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Neurosurgery and the dawning age of Brain-Machine Interfaces

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Abstract

Brain–machine interfaces (BMIs) are on the horizon for clinical neurosurgery. Electrocorticography-based platforms are less invasive than implanted microelectrodes, however, the latter are unmatched in their ability to achieve fine motor control of a robotic prosthesis capable of natural human behaviors. These technologies will be crucial to restoring neural function to a large population of patients with severe neurologic impairment – including those with spinal cord injury, stroke, limb amputation, and disabling neuromuscular disorders such as amyotrophic lateral sclerosis. On the opposite end of the spectrum are neural enhancement technologies for specialized applications such as combat. An ongoing ethical dialogue is imminent as we prepare for BMI platforms to enter the neurosurgical realm of clinical management.

Key Words: Brain–computer interface, braingate, brain–machine interface, DEKA arm, electrocorticography, electroencephalogram

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INTRODUCTION

In the mid-twentieth century, the notion that our brains operate similarly to computers was conceived as a result of the simultaneous development of digital microprocessors and modern neuroanatomical and electrophysiological techniques. Moreover, as knowledge of mammalian neuroanatomy became more established, models of sensorimotor control were described using circuit-based approaches. And today, as with computing devices, we view signaling in the brain in terms of complex, multilayered networks in which information is transmitted in temporal and frequency domains. Nevertheless, our ability to translate this neural code into an effective treatment for patients with devastating neurological conditions from disease, stroke, and trauma has been limited by less well understood processes within the sphere of consciousness, such as decision-making and goal-directed movement planning in three-dimensional space. Brain–computer interfaces, or the more generic term brain–machine interfaces (BMIs), are closed-loop systems that use neural activity to drive responsive devices, such as a computer, stimulating electrode, or robotic arm [Figure 1]. One of the first BMI devices was demonstrated in the 1990s by Wolpaw, *et al.*, who trained normal volunteers to deflect a cursor represented on a computer screen either up or down over the course of several weeks using electroencephalographic (EEG) activity alone.[23] However, the neuroscientific basis for BMI devices was conceptualized in the 1960s and 1970s using recordings in human behavioral experiments.[22] Today, these devices have advanced substantially and harbor the potential to provide a new therapeutic modality for patients paralyzed with spinal cord injury, brainstem stroke and neuromuscular disorders such as amyotrophic lateral sclerosis (ALS). They may also help elucidate some of

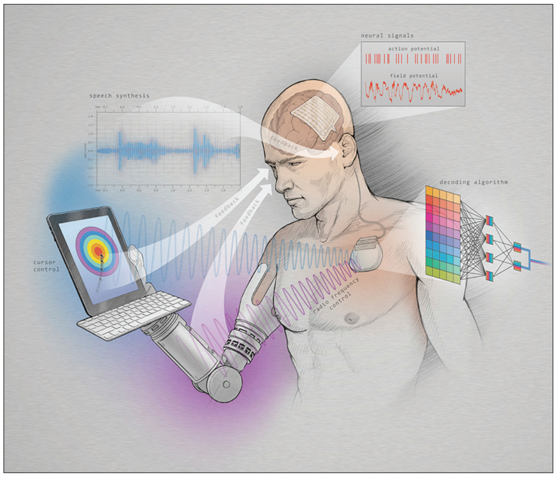

Figure 1: Schematic of a hypothetical closed-loop brain–machine interface system including an implantable electrocorticographic grid for recording and relaying neural signals to a decoding device that also controls multimodal actuators. These could take the form of computer commands such as cursor control, a speech synthesizer or movement of robotic-like limbs in three-dimensional space. Ongoing neural signals would feedback into the adaptive closed-loop system. Figure reprinted with permission from graphical artist

the most fundamental mechanisms of nervous system functioning, namely the relationships between planning, goals, and interaction with our environment.

As the technical development of BMIs proceeds, attention has begun to shift to the practical aspects of neurosurgical implantation and long-term use of these devices. Relevant questions for neurosurgeons are: How will these devices integrate into current practices? What is the lifespan of these devices? And what will the clinical demand for these devices look like over the next five years? Several BMI platforms have emerged, including EEG-, electrocorticography (ECOG)-, and multi-unit-based designs. The platforms are differentiated by the scale of neuronal populations from which they acquire data, and they are accordingly capable of varying complexity of actuation. In this article, we review several BMI technologies at the threshold of marketplace entry and the domain of neurosurgical management. Our goal is to identify the potential impact of this technology on current neurosurgical practice, including ethical implications that may accompany future use of these devices.

Electrocorticography – how good is it?

ECOG recordings represent the integrated neural signal of between 10^2 and 10^3 subjacent cortical neurons. These recordings are thus a type of population code of spiking activity surrounding an individual ECOG contact. Neurosurgeons specializing in epileptic focus resection have utilized ECOG since its development by Penfield and Wilder, and now it is being used in the first closed-loop BMI system to be tested in a clinical trial. The responsive neurostimulation (RNS) system by Neuropace, Inc.,® detects abnormal cortical activity from an implanted ECOG strip electrode or depth electrode and responds by delivering an electrical pulse through the electrode with abnormal activity.[1] Onboard processors that feature seizure detection algorithms fit inside a casing contoured to a full thickness cranioplasty. In a randomized, blinded, multisite clinical trial, patients undergoing RNS therapy experienced a 37.9% mean reduction in seizures compared with 17.3% in a sham control group ($P = 0.012$). Treated patients also showed secondary gains in verbal and memory tasks.[18] Food and Drug Administration (FDA) approval of this device is currently pending.

