Brain–Machine and Brain–Computer Interfaces

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***Abstract*—**The idea of connecting the human brain to a computer or machine directly is not novel and its potential has been explored in science fiction. With the rapid advances in the areas of information technology, miniaturization and neurosciences there has been a surge of interest in turning fiction into reality. In this paper the authors review the current state-of-the-art of brain–computer and brain–machine interfaces including neuroprostheses. The general principles and requirements to produce a successful connection between human and artificial intelligence are outlined and the authors' preliminary experience with a prototype brain–computer interface is reported. **(*Stroke*. 2004;35[suppl I]:2702-2705.)**

Key Words: electroencephalography ■ receptors, sensory ■ rehabilitation ■ stroke

For the past 40 years researchers have been trying to transform thought into action. Recent advances in neuroscience and neurotechnology have initiated a renewed interest in the development of brain–machine interfaces (BMIs) or brain–computer interfaces (BCIs) that can restore lost motor or sensory function. The currently available systems depend on neural activity input from cortical surface recording (electroencephalographic [EEG] signals) or extracellular brain recording. So far, several patients have benefited from BCI devices, although the current information transfer rate remains a limiting factor. This technology might be especially useful for patients who are otherwise unable to move or speak. This article provides a review of the current state of technology, with emphasis on neuromotor prosthetics. Furthermore, it summarizes the authors' experience in the development of a human BMI.

The idea of connecting a computer to a brain is not new. As early as the 1950s it was possible to implant single or multiple electrodes into the cortex of humans and animals for recording or stimulation.[1] The result was sometimes spectacular "control" of an animal's motor behavior or attempted influence of neurological disorders.[2,3] With the worldwide introduction of computers, and ongoing miniaturization, several research groups have started to look into the potential applicability of such BMIs, BCIs, or neural prostheses for use in patients. These devices, by extracting signals directly from the brain, might help to restore abilities to patients who have lost sensory or motor function because of disease or injury. In essence, the computer is used as a surrogate for the damaged region (eg, the spinal cord in quadriplegic patients) and, in the case of a neuromotor prosthesis, acts to interpret brain signals and drive the appropriate effector (eg, muscles or a robotic arm).

Review of Literature

Probably the most widely accepted neural prosthesis in human use is the cochlear implant,[4,5] which substitutes a small computer chip for the damaged inner ear control organ to enable sound waves to be transformed into electrical signals the brain can interpret. Other research has focused on restoring vision for the blind[6–10] with implantable systems to transmit visual information. One other possible application is the restoration of motor control for patients with movement disorders, a population numbering ≈2 million in the United States alone.[11] In an especially tragic situation, brain stem stroke can leave patients in a locked-in state with minimal eye movements and no speech, but full cognitive functions. Among the other diseases that could be helped by BMIs are degenerative disorders (amyotrophic lateral sclerosis or Lou Gehring disease, multiple sclerosis, muscular dystrophy), brain or spinal cord injury, or cerebral palsy. When a disconnection of the main motor pathway occurs, the information generated in the motor cortical areas cannot travel through the pyramidal tract to reach the executing organ, the muscles. There are several possible approaches in how to overcome this disconnect in the signal pathway: (1) activation of intrinsic alternate pathways (anatomical compensation); (2) repair or regeneration of the damaged pathway (anatomical recovery); and (3) bypassing the damaged area by means of a BMI (functional recovery).

Although BMIs are not capable of activating alternate pathways (anatomical compensation) or truly restoring the structural lesion to its original state (anatomical recovery), they may be helpful in restoring lost function (functional recovery).

Typically, motor BMIs consist of at least 3 distinct modules: (1) the data acquisition module; 2) the data interpretation module; and (3) the data output module. A functional

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neuroprosthesis must address each stage efficiently and safely. These 3 stages of the process are discussed here.

