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Brain–computer interface technology as a tool to augment plasticity and outcomes for neurological rehabilitation

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Brain–computer interfaces (BCIs) are a rehabilitation tool for tetraplegic patients that aim to improve quality of life by augmenting communication, control of the environment, and self-care. The neurobiology of both rehabilitation and BCI control depends upon learning to modify the efficacy of spared neural ensembles that represent movement, sensation and cognition through progressive practice with feedback and reward. To serve patients, BCI systems must become safe, reliable, cosmetically acceptable, quickly mastered with minimal ongoing technical support, and highly accurate even in the face of mental distractions and the uncontrolled environment beyond a laboratory. BCI technologies may raise ethical concerns if their availability affects the decisions of patients who become locked-in with brain stem stroke or amyotrophic lateral sclerosis to be sustained with ventilator support. If BCI technology becomes flexible and affordable, volitional control of cortical signals could be employed for the rehabilitation of motor and cognitive impairments in hemiplegic or paraplegic patients by offering on-line feedback about cortical activity associated with mental practice, motor intention, and other neural recruitment strategies during progressive task-oriented practice. Clinical trials with measures of quality of life will be necessary to demonstrate the value of near-term and future BCI applications.

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Neurological rehabilitation aims to lessen physical and cognitive impairments (e.g. weakness of the upper extremity after a stroke) and related disabilities (e.g. difficulty using the affected hand to reach and grasp items for dressing or toileting) and to increase independence so patients can participate in daily self-care and other activities and improve their health-related quality of life (QOL). Skills learning after stroke, traumatic brain or spinal cord injury and other diseases draws upon spared neural networks for movement, sensation, perception, memory, planning, motivation, reward, language and other aspects of cognition (Dobkin, 2004). The essence of therapy is progressive practice of subtasks and more complete intended goals using physical and cognitive cues with feedback about performance and results (Dobkin, 2005a). Patients must have some access to voluntary movement for motor interventions to work. If so, functional magnetic resonance imaging (fMRI), transcranial magnetic stimulation, and other techniques reveal some of the regional brain adaptations that may evolve as successful rehabilitation training optimizes parameters for voluntary actions (Dobkin et al. 2004; Koski et al. 2004; Weiskopf et al. 2004; Dobkin, 2005b; Winchester et al. 2005; Dong et al. 2006).

Brain–computer interface (BCI) systems are rehabilitation devices in every sense. Training-induced plasticity leads to intentional control of a computer cursor or a machine to permit communication and other functions that lessen disability and enhance health-related QOL. BCI technology requires patients to learn to manipulate disease-spared electrical potentials such as the mu rhythm (Wolpaw & McFarland, 2004), P300 (Sellers & Donchin, 2006), or an (Pham et al. 2005) evoked potential that is detected from the scalp or cortical surface. Intracortical strategies decode burst activity from a small number of neurons in the primary motor cortex (M1) or other regions via a multi-electrode array (Pomeroy et al. 2005; Hochberg et al. 2006). Successful deployment of BCI technology depends on the incorporation of cues and feedback during training and practice, as...
well as a mathematical algorithm to transform neural activity, especially from intracortical bursts, into a control signal. For example, self-regulation of slow cortical potentials (SCPs) may depend upon learned regulation of a cortico-striatal-thalamic loop that modulates local excitation thresholds of cortical ensembles (Hinterberger et al. 2005). Subjects appear to learn to regulate the excitatory thresholds of large neuronal assemblies as a prerequisite for direct brain communication using an SCP-driven BCI. These adaptations in the control of electrical potentials used for BCI may arise from changes in neuronal tuning to parameters of movement, in the variability of neuronal firing as practice and reward proceed, in Hebbian strengthening of neuronal ensembles with remapping of representations for movements, in recruitment of remote or correlated activity from ensembles within a network, and in other self-regulation and learning-associated processes. These mechanisms also serve the physiological basis for neurorehabilitation (Dobkin, 2004).

