

British Society of Rehabilitation Medicine

Brain-Computer Interfaces in neurological rehabilitation

Essay Prize Submission 2013

Kundan Iqbal
Newcastle University

During my third year clinical rotations, I met Melissa¹, a 12 year old who suffered a haemorrhagic stroke caused by an undetected brain tumour, which left her suffering with locked-in syndrome (LIS). LIS is a rare condition caused by brainstem damage resulting in sudden quadriplegia (sometimes sparing ocular muscles), with preserved consciousness and cognition. Sufferers are left severely limited. Meeting Melissa initiated my interest in therapies to improve the abilities and function of those with severe neuromuscular disorders including LIS.

¹ Name and age has been changed to preserve anonymity

INTRODUCTION	3
WHAT ARE BCIs?	3
TYPES OF BRAIN SIGNALS.....	3
HOW DO BCIs WORK?	5
Signal Acquisition	5
Feature Extraction.....	6
Feature Translation.....	6
Device Output	6
CLINICAL APPLICATIONS OF BCIs.....	6
SUBSTITUTION OF FUNCTION.....	6
Communication	7
Movement.....	7
Environmental Control.....	8
Locomotion.....	8
RESTORATION OF FUNCTION.....	8
DISCUSSION.....	10
CONCLUSION.....	11
REFERENCES.....	12

INTRODUCTION

Many neurological disorders including motor neurone disease, spinal cord injury, cerebral palsy, muscular dystrophies, multiple sclerosis and stroke can impair the neural pathways of muscle control or the muscles themselves. Severe disease can result in loss of all muscle function, including communication, leaving patients cognitively intact but entirely 'locked in' to their bodies[1]. Modern medical advances have increased longevity even in those with severe or progressive disease yet recovery is currently impossible[2, 3].

Management of such patients relies on rehabilitation, which aims to help patients compensate for physical and cognitive impairments, regain skills and re-participate in society[4].

Neurorehabilitation can thereby lessen disability, foster independence and increase quality of life (QOL), for affected individuals, their family and carers. However, patients require some voluntary movement for interventions to work[5] and for those without, current assistive technologies and rehabilitation methods are inadequate[6], resulting in prolonged and profound personal, social and economic burdens of disability[2, 3]. Therefore, developing alternatives is essential.

Recent advances in brain signal analysis and computer technology have generated substantial interest in a potentially transformative method of restoring function in patients with severe motor disabilities[1, 2, 6, 7]. Brain-Computer Interfaces (BCIs- also called Brain-Machine Interfaces) allow users to communicate or control external devices using brain signals rather than conventional pathways of peripheral nerves and muscles[2, 6]. Additionally, BCIs offer the exciting possibility of restoring motor function by inducing 'activity-dependent brain plasticity'[6]. This essay discusses principles of BCI technology, its applications for neurorehabilitation, current limitations and future prospects.

WHAT ARE BCIs?

BCIs recognise the user's intent through analysing their brain activity, which is then translated into commands that accomplish the user's desire, meaning communication and control of the external world can be achieved despite an impaired neuromuscular system[2, 5, 6].

TYPES OF BRAIN SIGNALS

Signals which can be used to monitor brain activity include electrophysiological, magnetic, or metabolic[6, 7].

Since the electroencephalogram (EEG) was first described by Berger in 1929[8] scientists have questioned if it could be used therapeutically as well as for diagnosis and investigation[2]. As illustrated in Figure 1, electrophysiological signals may be recorded using non-invasive over-the-scalp electrodes (EEG), or more invasively, from electrodes surgically placed on the cortical surface (electrocorticographic (ECoG)), or implanted within the brain (intracortical) which record 'local field potentials' (LFPs) and 'neuronal action potentials' (spikes)[6].

