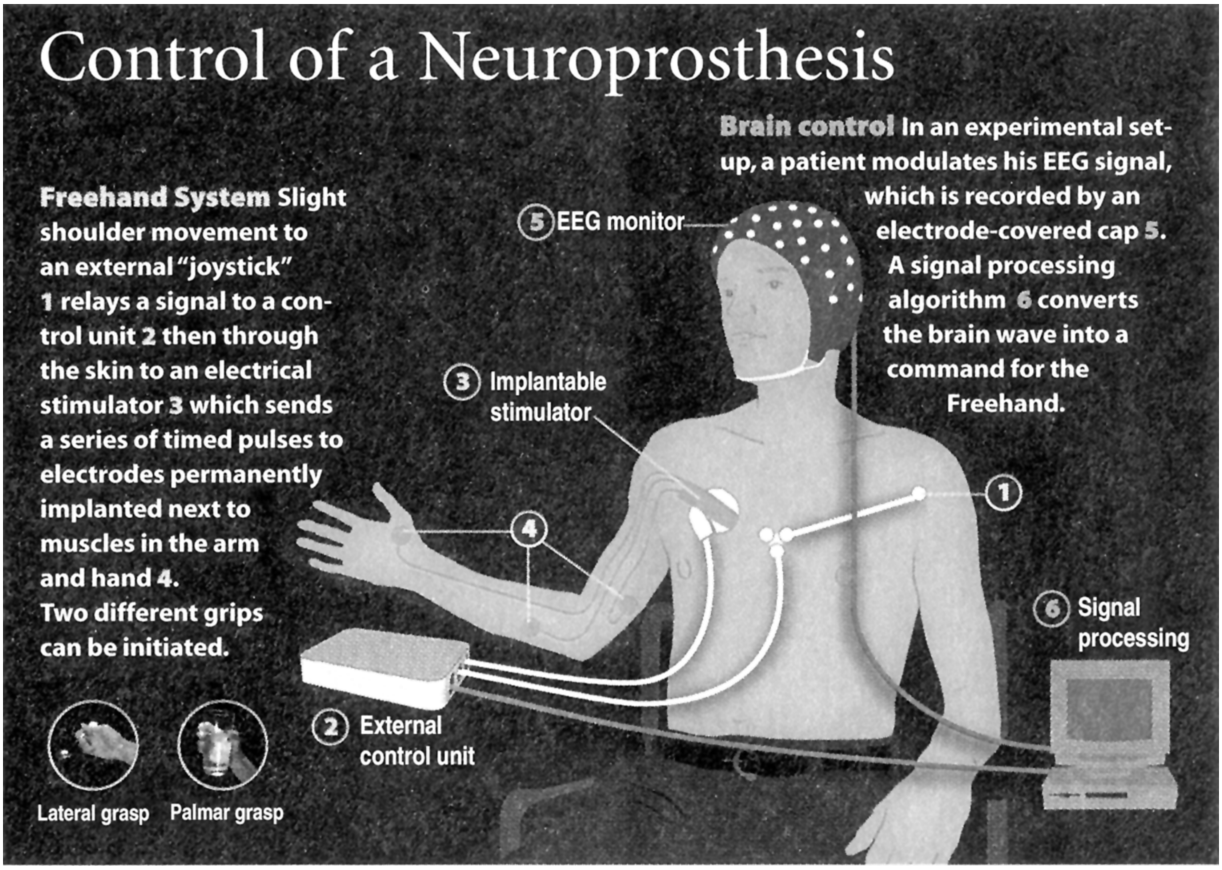
Although this "thought-translation" system is still far from practical, other research teams are now pressing hard to develop implants able to capture superior control signals directly from the brain's motor cortex, the area where volitional movement is thought to arise. In what seems like a page torn from a William Gibson novel, such cortical implants have already been used to restore communication to two patients "locked-in" by severe paralysis (*see box: "Tapping the Life Within"*). And some scientists believe that using these signals to control robotic arms or FES systems may no longer be a distant prospect. "We're getting to a point where developments in neurosurgical and electrophysiological procedures and in microelectronics are making this feasible," says Miguel Nicolelis, a neurobiologist at Duke University. "This is not science fiction anymore."

