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State-of-Science Review: SR-E29, Brain-Computer Interfaces and Cognitive Neural Prostheses

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Abstract

This review looks at recently developed technology that allows engineers to record signals from the brain, identify the subject's intent, and allow the subject to control prosthetic devices or communicate with others. It explores the current status of the technology, focusing on studies aimed at developing assistive devices for human subjects. Lastly, it reviews the impressive accomplishments to date, as well as limitations of the technology that will need to be overcome to enable the development of fully practical assistive technologies.

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Making the most of ourselves in the 21st century

State-of-Science Review: SR-E29

Brain-Computer Interfaces and Cognitive Neural Prostheses

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Summary

This review looks at recently developed technology that allows engineers to record signals from the brain, identify the subject's intent, and allow the subject to control prosthetic devices or communicate with others. It explores the current status of the technology, focusing on studies aimed at developing assistive devices for human subjects. Lastly, it reviews the impressive accomplishments to date, as well as limitations of the technology that will need to be overcome to enable the development of fully practical assistive technologies.

1. Introduction

The neuroscience revolution has given us the ability to craft new kinds of assistive devices for profoundly disabled individuals which interact ever more intimately with the brain. From at least 1965, biomedical engineers have been crafting devices that allow paralysed muscles to contract by applying electrical currents to the intact peripheral motor nerves innervating them (Vodovnik et al., 1965; Peckham, 2005). For many years biomedical engineers have been developing eye-motion-tracking devices to allow severely paralysed individuals to type words into a computer and perform other tasks.

It is now becoming possible to control prostheses of this kind, and other kinds as well, using advanced techniques that infer intent of the subjects from signals recorded directly in the patient's brain, bypassing parts of the brain or spinal cord that are damaged by diseases such as amyotrophic lateral sclerosis (ALS), stroke or injury. Using systems incorporating a brain-computer interface (BCI), patients can control prosthetic limbs, computer cursors, or stimulate their own muscles – by thought alone.

In this new and rapidly growing field, terminology is still developing. One authority defines the BCI as 'a system for controlling a device, e.g. computer, wheelchair or a neuroprosthesis by human intentions, which does not depend on the brain's normal output pathways of peripheral nerves and muscles' (Wolpaw et al., 2002). Donoghue et al. (2007) prefer the term neural interface system (NIS), referring to any system that transforms neurally-based motor intentions into electrical signals that can control physical apparatus. This second rubric might apply to a very broad range of systems, for example, a robot controlled by electrophysiological signals from a moth, which was developed in the laboratory of C.M. Higgins at the University of Arizona and recently described in media reports, though not as yet in a peer-reviewed scientific paper. This review focuses on BCIs for assisting profoundly disabled humans; it does not discuss basic research that is presently far removed from human use.

2. Current state of the art

In 2002, John Donoghue and colleagues at Brown University made a spectacular demonstration of the potential uses of BCIs (Serruya et al., 2002). He and his colleagues implanted electrodes in the motor cortex of monkeys trained to manipulate a joystick with their hands in order to control the cursor on a computer display. The cortical signals were simultaneously processed by computer and also used to control the cursor. Eventually, the investigators disabled the joystick and the monkeys continued to control the cursor, by thought alone. As of present writing, April 2008, their paper has been cited nearly 200 times since its publication, making it a convenient marker for the beginning of the present era of BCI research. These provocative results drew many other groups into the field, typically with the aim of developing prostheses for disabled individuals. A recent (April 2008) search of 'brain-computer interface' in the Medline database yielded 351 scientific papers, roughly 90% of them published since 2002. Recent reviews of BCIs and BCI-based prostheses have been published by Allison et al. (2007), Birbaumer (2006), Donoghue et al. (2007), and Mason (2007).