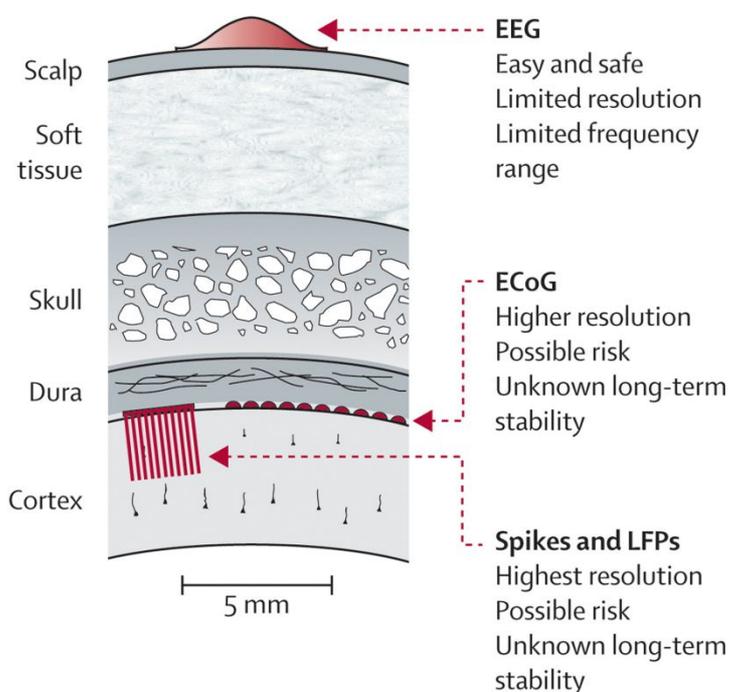


Figure 1 Recording locations for electrophysiological signals and their advantages and disadvantages. Modified from[6]

EEG is the simplest and safest recording method; however, it has limited frequency range, signal strength and spatial resolution, and is more susceptible to interference, for example from electromyographic (EMG) signals from facial muscles[2, 6, 7]. Both ECoG and intracortical recordings provide more sensitive data, resulting from their greater proximity to neurons[2, 6, 7]; however, some argue this is not significant[7]. Furthermore, they both require surgery with its attendant risks of tissue damage and infection, and their long-term safety and stability needs clarification[2, 6, 7]. Because of this, ECoG has been mainly trialled in presurgical epileptic patients and intracortical BCIs are mostly tested in primates[6, 7].

Non-invasively, magnetoencephalography (MEG) measures tiny magnetic fields produced by brain activity; and positron emission tomography (PET), functional magnetic resonance imaging (fMRI) and near-infrared spectroscopy (NIRS) measure blood oxygenation and flow, which correlates with neural activity[7]. However, whilst MEG, fMRI and NIRS show efficacy, their size, complexity and cost mean their use is restricted to research[7].

Each method of BCI has merits and weaknesses. However presently, only electrophysiological methods offer potentially practical BCIs due to their relatively short time constants and simple, inexpensive equipment. Consequently, these BCIs are in the most advanced state of development and the most studied in humans[2, 6]; therefore the remainder of this essay focuses on them.

HOW DO BCIs WORK?

All BCIs consist of four elements[6]: signal acquisition, feature extraction, feature translation, and device output, illustrated in Figure 2 along with potential applications.