Data Acquisition Module: EEG signals and Microelectrodes

The purpose of this module is to extract electrical signals from the brain with sufficient bandwidth and at a favorable signal-to-noise ratio. Although the EEG signals can be obtained in a noninvasive manner through single or multiple electrodes that are mounted on the head or assembled in headgear,[12–18] the signal represents a field potential rather than specific cellular activity. Patients and volunteers have been shown to be able to learn to self-regulate slow cortical potentials[19] or to voluntarily control a specific frequency component of the EEG.[20–22] Yet because the EEG signal, especially when recorded with noninvasive methods, is a gross potential generated by the synchronous activity of large numbers of neurons, its resolution is limited temporally and spatially. This means that the rate at which information, and therefore patient intent, is extractable from the EEG signal is limited. This limited bandwidth may be sufficient for many applications, such as interaction with a computer cursor, but may be insufficient for more complex signals, such as when detailed movement trajectories must be specified. In contrast, other groups have focused on obtaining signals from the cortex through invasive methods. Kennedy et al describe their method of implanting glass cone electrodes that are filled with a substrate containing nerve growth-stimulating substances.[23–25] This extracellular recording electrode is bioactive and requires nerve fibers to sprout into the glass cone, a process which occurs over a period of several weeks. With this device, the researchers were able to produce long-term recording from the' cerebral motor cortex of patients.[25–27] More commonly used are bio-inactive arrays that provide extracellular recording through multiple microwires[28,29] or multichannel electrode arrays in the more superficial motor areas[30] or deep brain structures.[31] It is of note that any of these electrodes are capable of recording from multiple neurons at the same time, a requirement for extraction of signals with the necessary bandwidth for use in prosthetics.

Recent research has focused on exploring various cortical and subcortical areas for optimum electrode array placement. Although traditionally the primary motor cortex (M1) was assumed to be the optimum location for extracting neural signals for use with BMIs designed to substitute for movement, the consensus is growing that alternative or multiple locations may provide the best signals. Among the alternative brain regions investigated are parietal cortex,[32–34] the premotor cortex,[35,36] or simultaneously across M1 and premotor cortices,[37] frontoparietal cortices,[29,38] or subcortically from the basal ganglia.[31] Because various regions' neural activities occur at varying times in the movement planning and execution process, signals from some areas may be more suited than others depending on the type of information extracted and computational algorithm used.

Data Interpretation Module

Once the signal has been obtained from the recording site, it is fed into a signal processing unit through telemetric communication[27] or direct wire contact.[30] Most researchers recommend early pre-amplification and digitization of the analog recording data to minimize the signal deterioration. The main goal of the interpretation module is to transform the digitized brain signal into a code that best-represents the desired action. For a motor prosthetic, this may be movement of a cursor, clicking of a button, or specification of a complex time-varying movement trajectory, such as reaching for a glass. Continuous movement such as in the hand tracking a moving target can be represented by a Cartesian X-Y-Z coordinate system in extrapersonal space. This approach has been used by several research groups and has resulted in very good approximation of 2-dimensional and 3-dimensional arm or hand movement.[15,27,28,32,39–42] Furthermore, distinct states of limb movement, ie, reaching versus grasping, can now be identified by interpretation modules.[38] The ability to distinguish between these different modes of desired action expands the usefulness of the system and may aid in increasing accuracy and decreasing the effects of errors in decoding. For example, if decoding of continuous motion results in some error, or jitter, around the desired position, holding a full glass of water may be problematic. However, if the system can determine that the user intends to hold the glass still, the position of the artificial effector can be held fixed by turning off the position decoding.

It will be important for a BMI to be able to decode discrete movement classes, such as initiation and termination, or selection between several choices, such as in typing, along with continuous decoding for optimum functionality.[37] The mathematical models used for interpretation and decoding of intent include linear regression algorithms, best fit models, and neural networks,[21,29,43–46] and the best BMI may use >1 of these simultaneously. Although initially decoding was performed off-line, it is now possible with advanced algorithms and recording systems to accurately predict movement in up to 90% of trials either in real time or with only milliseconds delay.[30,43,47] Moreover, accuracy of decoding may be augmented through feedback to the user. It is known that subjects have the ability to consciously alter their neural activity in certain brain areas with sufficient training.[48] Patients, then, should be able to improve decoding of their intent through practice. This reduces the burden on the algorithm and ameliorates potential concerns about drift in the population of neurons that is being observed.