This extensive literature includes many descriptions of BCIs and BCI-based prostheses, widely varying in approach. The applications can be broadly classified according to the location of the sensing element relative to the surface of the body. *Invasive* applications employ microelectrodes or electrode arrays implanted in various regions of the brain, which measure spikes from individual neurons, small groups of neurons, or local field potentials from larger aggregates of neurons. *Noninvasive* or minimally invasive techniques rely on signals from electrodes placed on the scalp or screwed into the skull but not penetrating the dura. Other noninvasive approaches use functional magnetic resonance imaging (fMRI) or near infrared spectroscopic techniques to sense brain activity. Noninvasive recording methods have the obvious advantage of avoiding the need for brain surgery on the patient, but generally suffer from slow rates of data transfer into the computer, noise, and other practical limitations. Invasive recording techniques, for example, using electrodes implanted into the motor cortex, provide cleaner signals (with higher signal-to-noise ratios) whose origin can be precisely localised within that brain but create obvious issues related to patient acceptability.

BCI systems can also be classified according to the type of signal recorded and its relation to cognitive and motor control functions of the brain. Signals that have been recorded noninvasively for BCIs include: slow cortical potentials of the EEG; EEG and MEG oscillations, mainly sensorimotor rhythms; and P300 and other event-related brain potentials (see the review by Birbaumer, 2006). These signals reflect brain activity at several levels. Motor-based prostheses rely on input from motor cortical areas, while cognitive neural prostheses utilise signals reflecting higher-level cognitive processes that organise behaviour (Donoghue et al., 2007; Pesaran et al., 2006).

Whatever the recording strategy employed, the BCI is used to infer the subject's intent from recordings of brain activity, and this information is used to control prostheses or other aspect of the world external to the patient. In a typical application, the subject is given a mental task, such as imagining a motion of part of the body (motor imagery), and the resulting change (modulation) of brain function is detected and interpreted by the computer. Remarkably, these changes persist even though the subject may be totally paralysed and incapable of actually carrying out the body motions themselves. Most BCI applications employ feedback training methods, during which the subject learns to control his or her EEG, rates of firing of specific cortical neurons, or other aspect of brain activity so as to increase the accuracy of the BCI. Other methods are based on signals such as the P300-evoked response which reflect cognitive processes of the subject and require little or no feedback training to succeed. While these methods are sometimes described in lay publications as "reading the thoughts" of the subject, perhaps a more accurate description is that they enable the subject to communicate with the outside world by modulating brain activity in ways that are at least partly under control of the subject.

Despite the large research activity in this field, prostheses using BCIs, and BCIs themselves, are still in their very early stages of development. Human studies are, in most cases, in proof-of-concept or Phase I stages. To illustrate the present state-of-art, different BCI-based prostheses are briefly described below.

2.1. *EEG-based systems*

Neuper et al. (2006) describe experiments with a BCI developed at the Graz University of Technology (Austria) that uses event-related desynchronisation (ERD) classification in the EEG to discriminate between different kinds of motor execution and motor imagery in human subjects. Subjects are required to imagine different body motions (moving left *versus* right hand, for example) while their EEG is recorded. Imaging these different motions produces slight changes in the frequency spectrum of the EEG, which can be translated into binary (yes/no) commands to a computer. With repeated training sessions extending over periods of weeks to a few months, subjects learn to control their ECG well enough to allow the computer to discriminate between two imagined motions, with high but not perfect accuracy. The authors describe teaching three patients using this BCI system to 'type' on a virtual keyboard shown on a computer display. One of these patients was a 60-year-old male with advanced ALS, who was completely paralysed and had lost nearly all ability to communicate. Over the course of 82 training sessions in 17 days of training, the classification accuracy of the BCI with this patient increased from 49% (roughly random responses for the 2-level discrimination employed in the BCI) to 83%. At the end of this period, the subject was able to type at a rate of approximately one letter per minute; the first word he typed was the name of his caregiver. "The results document that paralysed patients may retain the ability to generate neural signals for motor control, although their motor pathways may be severely disrupted" (Neuper et al., 2006).