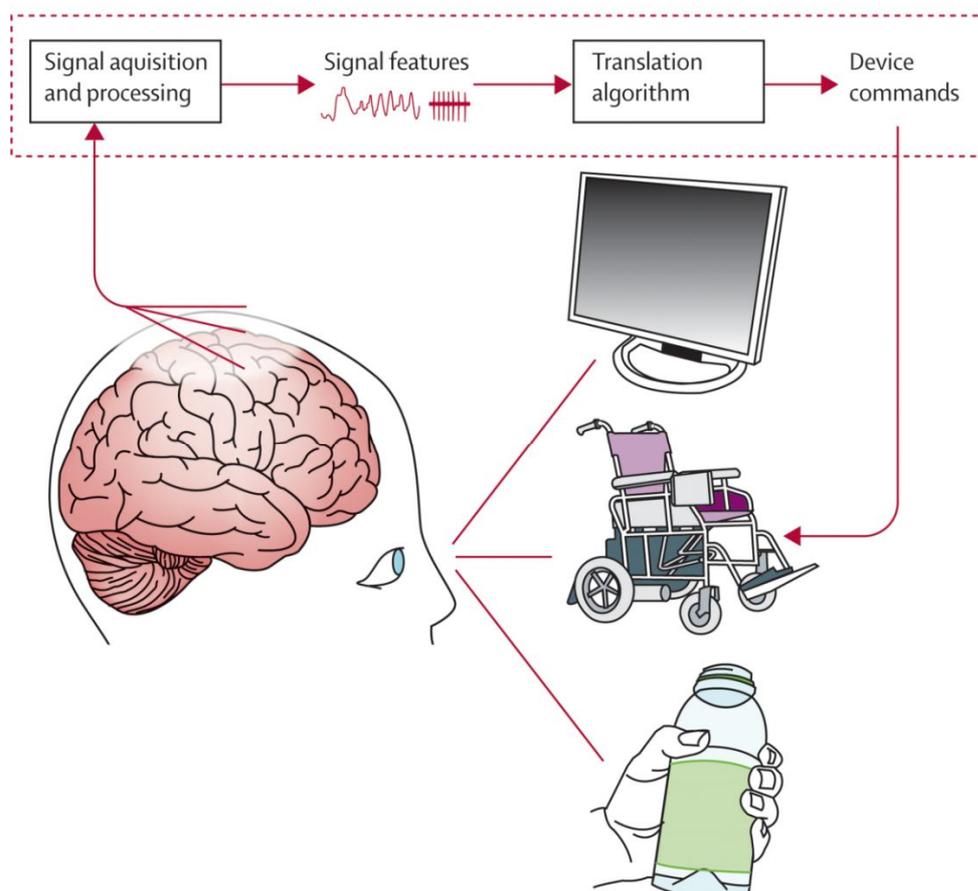


Figure 2 Overview of a BCI system. Modified from[6]

SIGNAL ACQUISITION

Brain electrical signals are acquired by the electrodes, amplified and digitalised.

FEATURE EXTRACTION

The signal is processed by accurately extracting the signals reflecting a person's intent and removing confounding artefacts, for example EMG activity.

Current systems commonly extract one of:

1. Slow cortical potentials (SCPs) - Voltage changes over 0.5-10.0s. Negative shifts represent cortical activation (e.g. movement) while positive shifts represent reduced activation.
2. Sensorimotor rhythms (SMRs) - recorded over sensorimotor cortex at 8–12 Hz (mu rhythm) and 18–26 Hz (beta rhythm), changes occur with sensorimotor stimulation or motor imagery.
3. P300 potentials- a significant peak in the EEG at a latency of 300 milliseconds following a visual or auditory stimulus of special significance[7].

FEATURE TRANSLATION

The signal is further processed by 'translating' the extracted signal features into commands using an algorithm. Crucially, translation algorithms must be dynamic and adaptable to the continuous changes of both the signal features and user's performance due to tiredness and so forth[6].

DEVICE OUTPUT

The commands thus created can be used to operate an external device, for example computer cursor or neuroprosthetic. BCI systems must enable real-time interaction between user and the outside world, to allow the user to receive feedback on the output, which might influence subsequent output. For example, "if a person uses a BCI to control a neuroprosthetic arm, the position of the arm after each movement will influence the person's intent for the next movement and affect the brain signals that encode that intent"[6].

CLINICAL APPLICATIONS OF BCIs

There are two ways to utilise BCIs to facilitate rehabilitation. Firstly, BCIs can substitute for lost neuromuscular function[2, 7, 9]. The second use is more complex and only recently begun to be explored. BCIs might restore motor function by inducing activity-dependent brain plasticity to restore more normal brain function[6].

SUBSTITUTION OF FUNCTION

COMMUNICATION

“Communication for people who are ‘locked in’ probably represents the most pressing area in need of intervention”[7] and capability for basic communication contributes significantly to QOL for severely paralysed patients[6].

Studies in people with amyotrophic lateral sclerosis (ALS) and other neurological diseases with various degrees of motor impairment confirmed SMR and SCP BCIs can provide basic communication ability via controlling computer-aided spelling systems, selecting icons and performing basic word processing[7, 10-14]. However, communication is very slow (1-3 letters/minute[13, 15]), error prone and significant user training (sometimes months) is required[13]. Nevertheless, it is a huge achievement which has improved the QOL of patients[11], and some argue speed is unimportant in “paralysed patients with a different life perspective and an urgent need to communicate”[13].

Alternatively, P300 spellers based on visual stimulus (e.g. grids of numbers, letters or symbols which flash in a random order, with the user focusing on the item s/he wishes to select) have been shown to be effective, with an acceptable communication rate[7, 16-18]. Importantly, they require minimal training because the P300 response occurs normally[7, 17]. Furthermore, auditory-based systems are being developed for patients with impaired visual systems[6, 18, 19].

