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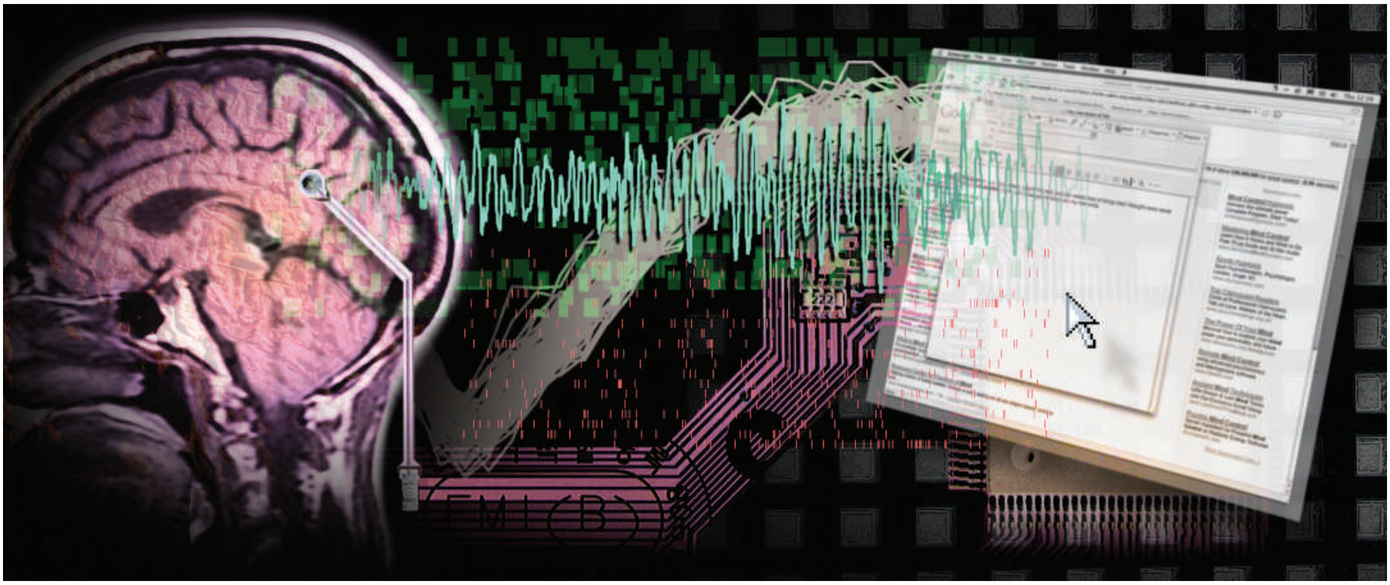

NEUROSCIENCE

Converting thoughts into action

Stephen H. Scott

There is a clear need to help people who have brain or spinal-cord damage to communicate and interact with the outside world. Progress to that end is being made with brain-implantation technology.

Using our thoughts to control a computer or robot used to be the realm of science-fiction writers. But scientists have been making concerted efforts to develop the technology required to convert brain signals into commands, to support communication, mobility and independence for paralysed people. In this issue, two papers shift the notion of such 'implantable neuromotor prosthetics' from science fiction towards reality. Hochberg *et al.* (page 164)[1] describe the first implantation of electrode arrays into the brain of a paralysed man; these allowed him to use his thoughts (motor intentions) to directly control devices such as a computer mouse. In addition, Santhanam and colleagues (page 195)[2] describe a new software approach for extracting intended actions from the neural activity in the brain of monkeys that dramatically improves the potential speed and performance of implantable neuromotor prosthetics.

Although it may someday be possible to reconnect damaged neural pathways by directing the regrowth of neurons, neuroprosthetics provide another potential approach to permit individuals with severe neurological injuries to interact with the environment. Damage to the nervous system means these individuals lose their motor control — that is, they can no longer directly control their muscles. Neuroprosthetics aim to bypass this damage by recording brain activity that reflects the individual's motor intentions. These signals are then used either to reanimate paralysed muscles using electrical stimulation, or to control physical devices directly, such as artificial limbs, computer cursors or wheelchairs. Several different approaches have been developed ranging from non-implantable technologies that record electroencephalographic (EEG) activity using removable electrodes placed on the scalp surface[3], to implantable devices that use microelectrodes to detect the activities of individual neurons[4–7].

Implantable neuromotor prosthetics build on basic research looking at the neural basis of the planning and control of movement, predominantly in monkeys. A brain region of particular interest for neuroprosthetic research is the primary motor cortex, a major region involved in controlling voluntary movements. Others include the premotor and posterior parietal cortex, which are principally involved in planning movements, providing instructions for the motor cortex to then act on. In monkeys, the activities of large numbers of neurons can be recorded simultaneously and be used to predict motor intention[4] and limb motion[5], or to move cursors on a computer screen[6,7]. Animal experimentation remains essential for testing and developing implantable neuroprosthetics, but obviously at some point the great leap into human patients needs to be made.

To this end, Hochberg *et al.*[1] recruited a man who can no longer move his limbs because his spinal cord is completely severed. They implanted an array of tiny electrodes into his primary motor cortex, and tested whether the activity of neurons recorded there could control prosthetic devices. Remarkably, the implanted electrodes allowed the patient to control a computer cursor and rudimentary movement of robotic devices (the associated videos are online in Supplementary Information[8]). This is not the first neuromotor prosthetic that has been implanted into a person — a previous experiment used a couple of implanted electrodes to generate limited horizontal control of a cursor[9]. But this study reports several significant advances.