Two other subjects in this study – a 32-year-old male with cerebral palsy and 33-year-old male with muscular dystrophy – also learned to type on the virtual keyboard. In the same report, Neuper et al. also describe two tetraplegic patients suffering from spinal cord injury. In these patients, the EEG-based BCI was used to control a device that electrically stimulated the peripheral nerves of the patients, restoring their ability to grasp objects with their hands.

Taking a considerably different approach, Rebsamen et al. (2007) describe a wheelchair controlled by a BCI that based on the P300 evoked potential. These signals, which can be measured on the scalp 300 milliseconds after a 'meaningful' stimulus is presented to a subject, can be used to infer the object of a subject's attention. The investigators presented the subject with a computer display with randomly flashing boxes indicating choices of destinations for the wheelchair ('my office', ' the lift', 'toilet'), and instructed the subject to focus attention on one of the boxes. By determining which flashing box elicited P300 waves in the subject, the investigators could identify the choice of the subject and, through a computer, send appropriate control signals to the wheelchair. Each of six fully enabled subjects succeeded in reaching their intended destination in an ordinary office environment in their first attempt. Remarkably (given the small amplitude of the P300-evoked response and the resulting need to average a number of responses to reliably detect the signal), subjects needed only about 15 seconds to issue a command through the BCI.

2.2. *BCIs using implanted electrodes*

The BrainGate neural interface system, currently under development by Cyberkinetics Neurotechnology Systems, Inc. (a firm founded by Donoghue) is the best publicised, and arguably most advanced, system of this type. Its system uses a rectangular array of 100 microelectrodes, 4mm on a side, placed against the primary motor cortex (MI) of the brain near the arm area (Donoghue et al., 2007). Preclinical data from able-bodied monkeys "showed that decoding can be implemented with sufficient speed and accuracy for a hand controlled mouse-driven cursor to be replaced with one that was driven by the decoded firing patterns from the MI arm area". (Donoghue et al, 2007).

To date, the company has enrolled four participants with tetraplegia (two with spinal cord injury, one with ALS, and one with a brainstem stroke). Action potentials could be recorded from the MI arm area of the motor cortex in these patients even years after their injuries had occurred, even if no body movement actually took place. 'These preliminary results provide initial proof of concept that a neuronally-based control system is feasible: signals can be detected, decoded and used for real-time operation of computer software, assistive technologies, and other devices', Donoghue et al. (2007) conclude.

Despite such promising results, the current generation of BCIs has significant limitations. EEG-based systems, in particular, suffer from "long training periods, noisy signals, the continuous professional attention necessary, slow spelling speed, electrode and skin problems with long recording times, and the controlled attention focus [required of the subject] during spelling". (Birbaumer, 2006). The current rate of information transfer between brain and computer in EEG-based BCIs is about 20-30 bits per minute, which corresponds to typing about two words per minute on a keyboard. Somewhat faster performance is possible with

BCIs that employ implanted electrodes: a recently described 'high performance' BCI using electrode arrays implanted in the monkey dorsal premotor cortex achieved data rates of up to 6.5 bits per second, equivalent to typing at a rate of about 15 words per minute (Santhanam et al., 2006). By comparison, speeds of up to 25 words a minute have been achieved with an eye-tracking system that does not employ a BCI (Ward and MacKay, 2002).

EEG-based systems (in particular) are also limited by high error rates of communication, even after long training times. In part this may be due to the small amplitude of the EEG, and the susceptibility of EEG recordings to artifacts resulting from body motion, eyeblinks, and other effects. In part this may also reflect underlying biological variability. Wolpaw (2007) noted a 'disconcerting variability' in performance of BCIs. It remains to be seen how fundamental a limitation this will turn out to be. Wolpaw suggests that performance of BCIs can be improved by shifting to a 'goal-selection' rather than a 'process-control' strategy. For example, the patient might choose the ultimate destination for a wheelchair, with the navigational details offloaded to a computer. Clearly, reliability and speed of communication is a crucial issue when using a BCI to control moving systems such as a wheelchair.