Invasive subcortical and intracortical BCIs have also been effective[20, 21]. However, death and medical complications interrupted communication in some studies[20]. Other studies in presurgical epileptic patients showed potential when patients attempted spelling or performed imagery tasks[22, 23]. However, whilst invasive BCIs confer greater precision and speed, they are less acceptable to patients who prefer non-invasive devices despite their slowness and error rate[2, 7, 13]. Furthermore, invasive BCI studies are currently too small to judge long-term efficacy[7]. Therefore, non-invasive BCIs “are and will remain the method of choice for communication in paralysed and...locked-in patients”[13]. Encouragingly, some individuals are already using EEG-based BCIs daily[6], including a scientist with ALS who uses it to run his research programme[6, 24].

MOVEMENT

Restoration of motor control is another key application. Both SMR and P300 BCIs have been tested in severely paralysed people[25]. An SMR BCI allowed a tetraplegic patient to grasp, open and close his paralysed hand by activating an orthosis[26, 27]. An implanted hand neuroprosthesis combined with a motor imagery-based system has been effective in a partially paralysed patient [25, 28].

Invasive BCIs can also be successful, as demonstrated by several studies performed in healthy monkeys which resulted in their performing skilled movements[29, 30]. More significantly, a partially paralysed human was able to open and close a prosthetic hand, and use a simple multi-jointed robotic limb to grasp and transport objects via intracortical electrodes[31]. Many efforts are focusing on further developing both invasive and non-invasive EEG-based BCIs for robotic or neuroprosthetic limb operation (for details see[6]).

ENVIRONMENTAL CONTROL

BCI-based environmental control (e.g. thermostat, lights, television etc.) could significantly improve the quality of life of severely disabled people[5, 15, 32] who are often home-bound.

A study by Cincotti et al[5, 32] integrated EEG-based BCI technology into a domestic environmental control system, allowing patients (suffering from muscular dystrophy or atrophy) to remotely operate lights, home entertainment, front door opener, a motorised bed and telephone, as well as monitor their surroundings using wireless cameras. Tested in a simulated home environment, they found it increased patients' sense of independence and relieved carer burden. Other systems are being developed[15].

LOCOMOTION

Restoring independent locomotion is another key issue. EEG BCI-controlled electric wheelchairs have been successfully developed, either allowing the user to send directional commands[33, 34] or choose a destination from a menu[35]. Whilst the latter is less demanding on the user, wheelchair control is limited to pre-set destinations. Further work is required to validate applicability of BCI-driven wheelchairs, for which, "due to considerations of safety, there must be stricter requirements for accuracy than for many other applications"[7].

RESTORATION OF FUNCTION

A robust evidence database shows activity-dependent brain plasticity (ADBP) results in ongoing motor learning and skill acquisition, not only in an intact central nervous system (CNS), but also following trauma or disease, for example stroke[3, 36-40]. Plasticity can occur at synaptic, neuronal and circuit levels[40, 41]. Current rehabilitation protocols work on the premise that repetitive movement practice will restore motor function via ADBP[6, 40, 42-44]. Crucially, ADBP can either lead to restoration of normal function or, if repetitive abnormal movements are made, exacerbate or even establish abnormal function[6]. Therefore, rehabilitation must be carefully targeted. Recently, there has been growing interest in using BCIs to promote rehabilitation. Two types of BCI-based motor learning strategies are possible[6], as illustrated in Figure 3.