Getting a Grip

PREVIOUS TO THE EXPERIMENT IN CLEVELAND, THE LAST time Jatich had thought his hand into motion was on a hot summer night in 1977. He and some friends had spent the day housepainting in Akron, Ohio, and decided to cool off with a swim in nearby Portage Lake. "I was the last one to dive in and I hit something," Jatich recalls matter-of-factly. "I saw stars and knew right away what happened. I was stunned and sank to the bottom, my face in seaweed."

There's still no cure for paralysis. But the merger of neuroprosthetics and brain-computer interfaces could offer a more normal life for some patients.

In that split-second, Jatich went from being a healthy junior engineer at tire-maker Firestone to a C5–C6 quadriplegic. The spinal damage, between his fifth and sixth cervical vertebrae, left Jatich's legs totally immobilized, though he retained some shoulder and arm movement, and could raise his left wrist. According to the National Spinal Cord Injury Statistical Center, accidents cause about 10,000 spinal cord injuries in the United States each



year. Of the estimated 200,000 paralysis victims in the United States, about half are paraplegics who've lost sensation and movement in their legs, and half are quadriplegics suffering from paralysis in all four limbs.

As he lay convalescing in Cleveland's Highland View Rehabilitation Hospital, Jatich was approached by Peckham, then a young Case Western Reserve scientist seeking a volunteer to work with him on an FES system for restoring hand motion. Patient and researcher were embarking on lifelong quests for new spinal cord injury treatments. Jatich was inspired by necessity. Peckham's motivation originated in a magazine article he'd read in college about mechanical heart valves, which opened his eyes to the notion that "engineers can do something to help mankind." In graduate school, Peckham fell in with a group of biomedical engineers involved in early efforts to use electrical stimulation to restore function to skeletal muscles; "I became fascinated with it," Peckham says, "and that was the last time I thought in depth about the vascular system."

FES experiments in the late 1970s and early 1980s were less than elegant. In his work with Peckham, Jatich saw wires threaded through his wrist with a needle in a trial-and-error hunt to provoke movement in the correct muscle groups. The protruding electrodes were connected to a computer in Peckham's lab, which fired off signals to the muscles in various configurations. The computer was large and stationary, and the electrodes broke frequently, yet Jatich's hand did move, and he was able to pick up objects, though his control was far from adequate.

It took two decades for Peckham to perfect his invention, now known as Freehand, and which in 1997 became the first implantable FES device to receive U.S. Food and Drug Administration approval for wide use. About 160 quadriplegics now use Freehand to write, feed themselves, perform personal grooming, and, in some cases, even manually operate a computer. The Cleveland company founded by Peckham to sell the device, NeuroControl, has just raised $4.5 million in venture capital money to step up marketing of Freehand and a bladder-control device called VOCARE.

Today, Jatich uses Freehand to close his right hand by activating a "joystick" taped to his left shoulder. Pushing his shoulder forward, the joystick signals a computer carried on his wheelchair, which then sends a series of timed electrical pulses to eight platinum electrodes implanted next to nerves feeding the muscles that close his hand. Separate shoulder commands let Jatich lock the grip, or release it.

Once a person who needed help to eat and thought his career was over, Jatich is now largely self-sufficient and has even begun an in-home business creating computerized engineering drawings. "I'm using my hand again. I'm picking up a fork to feed myself, and picking up a pen to write again," says Jatich. "That's a big emotional change in my life."

Think About It

IN THE PROCESS OF DEVELOPING FREEHAND, PECKHAM turned Cleveland into the world's focal point for FES development. In 1990, he was instrumental in founding the Cleveland FES Center, a consortium of medical centers where researchers are now driving Freehand technology in new directions. Current projects include systems that allow paraplegics to stand and move a few steps on their own, research aimed at finer muscle movement using more electrodes, as well as what Peckham terms "alternative strategies for control" that can bring more natural dexterity to paralyzed people. The most dramatic of these alternatives is mind over matter: direct brain-control.