Analogous closed-loop systems are in the conceptual stage for deep brain stimulation (DBS) therapies. Conventional DBS for movement disorders involves chronic, high-frequency stimulation of targets centered in the thalamus and basal ganglia. FDA-approved indications exist for essential tremor, Parkinson's disease and dystonia. The current generation of DBS devices differ from BMI systems, however, in that they operate in a continuous, open-loop fashion and are not used to drive external actuators. Nevertheless, long-term outcome studies (at 1, 5, and 10 years) indicate patients tolerate DBS implantation well with lasting improvements in both motor and nonmotor symptoms.[3,7] However, some patients are subjected to frequent revisits to clinical centers for reprogramming of device stimulation parameters. Several authors have proposed using electrophysiological signals to help optimize and possibly automate programming parameters,[2] and such signals could be derived from chronically implanted ECOG electrodes to complete the loop. Rosin, *et al*. demonstrated the first closed-loop DBS design in which stimulus pulses to the internal globus pallidus (GPi) in Parkinsonian animals triggered either by abnormal GPi and/or motor cortical activity resulted in superior motor control relative to open-loop stimulation.[19]

More complex actuators, such as motor prostheses, driven by ECOG signals are also in development. Leuthardt, *et al*. designed the first ECOG-based BMI platform in 2004 to allow epilepsy patients to control one-dimensional cursor movement on a computer screen. In these trials, ECOG signals were first recorded in patients performing actual movements coupled to either up or down cursor deflections on a computer screen. Unique signal profiles in the μ, β, and γ frequency bands were found to be associated with individual movement directions. This group then used imagined performance of these movements to accurately control the cursor in a training paradigm requiring less than half an hour.[15,16,21] This technology has now been extended to control of robotic prostheses. Yanagisawa, *et al*. constructed a decoding algorithm that allowed accurate mimicking by a robotic hand of imagined finger movements in a patient with stroke.[24] Notably, this capability has also been achieved by less robust systems based on EEG signals, in which each contact samples on the order of 10^5-10^8 neurons. However, the training time required for real-time control of EEG-based devices is considerably longer, and signal acquisition can suffer from contaminating internal and external electrical activity.[15] Thus, ECOG-based BMI designs capitalize on proximity to the electrical source in order to compute signals more closely representative of the intended action (i.e., more 'removed' from noise) and therefore require less practice.

Harnessing the power of multi-unit recording

One of the most complex BMI platforms still in development is the BrainGate array utilized by the Donoghue research group in collaboration with former biotechnology firm Cyberkinetics®. The system is composed of a 4 × 4 mm square array of 100 microelectrodes implanted into the 'hand knob' brain parenchyma of dominant primary motor cortex. The first generation of the BrainGate array implanted two patients with tetraplegic spinal cord injury who were both able to achieve rapid two-dimensional cursor control and more rudimentary multi-jointed limb movement using imagined performance.[11,13] The latest generation of this system (BrainGate 2) employs more advanced neural decoding algorithms and an upperlimb prosthetic device developed for the military to allow fine motor manipulation of objects in three-dimensional space.[12] The BrainGate system has received criticism for the invasiveness of its platform design, although the foundation for neuromotor prosthetic development has come almost exclusively from recordings using implanted microelectrode arrays in nonhuman primates.[8,10] Nevertheless, one of the challenges faced by these early pioneers, and also by the BrainGate group, is the gradual deterioration of signal quality over time, a feature that has not been an observed problem for EEG-or ECOG-based approaches. Various hypotheses have been offered to explain this phenomenon, including gliosis and micromotion of the electrodes.[20] Despite these issues, currently no other BMI platform is able to match the complexity and degrees of freedom of robotic limb control, and it is indeed possible that we may see multi-unit BMI devices with a more biocompatible, less invasive form factor in the near future. Although speculative, miniaturization and full implantation of a multi-unit system will have to be achieved before it can undergo a full clinical trial to demonstrate these important advances relative to the level of prosthetic control that ECOG-based approaches are also beginning to provide.

Ethical challenges of mind control – are we there yet?

Few studies have been published on the ethical dilemmas posed specifically by BMI technology.[5,6] From a technological standpoint, these devices operate similarly to implanted cardiac pacemakers that can be percutaneously or remotely interrogated and adjusted. However, the prospect of using DBS to treat psychiatric disorders has reintroduced the issue of personality-or 'mind'-altering therapies, and it is apropos to the discussion also centered around BMI devices for cognitive control. Christopher, *et al*. studied decision-making in patients with medically refractory depression considering DBS and found that current trials have developed ethically sound informed consent algorithms that achieve sufficient transparency on the likelihood of benefit for participants.[4,9,17] The Defense Advanced Research Projects Agency (DARPA) also has a substantial interest in BMI technology for enhancing capabilities of soldiers in combat, such as its 'Silent Talk' program, which aims to decode EEG signals of intended speech as a form of communication between field operatives.[14] These and other BMI platforms on the horizon will require incorporation into novel ethics frameworks accounting for both restoration and enhancement of neural function.

CONCLUSION

BMIs are an emerging technology that has been in development for several decades in basic neuroscience and engineering research laboratories. EEG-based designs were the first to demonstrate translational algorithms between brain activity and external computing devices. Nevertheless, EEG-based BMI systems have been replaced by chronically implantable ECOG and multi-unit recording electrodes that can achieve signal acquisition on finer timescales and thus drive more elaborate actuators with less extensive training protocols. Overall, BMI represents a new paradigm in the effort to restore function in patients with severe neurological impairment, including patients with spinal cord injury, stroke, neuromuscular disorders, and limb amputation – conditions in which all other therapeutic modalities have failed to recover any functional movement. BMI technology has now matured to the point where clinical applicability is imminent. Neurosurgeons will be required to gain familiarity with these various platforms, and our input is critical to the next generation of safer and more functional devices.

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