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Neuroprosthetic devices: how far are we from recovering movement in paralyzed patients?

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"Neuroprostheses offer the promise of restoring movement to paralyzed patients … ultimately allowing patients … greater independence and improving their quality of life."

In October 2008, Eberhard Fetz's group from the University of Washington demonstrated that a direct artificial connection from a region of the brain associated with the control of movement to muscles in the limb could restore movement induced by electrical stimulation in monkeys whose arms had been temporarily anesthetized. The report of this progress created tremendous public interest as a perceived milestone in the development of a seamless neurotechnological solution for restoring function in paralysis. This work relied on the combination of an implanted electrode array in the motor cortex and functional electrical stimulation (FES) to muscles in the paralyzed wrist. Indeed, the combination of FES, a technique that has achieved a track record of clinical utility, with brain–machine interfaces (BMIs) has become the subject of study for several research groups. Based on progress from these groups, we suggest that the technology has reached sufficient maturation that the proof-of-concept clinical demonstration could be accomplished within the next 5 years. In this editorial, we provide a brief overview of the key technologies and several key issues that are being explored, and also discuss the importance of supporting translational neuroprosthetics research and development to achieve this goal.

Paralysis resulting from neurological injury or disease places a significant burden on patients, their families and caregivers. Neuroprostheses offer the promise of restoring movement to paralyzed patients by bypassing damaged regions of the nervous system, ultimately giving patients the ability to live with greater independence and improving their quality of life. Indeed, the coordinated stimulation of paralyzed muscles through FES has been shown to be effective and safe for restoring hand grasp [1–3], bladder control [4–6] and respiration [7,8], and clinical feasibility has been shown for standing, walking [9–12] and coughing [13,14]. These neural interfaces function by delivering small levels of pulsed electrical current to intact presynaptic nerves to trigger stimulus–secretion coupling in target muscles. Although no longer receiving meaningful input from neural structures caudal to the lesion, the paralyzed muscles can be induced to contract through FES to restore purposeful movements for the patient. Several research participants have received multiple implantable devices, enabling them to achieve multiple functions, such as the use of both hands, standing and hand and postural control.

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Implantable devices used to provide these functions range from the BION™ [15], a small single-channel microstimulator that is readily implantable through a cannula, to multichannel implantable stimulator/telemeter systems [16] to a modular networked and wirelessly controlled system for stimulation and sensing [17–19].

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An implantable system for control of hand grasp achieved commercialization as the Freehand® in 1997, and has been used successfully by over 250 C5/C6 individuals with spinal cord injuries throughout the world [2]. Freehand recipients control hand grasp through operation of an external joystick, controlled by the movement of the opposing nonparalyzed shoulder, which through a radiofrequency-powered and -controlled implanted stimulator, delivers electrical stimulation [20,21]. Claims of utility of medical devices, as with other therapeutic interventions, are ultimately subject to validation through clinical trials. Importantly, a multicenter trial of the Freehand system based on 51 C5/C6 patients quantitatively demonstrated the efficacy of the system. Building from this success, the implantable FES technology is undergoing significant design improvements, which include the capability to use recorded neural and muscle potentials as command signal sources and the use of implanted rechargeable power and wireless telemetry. These improvements allow the user to be free of the encumbering external aspects of the technology and improve his/her control. However, the control of FES devices is currently rudimentary, relying on either movement or underlying muscle activation from a nonparalyzed body part to trigger the coordinated electrical stimulation of muscles in the paralyzed limb.

> "...neuroprosthetics have already provided many individuals with the capability to move and regain essential functions lost after their paralysis."

One of the most exciting recent advances in the neuroprosthetics field has been the emergence of BMI. Over 20 years ago, Georgopoulos and colleagues showed that the firing of individual neurons in the motor cortex could be correlated with specific movements [22]. With the use of microelectrode arrays in various brain regions responsible for movement planning or execution, populations of neurons could be recorded simultaneously. Based on the instantaneous firing rates across the population, limb kinematics or muscle-activation patterns responsible for limb movements could be decoded and predicted [23,24]. Advances in real-time computation have allowed the implementation of closed loop control of cursor movement and robotic limb control based on real-time recording and analysis of spike rates or field potentials [25–28].