As early as the 1960s, scientists discovered that people can control certain components of the electrical signals emitted by their brains, which are recorded from the scalp as electroencephalograms (EEGs). EEGs could therefore be used to issue simple commands to electronic devices, but the technology remained largely a laboratory curiosity. It's been explored by the Air Force as a futuristic means for pilots to fly jet planes, and has more recently found a concrete application in helping patients with severe paralysis to communicate via computer.

Starting in 1997, Peckham says he and graduate student Richard Lauer began attempting to use brain-computer interface technology to "acquire information from the brain and put it into the hand of a person." Their initial subject was Jatich, who agreed to wear what looks like an oversized, electrode-studded shower cap to help the scientists learn whether EEG signals could control his Freehand system directly, without the usual shoulder controller.

Lauer and Peckham zeroed in on a component of the EEG known as the beta-rhythm, which Jatich began learning to modulate in order to move a cursor on a computer screen. Thanks to the phenomenon known as biofeedback, Jatich was able to use the cursor's movements to gain conscious control over the strength of the beta-rhythm, even though he'd previously been completely unaware of it. After a dozen training sessions, Jatich had learned to move the cursor simply by thinking of a particular direction. The next step was to convert the cursor signal into a command for Jatich's Freehand. The switchover went smoothly: Jatich soon was opening his hand by thinking of moving the cursor up. By thinking down, he closed it. Since then, Jatich has learned to manipulate objects including a glass and a fork.

Dramatic as these results are, Peckham cautions that all Jatich is doing "is using the signal to tell his hand to close. It's a very rudimentary control." Indeed, thus far, EEG-control remains slower and less versatile than the shoulder controller. For instance, because the beta-rhythm provides only a single on/off signal, Jatich still can't lock his hand into position—instead he's got to continually think "hand closed." "We're saying pick up this fork, stab something and raise it to your mouth," explains Peckham, "but if the task was eat a meal, which requires holding onto the fork for an extended period of time, we would not have the same level of success."

Still, the initial results are "fairly promising," says Bill Heetderks, a physician who directs the National Institutes of Health's Neural Prosthesis Program, which, along with the Veteran's Administration and the National Science Foundation, provides the majority of the grants that support FES and BCI research. As Heetderks points out, only about ten percent of quadriplegics have enough shoulder and arm movement to operate Freehand. He says EEG control might allow people with injuries higher on their spinal cords, like the actor Christopher Reeve, to benefit from neuroprosthetics as well.

Over the next year, says Peckham, his team will be trying to establish whether or not the EEG signal is good enough to give full movement to current Freehand users. Confident, yet cautious, Peckham notes, "We are not certain yet whether the control is, in fact, fast enough and natural enough."