Data Output Module

After the data set is translated into appropriate coordinates or output classes, it can be used to drive a variety of output devices that become the "effector organ" in lieu of muscle-activated limbs. For one, the information has been successfully used to control a computer cursor.[14,15,17,26,27,35,41,42] This opens ample opportunities ranging from simple move-and-click functions to Internet and e-mail use or command or a virtual keyboard.[18] The same signal can also be used to control a robotic device for instance as a substitute for a moving human limb.[49–52] Possibly the most attractive yet difficult to achieve is provided when the computer generated signal can be fed back into the patient's own limb to activate muscles, for example, through a functional electrical stimulation system. One group has been able to train normal subjects and a neuroprosthesis user to control EEG rhythms to stimulate a motionless hand to open and close or to move a cursor to targets on a computer screen.[15] Although provocative, training took months, however, and ultimate functional movement was less than practical because of low resolution of the EEG signal.

Brown University Experience

Recently, research at Brown University has begun to focus on human control of neural activity, both on-line and off-line. We have been able to take advantage of the implantation of deep brain stimulators for improvement of motor disorders to explore the ability of patients to control their neural signals. Parkinson patients and essential tremor and dystonia patients who are unable to benefit from medication may opt to have a DBS implanted in one of several basal ganglia nuclei to improve tremor, rigidity, bradykinesia, or dyskinesias.[53] As part of this neurosurgical procedure, extracellular recording from brain regions "en route" to the basal ganglia target is routinely performed to give added localization information to the neurosurgeon. With institutional review board and patient permission, we have recorded from 4 to 6 neurons simultaneously in the premotor and prefrontal regions during visuomotor arm movement tasks. With a few minutes of practice, patients have been able to control their neural activity to bring a cursor to a target.[35] Off-line decoding using a maximum likelihood estimator revealed that small, pseudo-randomly selected neuronal ensembles in the human cortex contain information about movement direction and intent (to move or not to move)[36] (Ojakangas et al, data unpublished, 2004). These results are promising in that they demonstrate the possibility of using neuronal activity in nonprimary motor areas for neural prosthetic development, which may be required or even advantageous with certain types of patients.

Summary

With the current state of technology, all essential steps for development of a human motor neural prosthesis are in place. Research at multiple institutions continues to refine surgical implantation techniques and analysis algorithms, as well as computer software, that can take more efficient advantage of signals directly derived from human brains. Especially because Food and Drug Administration approval was recently granted for a pilot study using the Cyberkinetics, Inc Braingate electrode array system, the dream of turning "thought into action" may soon become reality for patients with severe motor disabilities.