**BCI for neurorehabilitation**

**Disability.** Candidates for BCI applications usually have no other means to control a computer interface, such as by triggering a microswitch with a minimal muscle, joint or eye movement. The most typical patient would have a locked-in syndrome. These persons are awake and conscious but de-efferented with no ability to produce speech, limb or facial movements. Acute ventral pontomedullary stroke and late stage amyotrophic lateral sclerosis are the most common causes. Other diagnoses of patients with minimal or no useful motor function include brain stem encephalitis, cerebral palsy with action-induced movement disorders or paralysis and severe dysarthria, traumatic brain injury with diffuse axonal white matter injury but no hypoxic–ischaemic cortical injury, and persistent disorders of the motor unit such as a Guillain-Barre syndrome with generalized polyneuropathy or a progressive muscular dystrophy. Patients with spinal cord injury with the lesion at or above the motoneurons for the diaphragm and shoulder muscles could benefit if other options, especially for a ventilator-dependent person, were not feasible for manipulating a computer cursor or environmental control system.

Many of the patients considered for a BCI system are fed by stomach tubes and require mechanical ventilation, frequent turning in bed or wheelchair to prevent skin ulcers, measures to empty the bowels and bladder, and other nursing care such as range of motion of joints and lubrication of the skin. Centrally acting medications, intermittent lung and bladder infections, autonomic dysfunction with fluxes in blood pressure, and co-morbidities from heart disease, diabetes mellitus, hypertension, and other toxic and metabolic complications are common in these immobile people. All of these factors can interfere with concentration, attention, learning and perhaps the reliability of intentional manipulation of cortical signals.

Much of the experimental proof-of-principle in BCI work has involved healthy subjects, rodents and monkeys or patients who retained some head, facial or limb movement. Animal models of cell recordings for BCI control have provided great insight into the functional tuning of neurons and have revealed the promise of BCI. Direct translation from animal experiments of a BCI to human studies of neurologically impaired patients can become as misleading as the translation of cellular transplantation experiments from rodents to man for spinal cord injury repair (Dobkin et al. 2006). The rodents and monkeys have been deprived of the ethologically typical environs for which their neural and humoral systems evolved. With little competition for use of a cell population and with hunger or thirst as the reward for performance, the control and maintenance of a BCI signal may be easier in caged animals than in human subjects. In many published studies and videotaped demonstrations of an invasive or non-invasive BCI system, the tongue or lips of the person or monkey may purse, the head and neck may move, unmonitored muscle and eye movements may occur or the subject may even vocalize (Serruya et al. 2002; Hochberg et al. 2006). Thus, the BCI signal may be driven in part by a distributed network activated by this overflow of motor output. Early results in patients, however, are very promising.

**Applications.** Progress in the detection, control and analysis of brain signals is opening the way for robust applications that may diminish disability for patients who cannot use a microswitch (Wolpaw et al. 2006). Communication is perhaps the most fulfilling immediate use of BCI systems for patient, family and caregivers when no intelligible interaction can otherwise take place. Even simple interactions to make needs known, answer questions with a simple yes or no, and select among a small matrix of choices may reintegrate the isolated patient with others. Communication systems already exist that use microswitches to choose letters and words to write text and converse with synthetic speech. Other extant systems can be used to manipulate the environment by adjusting appliances, altering body position in an electric bed or wheelchair for comfort and to decrease the chance for developing a bed sore, and to manoeuvre a powered wheelchair. Socialization, education, entertainment and even support groups are feasible using BCI interaction with the Internet for email, chat lines, games, movies and music (Karim et al. 2006). Virtual environment interactions may further the possibilities for travel and entertainment in the near future.
Patients who can formulate and command movements, but not physically enact the intention, could benefit from a brain–machine interface. Both non-invasive and invasive BCI systems may be able to utilize cortical signals to control a robotic arm or an exoskeleton for the patient’s arm to manage reach and grasp functional activities in peripersonal space. Although the notion of controlling a robotic arm to aid self-care is exciting from the view of neuroscience and engineering, the difficult goal will be a cost-effective robotic arm that performs enough actions to lessen caregiver burden. For patients with intact lower motor neuron and peripheral nerve function, cortical BCI commands may also control a neuromuscular stimulation system for movements of the upper extremity for reach and pinch to enable more self-care. Both actuator-driven and neuromuscular stimulation systems may also come to be designed to permit standing and stepping.