Clearly, BMI has enormous implications for individuals living with severe disabilities. By tapping into one or more regions of the brain responsible for the control of movement, BMI may provide natural and complex upper extremity control by relying on volitional signals recorded from brain regions integral to movement control. However, the state of the science is somewhat in flux from basic to the translational/clinical domain and, as a result, there are a number of issues that will need to be resolved. First, there is the question of whether or not paralyzed individuals retain the ability to generate stable patterns that can be decoded to ascertain movement intent. Through a pilot clinical feasibility study initiated by Cyberkinetics Neurotechnology Systems Inc., Hochberg and Donoghue demonstrated that an individual paralyzed for up to 3 years could modulate cortical activity to drive cursor movement with the BrainGate™ system [29]. It remains to be determined how generalized these observations will be and, importantly, how stable the recordings are in patients.

Based on experimental studies involving healthy nonhuman primates, it is well known that quality recordings are typically obtained for no more than several months to 1 year after paralysis, regardless of the microelectrode array platform employed [30]. A recent preliminary report suggests that the clinical outlook for existing devices may be more optimistic [31].

Second, the leadership in the BMI field has been largely driven by the fundamental questions pertaining to how the brain controls movement. For example, does the brain encode limb kinematics (e.g., direction and velocity) or the activity of muscles, which ultimately result in limb kinematics? How can proprioceptive and/or tactile information, perhaps delivered through microstimulation of the somatosensory cortex, improve BMI performance [32]? These are undoubtedly important scientific questions, but to move forward with the clinical integration of FES and BMI, the field needs to develop design specifications for BMI as a source of control signals for FES systems. Musculoskeletal modeling, which captures the activation and dynamics of limb control in real time, may be used to simulate useful movements [33]. By varying the BMI characteristics, such as the number of recorded neurons, the stability of the recordings and the decoding methodology, one may empirically derive the minimum performance requirements for a useful control signal source. Robert Kirsch's group at Case Western Reserve University/Cleveland VA Medical Center working in conjunction with Leigh Hochberg at Brown University/Massachusetts General Hospital is actively pursuing this area by coupling their dynamic limb simulator to the data stream from BrainGate patient recordings [34].

Third, BMI systems need to be fully implantable to minimize risk associated with infection and to enhance the mobility of users. Several groups are working toward the development of a wireless system and, in at least two cases, they are leveraging against the Utah array architecture that underlies the BrainGate system [35–38].

Finally, funding sources that enable translational and pilot clinical feasibility studies for neural prosthetics need to be in place. The NIH Neural Prosthesis Program, initiated in the 1970s, enabled targeted basic, translational and clinical neural engineering projects through contract-based initiatives. With the widespread recognition of bioengineering as an academic discipline, translational neural prosthetics projects have attempted to compete for grant funding with basic science, ultimately with mixed results. Recognizing this gap, several institutes at the NIH have partnered to offer a new program announcement on neural prosthetics, encouraging translational and pilot clinical studies. This program will enable support for milestone-driven projects for the design, development and demonstration of clinically useful neural prosthetic devices. Activities to be supported in this program include implementation of clinical prototype devices, preclinical safety and efficacy testing, design verification and validation activities, pursuit of regulatory approval for clinical study, and proof-of-concept or pilot clinical studies.

In summary, neuroprosthetics have already provided many individuals with the capability to move and regain essential functions lost after their paralysis. FES-based devices have proven to be safe and effective in the body for decades without deterioration of function, and the users continue to use them on a nearly daily basis. However, control must be made even more natural to the user, enabling them to accomplish movement in a fluid and transparent way. With the recent advances in BMI, including the emergence of wireless systems, we suggest that these technologies are reaching sufficient maturation that the proof-of-concept clinical demonstration of a combined BMI and FES system could be accomplished within the next 5 years. Finally, programs are in place to enable the translation of findings from the research laboratory to the clinic, such that a neuroprosthetic solution can become a component of routine clinical care for individuals who have become paralyzed.

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