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References

1. Delgado JM, Hamlin H, Chapman WP. Technique of intracranial electrode emplacement for recording and stimulation and its possible therapeutic value in psychotic patients. *Confin Neurol*. 1952;12:315–319.
2. Delgado JM. *Physical Control of the Mind.* New York: Harper and Rowe; 1969.
3. Evarts EV. Pyramidal tract activity associated with a conditioned hand movement in the monkey. *J Neurophysiol*. 1966;29:1011–1027.
4. Parmet S, Lynm C, Glass RM. JAMA patient page. Cochlear implants. *JAMA*. 2004;291:2398.
5. Spahr AJ, Dorman MF. Performance of subjects fit with the advanced bionics CII and nucleus 3G cochlear implant devices. *Arch Otolaryngol Head Neck Surg*. 2004;130:624–628.
6. Hetling JR, Baig-Silva MS. Neural prostheses for vision: designing a functional interface with retinal neurons. *Neurol Res*. 2004;26:21–34.
7. Veraart C, Wanet-Defalque MC, Gerard B, Vanlierde A, Delbeke J. Pattern recognition with the optic nerve visual prosthesis. *Artif Organs*. 2003;27:996–1004.
8. Maynard EM. Visual prostheses. *Annu Rev Biomed Eng*. 2001;3: 145–168.
9. Dobelle WH. Artificial vision for the blind by connecting a television camera to the visual cortex. *ASAIO J*. 2000;46:3–9.
10. Dobelle WH. Willem J. Kolff and artificial vision for the blind. *Artif Organs*. 1998;22:966–968.
11. Murray CJL, Lopez AD. *The Global Burden of Disease: A Comprehensive Assessment of Mortality and Disability From Diseases, Injuries and Risk Factors in 1990 Projected to 2020.* Boston: Harvard University Press; 1996.
12. Birbaumer N, Kubler A, Ghanayim N, et al. The thought translation device (TTD) for completely paralyzed patients. *IEEE Trans Rehabil Eng*. 2000;8:190–193.
13. Guger C, Edlinger G, Harkam W, Niedermayer I, Pfurtscheller G. How many people are able to operate an EEG-based brain-computer interface (BCI)? *IEEE Trans Neural Syst Rehabil Eng*. 2003;11:145–147.
14. Kostov A, Polak M. Parallel man-machine training in development of EEG-based cursor control. *IEEE Trans Rehabil Eng*. 2000;8:203–205.
15. Lauer RT, Peckham PH, Kilgore KL. EEG-based control of a hand grasp neuroprosthesis. *Neuroreport*. 1999;10:1767–1771.
16. Obermaier B, Neuper C, Guger C, Pfurtscheller G. Information transfer rate in a five-classes brain-computer interface. *IEEE Trans Neural Syst Rehabil Eng*. 2001;9:283–288.
17. Obermaier B, Muller GR, Pfurtscheller G. "Virtual keyboard" controlled by spontaneous EEG activity. *IEEE Trans Neural Syst Rehabil Eng*. 2003;11:422–426.
18. Sheikh H, McFarland DJ, Sarnacki WA, Wolpaw JR. Electroencephalographic(EEG)-based communication: EEG control versus system performance in humans. *Neurosci Lett*. 2003;345:89–92.
19. Kubler A, Neumann N, Kaiser J, Kotchoubey B, Hinterberger T, Birbaumer NP. Brain-computer communication: self-regulation of slow cortical potentials for verbal communication. *Arch Phys Med Rehabil*. 2001;82:1533–1539.
20. McFarland DJ, Sarnacki WA, Wolpaw JR. Brain-computer interface (BCI) operation: optimizing information transfer rates. *Biol Psychol*. 2003;63:237–251.
21. McFarland DJ, Wolpaw JR. EEG-based communication and control: speed-accuracy relationships. *Appl Psychophysiol Biofeedback*. 2003;28: 217–231.
22. Pfurtscheller G, Neuper C, Muller GR et al. Graz-BCI: state of the art and clinical applications. *IEEE Trans Neural Syst Rehabil Eng*. 2003;11: 177–180.
23. Kennedy PR. The cone electrode: a long-term electrode that records from neurites grown onto its recording surface. *J Neurosci Methods*. 1989;29: 181–193.
24. Kennedy PR, Mirra SS, Bakay RA. The cone electrode: ultrastructural studies following long-term recording in rat and monkey cortex. *Neurosci Lett*. 1992;142:89–94.
25. Kennedy PR, Bakay RA. Activity of single action potentials in monkey motor cortex during long-term task learning. *Brain Res*. 1997;760: 251–254.
26. Kennedy PR, Bakay RA. Restoration of neural output from a paralyzed patient by a direct brain connection. *Neuroreport*. 1998;9:1707–1711.
27. Kennedy PR, Bakay RA, Moore MM, Adams K, Goldwaithe J. Direct control of a computer from the human central nervous system. *IEEE Trans Rehabil Eng*. 2000;8:198–202.
28. Taylor DM, Tillery SI, Schwartz AB. Direct cortical control of 3D neuroprosthetic devices. *Science*. 2000;296:1829–1832.
29. Wessberg J, Stambaugh CR, Kralik JD et al. Real-time prediction of hand trajectory by ensembles of cortical neurons in primates. *Nature*. 2000; 408:361–365.