Another limitation is patient acceptance, particularly with invasive BCIs. In an informal survey of 100 BCI investigators in 2005 conducted by a leading investigator in this field, the majority of respondents considered noninvasive BCIs to be more desirable than invasive types over the next decade, largely because of patient acceptability issues surrounding invasive devices (Birbaumer, 2006). In a previous (2005) report, Birbaumer described a group of 17 patients with end-stage ALS, only one of whom consented to have electrodes implanted in the brain for a BCI. The remaining patients preferred a much slower and more error-prone system employing external electrodes. These systems require the continued concentration of the patient, and their usability by patients over extended times remains to be seen.

While some of these limits can be overcome by improved technology, biology poses fundamental limits as well. The goal of the BCI is to infer the intent of the subject from specific changes in brain activity that may be at least partly under the control of the subject. However, the ability of a subject to voluntarily modulate brain activity is limited by a number of biological factors, not least of which is the immense complexity of brain function. Even the simplest action requires the coordinated activity of many neurons, which have a high level of interaction among them. This leads to what one expert calls the "complex transforms of neural activity to output parameters" of a BCI (Fetz, 2007). Moroever, effective communication via a BCI may require the patient to elicit unnatural responses in the brain. In the words of another expert, "a BCI attempts to assign to cortical neurons the role normally performed by spinal motoneurons. Thus, a BCI requires that the many CNS [central nervous system] areas involved in producing normal motor actions change their roles so as to optimise the control of cortical neurons rather than spinal motoneurons. The disconcerting variability of BCI performance may stem in large part from the challenge presented by the need for this unnatural adaptation." (Wolpaw, 2007). To the extent that the accuracy of a BCI in decoding the subject's intentions is limited by such biological factors, it may be difficult to improve by technical advances in signal processing or computer technology alone. How far technology can advance in the face of underlying biological limitations is, at present, still an open question.

3. Restoring cognitive loss

The systems discussed above are intended to enable profoundly disabled individuals to communicate with or control aspects of the outside world or (when the BCI is coupled to functional electrical stimulation) to partially restore their motor function. Other investigators are working to develop prostheses to interact directly with the central nervous system, to help restore cognitive function. These employ so-called 'silicon neurons' – microchips that are intended to be implanted in the brain. The circuits are designed to interface with healthy neurons and carry out calculations that would otherwise be lost to the patient by brain damage or disease. An example is a prosthetic hippocampal-cortical neural prosthesis described by Theodore Berger at the University of Southern California, which may eventually help to improve memory in patients with Alzheimer's disease or suffering from stroke. (For an accessible review see Berger et al., 2005).

Prostheses of this sort, which employ microchips implanted in the brain to carry out computations ordinarily done by neurons in intact tissue, are far from use in humans. Indeed, basic questions about their feasibility remain. "To operate as a 'cognitive prosthesis', [such a device] would require effective communication between neural and electronic circuits at both input and output [of the damaged region of brain] – a formidable technical challenge given the parallel distributed operations of biological neurons" (Fetz, 2007).

4. Future developments

These early results show the great potential of BCIs and cognitive neural prostheses for enhancing the lives of patients with severe disability. This review concludes by considering future developments in this technology both in the near future (<10 years) and long-term.

4.1. *Near-term: next ten years*

Certainly, as research moves out of the proof-of-concept and Phase I stages of human experimentation, BCI-based prostheses will become smaller, cheaper, more reliable, and easier to use than the systems discussed here. Wolpaw's group has already described an EEG-based BCI system that costs US$4,000 to build – a figure that is expected to decrease still more in the future. Apart from the small amplitude of the P300 and other signals recorded on the scalp, there are few technical obstacles to producing EEG-based BCIs; such systems are easily in the range of student projects. The surgery needed to implant electrodes against the motor cortex is minor (as brain surgery goes), and experience with cochlear implants and other devices using electrodes chronically implanted in the head suggests that issues related to infection and long-term performance of electrodes in the brain can be managed. At least in the US, BCI-based prostheses for profoundly disabled patients are likely to gain regulatory approval rather easily on humanitarian grounds. The number of potential candidates for BCI-based prostheses is very large. These might include people who are paralysed by spinal cord injuries, strokes, ALS, cerebral palsy and other neuromuscular diseases. Wolpaw estimates that about 70-80% of people with severe disabilities could use his current system. And many such individuals exist: one source estimates that there are one million potential users in New York State alone, out of a total (2006) population of 19 million.