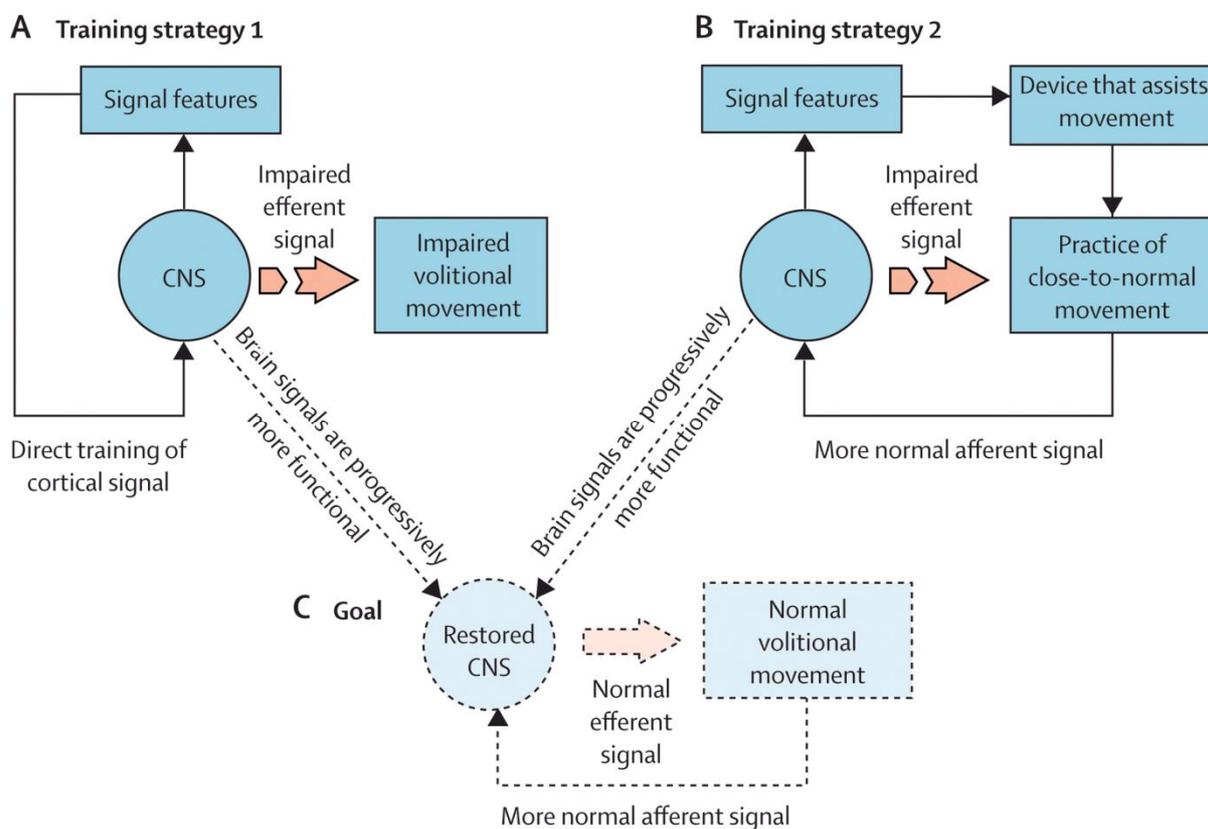


Figure 3 Two BCI-based training strategies to guide CNS plasticity to improve motor function[6]

The first strategy aims to train patients to produce more normal brain activity to control motor function, by using a BCI to provide EEG feedback on the current state of brain activity, enabling patients to gain control of specific brain activity patterns and lower abnormal activity[6]. Paralleling research first initiated several decades ago on training patients with epilepsy to control EEG features as a way of decreasing seizure frequency (amongst other conditions)[45-50], several studies have confirmed training can change features of EEG, ECoG or single-neuron activity[6]. For example, studies in stroke patients show they can gain control of specific EEG features[29, 51]; BCI-based sensorimotor rehabilitation improved motor function after CNS injury[52]; and EEG features changed in parallel with motor function improvement after EEG-based neurorehabilitation[53]. However, it remains uncertain “whether training a patient to produce more normal brain signal features will improve motor function that involves the same areas that produce those signals”[6].

The second strategy uses brain signals to activate assistive devices, on the basis that “CNS plasticity induced by the sensory input produced during the improved motor function provided by the device will lead to improved motor control”[7]. This is supported by studies demonstrating observation and practise of movements that are as normal as possible may help improve motor function[6, 54-56]and guide nascent ADBP[41, 57].

Brain signals might be used to activate a device that activates functional electrical stimulation (FES) or assistive robotics. Studies are encouraging, demonstrating both BCIs with FES[26, 58-61] or assistive robotics[28, 31] may aid motor relearning in patients with impairments from stroke. However, not all patients improved, or improved but didn't necessarily regain normal motor control[6]. Despite this, this method can be successful in some patients, particularly those with moderate-severe deficits following stroke[6].

BCI-based therapy might provide a useful adjunct to standard neurorehabilitation and might lower cost by reducing need for constant supervision by rehabilitation therapists[6, 7].