Monkey See, Robot Do

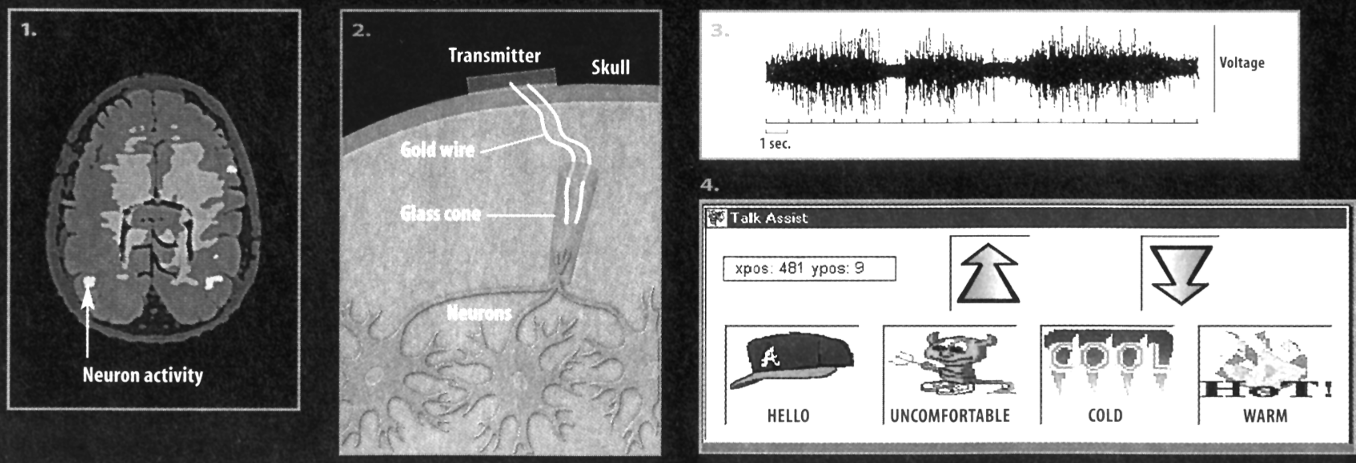
PART OF WHAT LIMITS EEG SIGNALS IS THAT WHEN ONE thinks about moving a cursor, or an arm, thousands of brain cells fire off simultaneously. Surface electrodes pick up all of the brain waves at once in a cacophony of electrical activity. That's why a growing number of researchers are working on what's termed "invasive" brain-computer interfaces. By tapping directly into the motor cortex, they hope that they can get past the EEG's cocktail party chatter to tune into individual neurons, an advance they think could be key to helping the paralyzed operate FES devices.

Already, a number of animal experiments are suggesting this is precisely the case. In a startling result published last summer in the journal *Nature Neuroscience,* Duke's Nicolelis and John Chapin, a neuroscientist at Hahnemann University in Philadelphia, reported that they had been able to get a rat to operate a robotic lever in real time via two dozen electrodes implanted in the area of the motor cortex that controls paw movement.

Several academic teams, including Chapin's as well as groups at Brown University and the California Institute of Technology, are trying to reproduce similar results in monkeys, whose brains are more like our own. So far, some of the most exciting results have come from neurophysiologist Andrew Schwartz at San Diego's Neurosciences Institute and collaborators at Arizona State University. Using dozens of hair-width electrodes implanted in the brain of a rhesus monkey, Schwartz simultaneously recorded signals from about 50 individual neurons, which he fed through a data-crunching algorithm to a robotic arm in a separate room. "And we see,"

Unlocking a Mind *(see box, "Tapping the Life Within")*

1. A functional magnetic resonance image (fMRI) of the brain shows areas of neuron activity when a paralyzed patient imagines closing his left hand. 2. Neurons grow into an electrode implanted in the active region. 3. Measurements of neuron firing rates provide a control signal that the patient uses to move a computer cursor. 4. A computer program allows the patient to communicate basic needs.



he says, "that the robotic arm moves close to the same trajectory that the monkey moved its arm." A split-screen movie of the result can be seen on the Web at http://www.nsi. edu/motorlab.

This feat is possible even though scientists still know very little about how the brain creates movement. The trick, Schwartz explains, is that although there are millions of neurons in the motor cortex, measuring the "firing rates" of just a few cells can give a surprisingly accurate picture of where and how fast the monkey's arm is moving. "It's like doing a survey. You're not going to get every person, but if you have enough samples you can get a pretty good idea of what's going on," he says.

Although Schwartz's primates were unaware of the robot mimicking their movements, he's now working on an experiment in which he'll challenge restrained monkeys to use a thought- driven arm to feed themselves. A positive outcome would be proof-of-principle that a cortical signal could give quadriplegics precise control over FES devices like Freehand. In fact, Schwartz predicts that a rudimentary brain-activated robotic arm will be ready for human use within five years.

Even a successful human test won't automatically translate into a working device. The development of invasive recording electrodes has been going on for some 30 years, but is still plagued with problems. In animal studies, signals from implanted electrodes tend to diminish over time, which may be due to scar tissue or shifting of the electrode caused by the brain's normal movement within the skull. Schwartz calls "the long-term survival of the electrodes" a key problem, and admits that the Teflon-coated stainless steel wires he uses are "really crude devices."