30. Serruya MD, Hatsopoulos NG, Paninski L, Fellows MR, Donoghue JP. Instant neural control of a movement signal. *Nature*. 2002;416:141–142.
31. Patil PG, Carmena JM, Nicolelis MA, Turner DA. Ensemble Recordings of Human Subcortical Neurons as a Source of Motor Control Signals for a Brain-Machine Interface. *Neuorsurgery*. 2004;55:1–10.
32. Shenoy KV, Meeker D, Cao S et al. Neural prosthetic control signals from plan activity. *Neuroreport*. 2003;14:591–596.
33. Pesaran B, Pezaris JS, Sahani M, Mitra PP, Andersen RA. Temporal structure in neuronal activity during working memory in macaque parietal cortex. *Nat Neurosci*. 2002;5:805–811.
34. Cohen YE, Batista AP, Andersen RA. Comparison of neural activity preceding reaches to auditory and visual stimuli in the parietal reach region. *Neuroreport*. 2002;13:891–894.
35. Donoghue JP, Saleh M, Caplan A et al. Direct Control of a Computer Cursor by Frontal Cortical Ensembles in Humans: Prospects for Neural Prosthetic Control. *Society for Neuroscience Abstract*. 2003;9:607.
36. Ojakangas CL, Caplan A, Serruya M, Ramchandani S, Donoghue JP, Friehs GM. Properties of Human Frontal Cortex Neurons during Visuomotor Tasks. *Society for Neuroscience Abstract*. 2003;14:919.
37. Hatsopoulos N, Joshi J, O'Leary JG. Decoding continuous and discrete motor behaviors using motor and premotor cortical ensembles. *J Neurophysiol*. 2004;in press.
38. Carmena JM, Lebedev MA, Crist RE et al. Learning to control a brain-machine interface for reaching and grasping by primates. *PLoS Biol*. 2003;1:E42.
39. Graimann B, Huggins JE, Schlogl A, Levine SP, Pfurtscheller G. Detection of movement-related desynchronization patterns in ongoing single-channel electrocorticogram. *IEEE Trans Neural Syst Rehabil Eng*. 2003;11:276–281.
40. Muller GR, Neuper C, Rupp R, Keinrath C, Gerner HJ, Pfurtscheller G. Event-related beta EEG changes during wrist movements induced by functional electrical stimulation of forearm muscles in man. *Neurosci Lett*. 2003;340:143–147.
41. Neuper C, Muller GR, Kubler A, Birbaumer N, Pfurtscheller G. Clinical application of an EEG-based brain-computer interface: a case study in a patient with severe motor impairment. *Clin Neurophysiol*. 2003;114: 399–409.
42. Pfurtscheller G, Muller GR, Pfurtscheller J, Gerner HJ, Rupp R. "Thought"–control of functional electrical stimulation to restore hand grasp in a patient with tetraplegia. *Neurosci Lett*. 2003;351:33–36.
43. Helms Tillery SI, Taylor DM, Schwartz AB. Training in cortical control of neuroprosthetic devices improves signal extraction from small neuronal ensembles. *Rev Neurosci*. 2003;14:107–119.
44. Schwartz AB, Taylor DM, Tillery SI. Extraction algorithms for cortical control of arm prosthetics. *Curr Opin Neurobiol*. 2001;11:701–707.
45. Serruya M, Hatsopoulos N, Fellows M, Paninski L, Donoghue J. Robustness of neuroprosthetic decoding algorithms. *Biol Cybern*. 2003; 88:219–228.
46. Paninski L, Fellows MR, Hatsopoulos NG, Donoghue JP. Spatiotemporal tuning of motor cortical neurons for hand position and velocity. *J Neurophysiol*. 2004;91:515–532.
47. Isaacs RE, Weber DJ, Schwartz AB. Work toward real-time control of a cortical neural prothesis. *IEEE Trans Rehabil Eng*. 2000;8:196–198.
48. Fetz EE, Finocchio DV. Operant conditioning of isolated activity in specific muscles and precentral cells. *Brain Res*. 1972;40:19–23.
49. Chapin JK, Moxon KA, Markowitz RS, Nicolelis MA. Real-time control of a robot arm using simultaneously recorded neurons in the motor cortex. *Nat Neurosci*. 1999;2:664–670.
50. Craelius W. The bionic man: restoring mobility. *Science*. 2002;295: 1018–1021.
51. Fetz EE. Real-time control of a robotic arm by neuronal ensembles. *Nat Neurosci*. 1999;2:583–584.
52. Taylor DM, Tillery SI, Schwartz AB. Information conveyed through brain-control: cursor versus robot. *IEEE Trans Neural Syst Rehabil Eng*. 2003;11:195–199.
53. Benabid AL, Pollak P, Hommel M, Gaio JM, de Rougemont J, Perret J. [Treatment of Parkinson tremor by chronic stimulation of the ventral intermediate nucleus of the thalamus]. *Rev Neurol (Paris)*. 1989;145: 320–323.