However, many questions remain to be resolved, including the extent to which patients have detectable brain signals that can support either of the strategies; which brain signal features are most suitable and how they can be used most effectively; and how to provide training and guidance to patients to maximise performance[6].

DISCUSSION

As discussed, BCI technology can be used for many functions and consequently, could substantially improve QOL in people with devastating neurological diseases such as ALS. Whilst some EEG-based BCIs for simple communication and environmental control are currently practical[7] and indeed are being used by a small number of patients day-to-day[24], issues remain which must be addressed in order to fully transfer BCIs from laboratories to homes and clinics[62].

Effective BCI use is a skill that needs to be acquired and maintained[2, 6]. BCIs require intense concentration which can lead to rapid fatigue and inconsistent performance[7, 20, 35, 63]. Such variability and that due to distraction, disease progression and so on require continuing mutual adaptation between the user and the system[6]. Managing this adaptation "is one of the most difficult and important challenges" facing BCIs[6]; this could be reduced by developing "intelligent adaptation" and learning algorithms[7].

All current BCIs require significant efforts to set up, calibrate, and operate[62] alongside continuous and costly expert technical support[7, 62]; therefore, they must improve in ease and convenience of daily use as well as long-term maintenance. Furthermore, BCIs must improve in areas as diverse as speed, accuracy, consistency, safety, reliability, practicality and cosmesis[7, 9] to fulfil their potential.

Finally, motivational factors, such as acceptability and whether use improves the user's QOL can be crucial[2]. Changes in an individual's physical or social environment and interactions can

considerably affect the extent of BCI use[2] and customising BCIs to suit the needs of the individual user is important[62]. Importantly, "to avoid unrealistic expectations and disappointment, [prospective] users and their families should be made aware of the modest capacities of present-day BCI technology"[7, 62] through good communication.

CONCLUSION

Both the study and use of BCIs in neurorehabilitation remains in its early stages with many challenges. Successful dissemination into clinical medicine and the home depends firstly on further research and clinical validation, and secondly, "interdisciplinary cooperation between neuroscientists, engineers, computer programmers, psychologists, and rehabilitation specialists[9]. Nevertheless, BCIs represent an exciting and promising rehabilitation technique, and one that is making significant advances.

Word Count (not including title page and contents page): 2498

REFERENCES

1. Graimann, B., B. Allison, and G. Pfurtscheller, *Brain- Computer Interfaces: Revolutionizing Human-Computer Interaction*, ed. A.C. Elitzur, et al. 2010, Germany: Springer.
2. Wolpaw, J.R., et al., *Brain-computer interfaces for communication and control*. *Clinical Neurophysiology*, 2002. **113**(6): p. 767-791.
3. Kleim, J.A., *Neural plasticity and neurorehabilitation: Teaching the new brain old tricks*. *Journal of Communication Disorders*, 2011. **44**(5): p. 521-528.
4. Carter, G.T., *Rehabilitation management in neuromuscular disease*. *Journal of Neurologic Rehabilitation*, 1997. **11**(2): p. 69-80.
5. Cincotti, F., et al., *Non-invasive brain-computer interface system: Towards its application as assistive technology*. *Brain Research Bulletin*, 2008. **75**(6): p. 796-803.
6. Daly, J.J. and J.R. Wolpaw, *Brain-computer interfaces in neurological rehabilitation*. *The Lancet Neurology*, 2008. **7**(11): p. 1032-1043.
7. Mak, J.N. and J.R. Wolpaw, *Clinical Applications of Brain-Computer Interfaces: Current State and Future Prospects*. *Biomedical Engineering, IEEE Reviews in*, 2009. **2**: p. 187-199.
8. Berger, H., *Über das Elektrenkephalogramm des Menschen*. *Archiv für Psychiatrie und Nervenkrankheiten*, 1929. **87**(1): p. 527-570.
9. Wolpaw, J.R., et al., *Brain-computer interface technology: a review of the first international meeting*. *Rehabilitation Engineering, IEEE Transactions on*, 2000. **8**(2): p. 164-173.
10. Kübler, A., et al., *Brain-computer communication: Self-regulation of slow cortical potentials for verbal communication*. *Archives of physical medicine and rehabilitation*, 2001. **82**(11): p. 1533-1539.
11. Birbaumer, N., et al., *A spelling device for the paralysed*. *Nature*, 1999. **398**(6725): p. 297-298.
12. Hinterberger, T., et al., *A brain-computer interface (BCI) for the locked-in: comparison of different EEG classifications for the thought translation device*. *Clinical Neurophysiology*, 2003. **114**(3): p. 416-425.
13. Birbaumer, N., *Breaking the silence: Brain-computer interfaces (BCI) for communication and motor control*. *Psychophysiology*, 2006. **43**(6): p. 517-532.
14. Birbaumer, N., et al., *The thought translation device (TTD) for completely paralyzed patients*. *Rehabilitation Engineering, IEEE Transactions on*, 2000. **8**(2): p. 190-193.
15. Moore, M.M., *Real-world applications for brain-computer interface technology*. *Neural Systems and Rehabilitation Engineering, IEEE Transactions on*, 2003. **11**(2): p. 162-165.
16. Hoffmann, U., et al., *An efficient P300-based brain-computer interface for disabled subjects*. *Journal of Neuroscience Methods*, 2008. **167**(1): p. 115-125.
17. Piccione, F., et al., *P300-based brain computer interface: Reliability and performance in healthy and paralysed participants*. *Clinical Neurophysiology*, 2006. **117**(3): p. 531-537.
18. Sellers, E.W., A. Kubler, and E. Donchin, *Brain-computer interface research at the university of south Florida cognitive psychophysiology laboratory: the P300 speller*. *Neural Systems and Rehabilitation Engineering, IEEE Transactions on*, 2006. **14**(2): p. 221-224.
19. Furdea, A., et al., *An auditory oddball (P300) spelling system for brain-computer interfaces*. *Psychophysiology*, 2009. **46**(3): p. 617-625.
20. Kennedy, P.R., et al., *Direct control of a computer from the human central nervous system*. *IEEE transactions on rehabilitation engineering : a publication of the IEEE Engineering in Medicine and Biology Society*, 2000. **8**(2): p. 198-202.