Simplicity of connection and control is necessary if BCI systems are to play multipurpose roles in the daily needs of disabled persons. Eventually, standardized systems may allow the use of different cortical signals so patients can decide which one best operates applications. Subjects have been reported who could not master the manipulation of a particular signal but could use another. Other factors will affect the utilization of BCI systems. Operant learning to consistently control the brain signal must be reasonably easy to achieve and retain. Software must be user-friendly for patients and caregivers. Home systems must be simple to set up and calibrate, reliable, affordable, require infrequent maintenance, and not depend on a corps of engineers to be at hand. The transfer rate of information from brain signals must be rapid. Typing systems would ideally aim for a character at least every 5 s and employ a logic system that anticipates words and phrases. Accuracy ought to reach 90%. The level of concentration for signal control should allow for divided attention. In the home, numerous distractions could interfere with modulation of the BCI signal. The environment of care is usually tight and filled with apparatus such as suctioning and respirator machines and easily spilled liquids. Systems ought to be mobile, sturdy and take up little space, so they can be used from bed and wheelchair. Brain and interface signals must not degrade in the presence of ventilators and electronic appliances. They should also meet some level of cosmetic acceptability. These criteria are gradually being met (Wolpaw et al. 2006). Indeed, for the larger population of neurologically disabled patients who are not locked-in, highly robust BCI systems could eventually aid communication, environmental control, and the use of assistive appliances.

Clinical trials. Safety and proof-of-principle trials for implantable BCI devices as well as for non-invasive strategies are in progress. After the reliability, flexibility and a practical means to maintain systems has been established, efficacy trials will probably be necessary before devices obtain regulatory approval and health care insurers become willing to help pay for applications. In subjects who can still make small, non-fatiguing movements, a comparison between a BCI system and a microswitch system in a randomized parallel group or a cross-over trial could determine whether neurally driven versus switch-driven 2-dimensional controllers serve more needs. In completely locked-in subjects, a crossover design could compare patient and family satisfaction between no device and a BCI system. Outcome measures would aim to reveal whether a system benefits patients by reducing medical complications and improving health-related QOL. Being able to communicate about symptoms, such as shortness of breath, urinary burning, pain and its location or a change in cognition or mood, may enable the detection of medical complications well before a drug side-effect or organ dysfunction becomes evident from vital signs and tests. Frequency and duration of daily use of applications are also valuable outcome measures for clinical trials.

Quality of life. Measures of QOL have become an important outcome in clinical trials of medical and rehabilitation interventions (Dobkin et al. 2003; Winston et al. 2003). For example, a primary outcome measure in a randomized trial of a medication for epilepsy may reach statistical significance when compared to another drug for reducing the number of monthly seizures, but may not be clinically meaningful if the frequency of seizures still interferes with school, work and personal safety. QOL measures help focus how a treatment affects a patient’s perception of physical, mental and social functioning, and overall satisfaction. QOL may be far better for a disabled person with amyotrophic lateral sclerosis (ALS), for example, than a healthy person might expect (Kubler et al. 2005). Patients with tetraplegia, even if they require a ventilator, judge their quality of life to be high if they have good social support and are free from chronic pain. QOL measures relevant to BCI trials fall into the domains shown in Table 1. Communication about needs, level of integration into the life of the home and family, sense of psychological and emotional well-being, and life satisfaction can be assessed before and after a BCI system comes into use. Responses are usually made on a 3–5 level Likert scale in which the subject compares present experience to the recent past.

Ethical considerations for BCI interventions

For the suddenly locked-in patient or the person with ALS who has become tetraplegic, aphagic, and chooses to be placed on mechanical ventilation, a BCI system for communication ought to enhance QOL. It is uncertain, however, whether benefits will outweigh the burden of physical, emotional and financial strain on the patient and
The decision to use BCI technology, then, will be a highly personal one. The BCI community can only try to provide what patients may find to be of value.

More theoretical concerns also arise. Repetitive use of stereotyped brain signals within the context of BCI and neurological disease could produce aberrant synaptic efficacy. Unintended movement signals, perhaps like a tic, and obsessive or delusional thoughts from correlative brain activity could evolve. In addition, perceptual distortion could follow the assimilation of a neuroprosthesis into the brain's representations as an extension of the self. Researchers must monitor patients for symptoms of peculiar neural reorganization.