But improved electrodes is an engineering challenge that several teams are already looking to meet. Some of the most successful work to date has been accomplished by neurologist Phillip Kennedy of Atlanta, Ga., who was the first to implant cortical recording electrodes in a human being. And the Duke group has helped develop a matrix of 16 electrodes, just a square centimeter in area, which Plexon Inc., of Dallas, Texas, is now manufacturing. The electrodes are working well in primate experiments, but Nicolelis adds that "we need to evolve to a new generation." Already looking ahead to applications in people, Duke is designing a telemetry chip to connect to the electrode array and transmit neuron recordings to an external computer, without wires coming through the skull.

Thoughts and Dreams

DESPITE THE PROGRESS TO DATE, SCIENTISTS DON'T YET KNOW whether BCI and FES devices will ever come together to restore precise natural movement to paralyzed human limbs. For instance, even given a perfect cortical signal, FES researchers might be unable to make full use of it. Nicolelis warns that, "It's a complex problem to coordinate the muscles to produce the kind of spatial-temporal patterns you need."

And yet there is a reserved consensus among FES experts that many of the same technological innovations that are driving BCI research, in particular better microelectronics and improved electrodes, are also paving the way for an increase in the speed of FES development. As Peckham puts it, "I think you could make a pretty good

Tapping the Life Within

Imagine being wide awake and yet completely unable to move. For almost 2,500 patients in the United States who are victims of severe strokes and conditions such as amyotrophic lateral sclerosis (Lou Gehrig's disease, or ALS), this scenario is a real-life nightmare. Bound and gagged by near-total paralysis, these patients must be fed intravenously, rely on machines to breathe, and in some cases, must have their eyelids taped open so they can see. Perhaps worst of all, although they remain aware, these "locked-in" patients cannot communicate.

Over the last two years, neurologist Phillip Kennedy and his colleague Roy Bakay, a neurosurgeon, both with the Department of Neurosurgery at Emory University, Atlanta, Ga., have uncorked the thoughts of two locked-in patients with "neurotrophic electrodes" implanted into the motor cortex areas of their brains. Neurons grow into the devices—glass tubes containing minuscule low-impedance wires—allowing the researchers to measure the cells' electrical activity (*see "Unlocking a Mind"*).

The second patient, John Ray—who goes by JR—is a 53-year-old who had been a drywall contractor until a 1997 brainstem stroke rendered him locked-in. "He can laugh and cry, but he can't speak; he can't move. Yet his attitude is absolutely incredible. He's got great energy," says Kennedy, who with Bakay implanted two electrodes into JR's brain in March of 1998. Since then, their patient has learned to use his thoughts to operate a computer program designed by Georgia State University that lets him select letters and produce audible responses. Kennedy has formed a company called Neural Signals to fund further development of the technology.

Researchers in the United States and Europe have also released locked-in patients with noninvasive systems that use electrodes placed on the outside of a person's skull to pick up EEG signals. "We have several patients who are able to communicate and write letters," says psychologist Nils Birbaumer of the University of Tübingen, Germany, who works with ALS patients. Although Kennedy believes the invasive implants promise a superior signal, the results of both approaches have, thus far, been surprisingly similar—three or four characters per minute.

Although that may sound agonizingly slow, even a few words can make a big difference. "This is probably one of the most terrifying states a human being can be in," and many locked-in patients die "because of hopelessness and not because of disease," Birbaumer says. "Most of our patients are now much older than was predicted by their physicians because their psychological health is improving."

argument that we're just getting the tools available now to make substantial clinical impacts."

Today, spinal cord injury is still a condition without a cure. Yet every paralysis victim dreams one will happen soon enough to make a difference in his lifetime. Where will the cure come from? The biomedical engineering approach expressed in Freehand has already achieved what millions spent on drug research and recent scientific progress in regrowing nerve cells haven't yet: a degree of normality in the lives of quadriplegics such as Jatich. Now the merger of neuroprosthetics with brain-computer interfaces, while still in the research-prototype stage, promises another stride toward helping people whose bodies are immobile, but in whose minds hope steps lively.