21. Kennedy, P.R., et al., *Computer control using human intracortical local field potentials*. Neural Systems and Rehabilitation Engineering, IEEE Transactions on, 2004. **12**(3): p. 339-344.
22. Lal, T.N., et al., *Methods towards invasive human brain computer interfaces*. 2005.
23. Leuthardt, E.C., et al., *A brain-computer interface using electrocorticographic signals in humans*. J Neural Eng, 2004. **1**(2): p. 63-71.
24. Vaughan, T.M., et al., *The wadsworth BCI research and development program: at home with BCI*. Neural Systems and Rehabilitation Engineering, IEEE Transactions on, 2006. **14**(2): p. 229-233.
25. Lebedev, M.A. and M.A.L. Nicolelis, *Brain-machine interfaces: past, present and future*. Trends in Neurosciences, 2006. **29**(9): p. 536-546.
26. Pfurtscheller, G., et al., *'Thought' – control of functional electrical stimulation to restore hand grasp in a patient with tetraplegia*. Neuroscience Letters, 2003. **351**(1): p. 33-36.
27. Pfurtscheller, G., et al., *Brain oscillations control hand orthosis in a tetraplegic*. Neuroscience Letters, 2000. **292**(3): p. 211-214.
28. Müller-Putz, G.R., et al., *EEG-based neuroprosthesis control: A step towards clinical practice*. Neuroscience Letters. **382**(1-2): p. 169-174.
29. Birbaumer, N. and L.G. Cohen, *Brain-computer interfaces: communication and restoration of movement in paralysis*. J Physiol, 2007. **579**(Pt 3): p. 621-36.
30. Nicolelis, M.A.L., *Brain-machine interfaces to restore motor function and probe neural circuits*. Nat Rev Neurosci, 2003. **4**(5): p. 417-422.
31. Hochberg, L.R., et al., *Neuronal ensemble control of prosthetic devices by a human with tetraplegia*. Nature, 2006. **442**(7099): p. 164-171.
32. Cincotti, F., et al. *Non-Invasive Brain-Computer Interface System to Operate Assistive Devices*. in *Engineering in Medicine and Biology Society, 2007. EMBS 2007. 29th Annual International Conference of the IEEE*. 2007.
33. Tanaka, K., K. Matsunaga, and H.O. Wang, *Electroencephalogram-Based Control of an Electric Wheelchair*. Robotics, IEEE Transactions on, 2005. **21**(4): p. 762-766.
34. Vanacker, G., et al., *Context-Based Filtering for Assisted Brain-Actuated Wheelchair Driving*. Computational Intelligence and Neuroscience, 2007. **2007**.
35. Brice, R., *Controlling a Wheelchair Indoors Using Thought*, B. Etienne, et al., Editors. 2007. p. 18-24.
36. Liepert, J., et al., *Motor cortex plasticity during forced-use therapy in stroke patients: A preliminary study*. Journal of Neurology, 2001. **248**(4): p. 315-321.
37. Marshall, R.S., et al., *Evolution of Cortical Activation During Recovery From Corticospinal Tract Infarction*. Stroke, 2000. **31**(3): p. 656-661.
38. Wieloch, T. and K. Nikolich, *Mechanisms of neural plasticity following brain injury*. Current Opinion in Neurobiology, 2006. **16**(3): p. 258-264.
39. Nudo, R.J., *Adaptive plasticity in motor cortex: implications for rehabilitation after brain injury*. J Rehabil Med, 2003(41 Suppl): p. 7-10.
40. Chen, H., J. Epstein, and E. Stern, *Neural Plasticity After Acquired Brain Injury: Evidence from Functional Neuroimaging*. PM&R, 2010. **2**(12, Supplement): p. S306-S312.
41. Nudo, R.J., *Mechanisms for recovery of motor function following cortical damage*. Current Opinion in Neurobiology, 2006. **16**(6): p. 638-644.
42. Johansen - Berg, H., et al., *Correlation between motor improvements and altered fMRI activity after rehabilitative therapy*. Brain, 2002. **125**(12): p. 2731-2742.
43. Bütefisch, C., et al., *Repetitive training of isolated movements improves the outcome of motor rehabilitation of the centrally paretic hand*. Journal of the Neurological Sciences, 1995. **130**(1): p. 59-68.
44. Dean, C.M. and R.B. Shepherd, *Task-Related Training Improves Performance of Seated Reaching Tasks After Stroke: A Randomized Controlled Trial*. Stroke, 1997. **28**(4): p. 722-728.
45. Walker, J.E. and G.P. Kozlowski, *Neurofeedback treatment of epilepsy*. Child and Adolescent Psychiatric Clinics of North America, 2005. **14**(1): p. 163-176.