However, given the present state of development of such prostheses, the number of patients who might actually use them is far smaller than this. For the foreseeable future, BCIs would appear best suited to enhance communication in severely disabled individuals. However, even for those applications, the performance of current devices leaves a lot to be desired – and a variety of other aids is available that may offer considerably better performance to the subject.

The potential rate of adoption of BCIs for motor restoration is more problematic, at least in the near-term. In his presidential address in 2005 to the Society for Psychophysiological Research, Niels Birbaumer said: "None of the paralysed patients reported in the literature is using the motor BCI in everyday-life situations as long as voluntary upper face and shoulder movements can activate an artificial limb. Therefore, in spinal cord lesioned patients, invasive and noninvasive BCIs (BMIs) may be useful in the future for the few patients with extremely high spinal cord lesions only." (Birbaumer, 2006). The growth (and even existence) of a future market for BCI-based assistive devices will depend on the rate of improvement of the technology, which will be constrained by fundamental biological limitations. This uncertainty makes it difficult to predict the extent of the ultimate success of BCI technologies.

In addition to their use as assistive devices, BCIs have other applications as well. A video game interface employing EEG-based BCIs was recently described (Krepki et al., 2007; Miller et al., 2007) and a San Francisco company, Emotiv reports that it will introduce a headset for EEG-based video games during 2008. Despite hyperbolic claims on the company's website (www.emotiv.com), the actual performance of the system remains to be seen. Few computer gamers would be satisfied with a system that communicates at the very slow rates that are typical of present BCIs.

4.2. *Distant future: 10 years or more*

In such a rapidly progressing field, it is difficult to predict what the next year will bring, let alone foretell the state of the technology a decade in the future. The long-term prospects for cognitive neural prostheses and other assistive devices using BCIs will depend on the degree of success of scientists and biomedical engineers in overcoming the difficult limitations posed by biology. These limitations cannot necessarily be addressed by purely technical advances such as further miniaturisation of sensors and increasing speed of computers.

There are certainly grounds for optimism about successful applications of the technology. Within a decade, assistive devices based on BCIs may have become truly practical for a large number of disabled individuals. Certainly, proof-of-concept for a number of such systems has already been obtained, even though few, if any, of these systems presently remain in use by patients after experiments have concluded.

One can hope that this technology will find important applications apart from assisting disabled individuals. Some expert groups have predicted that, in the distant future, very advanced BCIs will become available for greatly enhancing the capabilities of normally-enabled individuals. In developing such devices, ethical constraints would become important. It is one thing to implant electrodes surgically in the brain of a locked-in patient in an attempt to give him or her the ability to communicate; it is quite another to carry out brain surgery on a fully-enabled individual in order to position devices intended to 'improve' his or her performance.

For example, a European Commission-sponsored report (Nordmann, 2004) predicted the use of brain implants connected to sensory organs or to brain-cortex areas to allow pilots to respond more quickly to sudden threats. However, the report noted:'communicating complex sensory impressions or thoughts… requires fundamental progress in brain research and a reduced barrier against human experiments.' One can expect great advances in brain science in the coming years, while at the same time hoping that ethical limits to human experimentation will continue to be respected as well.

Even farther out on the horizon are implantable computer systems for the brain that will interface with neurons and carry out computations lost due to disease or injury. From today's perspective, developing such devices poses formidable technical challenges. The nature and capabilities of any successful device – as with the ultimate outcome of the neuroscience revolution – can only, at present, be a matter of speculation.

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