Future training applications
In less profoundly disabled persons, highly practical BCI systems could be used as a tool to recruit and reinforce spared neural representations and networks by using feedback from generated brain signals to enhance skills learning. More simple forms of sensorimotor biofeedback have a long tradition in rehabilitation, but their efficacy is still uncertain.

Using BCI signals, researchers and therapists may be able to improve the effects of a rehabilitation treatment aimed at impairment and disability. BCI signals may enhance training by providing a window on whether the subject is engaging a network for mental rehearsal or goal-directed action. For example, therapists could use the change in the mu rhythm to get immediate feedback about whether a subject is optimally prepared to make a movement and has focused his motor attention. This feedback may enhance presynaptic drive to a cell population and network that participates in extending the fingers to preshape the hand prior to grasping an item or to plan the trajectory of the foot for walking, which in turn may increase motor output and improve the timing and completeness of movements. Patients with incomplete lesions of the motor network often have great difficulty initiating a movement. Some patients with stroke and spinal cord injury intermittently twitch a muscle or slightly move a joint early in their recovery. This action may gain strength and precision if they can find a way to practise. This problem in motor control may arise from difficulty

Table 1. Dimensions of health-related quality of life (QOL) in BCI applications

<table>
<thead>
<tr>
<th>Dimension</th>
<th>Description</th>
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<tbody>
<tr>
<td>Physical well-being</td>
<td>Mobility and self-care dependence; level of activity; symptoms (e.g. pain, side-effects of treatments); immobility-related role limitations with family.</td>
</tr>
<tr>
<td>Mental well-being</td>
<td>Psychological and emotional well-being and stress; mood; cognitive functioning and stress; participation in family and cultural life; self-control of decision-making.</td>
</tr>
<tr>
<td>Social well-being</td>
<td>Social support and integration; home and social roles, contacts, and interactions; participation in work or hobbies; role limitations.</td>
</tr>
<tr>
<td>General health</td>
<td>Energy and fatigue; life satisfaction; perception of health; overall perception of QOL.</td>
</tr>
<tr>
<td>Caregiver QOL</td>
<td>Financial stresses about health costs; physical, mental, social and emotional well-being in role as caregiver; stressors and organizational efforts in maintaining normalcy in home life.</td>
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in finding a strategy to activate or summate enough motor units in the residual pathway or from rapid overuse with central or peripheral fatigue. Feedback could help improve the recruitment or order of recruitment of motor pools or enhance presynaptic activity to M1 to better drive the most effective residual pathway for motor control for a task. At the same time, this process could enhance Hebbian plasticity for skills learning. Thus, just as immediate feedback serves a locked-in patient about the propensity of a modulated neural signal to control a cursor or robotic arm, the signal could be used for the retraining of interactive motor, auditory, visual and cognitive networks to enhance practice and skills learning in less impaired patients with hemiparetic stroke or incomplete spinal cord injury (SCI).

The BCI Neurochip, which is being developed as an autonomous interface between an implanted computer chip and recording and stimulating electrodes, converts neural activity from one region (M1) and then stimulates another (cervical spinal cord) to evoke functional synergistic movements of the arm (Jackson et al. 2006). Computing chips could also connect with axons. In another potentially remarkable BCI application, minimally invasive techniques for intracortical recordings could help identify the most robust neural tuning parameters through behavioural training (Nicolelis, 2003). Parameters related to the direction, velocity, acceleration, position in space, grip force, kinematics and others would be recorded. Therapeutic training strategies would then consider which features of a movement were best practised within the patient’s ability to make use of each parameter.

Combational approaches are likely to be employed for the future neurorehabilitation of highly impaired patients. BCI may aid training and augment the actions of neuromodulating medications (Ziemann et al. 2006), exogenous cortical stimulation for excitation or inhibition of a network (Beekhuizen & Field-Fote, 2005), and neural repair strategies to incorporate new cells, axons, and dendrites into functionally useful pathways (Dobkin, 2006). Thus, whereas the near-term promise of BCI strategies is to enhance QOL for highly disabled persons, continuously improving technology may create tools to better engage a network and engrain practice parameters with the goal of lessening impairment and disability.

References


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