First, even though the patient had been paralysed three years earlier, the neural activity in his primary motor cortex seemed relatively normal. The neurons were spontaneously active and the subject could modulate this activity based on instructions such as, "Move your arm". This shows that activity in this region can still be modulated by a subject's motor intentions, even though axons projecting from this region to the spinal cord have been severed and the brain region has not been used to control limb movements for several years.

Second, the calibration of the device was achieved by simply asking the subject to imagine moving his hand to track a moving cursor on the computer screen. This process took only minutes, much less than the weeks or months of training required for current non-invasive EEG systems.

Third, after this calibration, the subject was immediately able to perform, to some degree, other computer-based tasks including reading e-mail and playing simple computer games. He could also control a television and even simple robotic devices. This flexibility in the use of neural signals is notable because the user of a similar neuroprosthetic will potentially be able to control a range of devices from computers to wheelchairs.

This research suggests that implanted prosthetics are a viable approach for assisting severely impaired individuals to communicate and interact with the environment. But there have also been substantial advances in non-invasive approaches to recording brain activity that allow comparable control of cursor motion[3]. So why use an invasive technology, with all the risks related to surgery and the long-term care inherent in implantable devices, when non-invasive technologies are available?

Several differences between the neural signals recorded from invasive and non-invasive electrodes suggest that implantable prosthetics will have greater long-term potential. EEG recordings reflect the averaged activity of millions of neurons, creating a signal with limited spatial and temporal resolution. By contrast, direct recordings using hundreds of microelectrodes, each monitoring the activity of a single or a small number of neurons, can create highly complex control signals.

The potential speed of implantable neuromotor prosthetics is demonstrated by Santhanam *et al.*[2]. A common strategy for the software algorithms used to convert neural recordings into a usable output (including the one used by Hochberg *et al.*[1]) is to translate neural activity into an estimate of hand trajectory or cursor motion. Santhanam *et al.* simplified the problem by using neural activity from the premotor cortex of monkeys to predict the location of spatial targets. By optimizing for the number of potential targets and the time period used to sample neural activities, they were able to extract the correct spatial location in about 250 ms from about 100 single and multi-unit recordings. This performance corresponds to retrieving about 6.5 bits of information per second — which would allow a person to type at approximately 15 words per minute. This is substantially faster than can be done using existing implantable or non-implantable technologies.

The algorithm developed by Santhanam and colleagues is not directly applicable to neuroprosthetics because it relies on the animal's learned response to a visual stimulus. However, this approach should be easily modified for humans and be driven not by sensory stimuli, but by the patient's own intentions, much as one converts a word into a series of key presses on a computer keyboard.

Many considerable problems must be addressed before this technology can be put to regular clinical use. It is not clear for how long the very fine microelectrodes can be used to record neural activity. Patients with spinal-cord injuries are often young and would need to use these technologies for many decades. Moreover, the device used by Hochberg *et al.* involved passing a large bundle of wires directly through the skin to a connector attached to the skull, and all signal processing was done by an external computer. Wires passing through the skin promote infection, so for a clinical device, the power into and neural signals out of the implant must be transmitted using telemetry across the skin. Unlike Hochberg and colleagues' prototype device, a clinical implant would therefore have to minimize data transfer by carrying out a considerable amount of signal processing within the implanted component of the neuroprosthetic. However, these types of problem are not insurmountable; indeed, they were overcome during the development of cochlear implants — the most successful neuroprosthetic so far (Box 1).

Animal-based studies tend to have three degrees of control or fewer because implantable neuromotor prosthetics are developed to predict an animal's movement when it reaches towards a spatial target. Human neuroprosthetics can use many more degrees of control because the level of involvement of the subject in calibrating the device will be so much greater — for instance, if the subject is asked to move each of their individual joints separately. As shown by Santhanam and colleagues, other control signals can be created based only on the patient's intentions but not actual actions. Importantly, neural processing in motor cortical regions is highly adaptable[10], probably reflecting our ability to acquire novel motor skills throughout life. So, using neuroprosthetic technologies should actually shape and modify brain processing to improve control of each prosthetic technology and facilitate the ability of paralysed individuals to convert their motor intentions into purposeful communication and interaction with the world. ■

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Box 1 | Cochlear implants — the first successful neuroprosthetics

Human speech creates a complex spatio-temporal pattern of acoustic frequencies that is converted into neural activity by thousands of hair cells in the cochlea. Genetic factors, various diseases and pharmaceutical drugs can damage these cells, resulting in deafness (sensorineural hearing loss).

In the 1960s, implants began to be tested with the aim of using electrodes positioned within the cochlea to stimulate the neurons that are connected up to dysfunctional hair cells. Originally the devices included only a single stimulating electrode, but further advances led to four and then 22 electrodes being used by the 1980s. These devices have an external headpiece and processor that pick up sound from the environment and convert it into patterns of digital signals. These are transmitted through the skin to the implant attached to the skull and converted into a pattern of stimulation for each electrode.

It had been assumed that speech perception required much of the detailed pattern of acoustic frequencies to be sensed by the hair cells[11], suggesting that such a small number of independent sites of stimulation on the cochlea would provide only modest improvements in hearing — the initial devices were developed merely with the hope that they would aid lip reading. In practice, however, implant users were often surprisingly successful at understanding speech, forcing a re-evaluation of theories on speech perception.

More than 100,000 people now have cochlear implants, and many of these are young children who are given implants before they learn to speak to ensure the best development of auditory and speech skills. I can testify to the success of this neuroprosthetic technology and the improvement it makes in the quality of life of deaf individuals, as my son has a cochlear implant. He nonetheless attends classes in a regular school and has average to above-average auditory and speech skills compared with 'hearing' children his age.

It may be that other neuroprosthetic devices will surprise us by the extent of their usefulness, and provide unexpected insights into how the brain processes thoughts. **S.H.S.**

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