46. Monastra, V.J., et al., *Electroencephalographic biofeedback in the treatment of attention-deficit/hyperactivity disorder*. Applied Psychophysiology Biofeedback, 2005. **30**(2): p. 95-114.
47. Monderer, R.S., D.M. Harrison, and S.R. Haut, *Neurofeedback and epilepsy*. Epilepsy & Behavior, 2002. **3**(3): p. 214-218.
48. Angelakis, E., et al., *EEG neurofeedback: A brief overview and an example of peak alpha frequency training for cognitive enhancement in the elderly*. Clinical Neuropsychologist, 2007. **21**(1): p. 110-129.
49. Serman, M.B. and T. Egner, *Foundation and practice of neurofeedback for the treatment of epilepsy*. Applied Psychophysiology Biofeedback, 2006. **31**(1): p. 21-35.
50. Lubar, J., et al., *Evaluation of the effectiveness of EEG neurofeedback training for ADHD in a clinical setting as measured by changes in T.O.V.A. scores, behavioral ratings, and WISC-R performance*. Biofeedback and Self-regulation, 1995. **20**(1): p. 83-99.
51. Buch, E., et al., *Think to Move: a Neuromagnetic Brain-Computer Interface (BCI) System for Chronic Stroke*. Stroke, 2008. **39**(3): p. 910-917.
52. Enzinger, C., et al., *Brain motor system function in a patient with complete spinal cord injury following extensive brain-computer interface training*. Exp Brain Res, 2008. **190**(2): p. 215-23.
53. Daly, J.J., et al., *Prolonged cognitive planning time, elevated cognitive effort, and relationship to coordination and motor control following stroke*. IEEE Trans Neural Syst Rehabil Eng, 2006. **14**(2): p. 168-71.
54. Iacoboni, M., et al., *Reafferent copies of imitated actions in the right superior temporal cortex*. Proceedings of the National Academy of Sciences of the United States of America, 2001. **98**(24): p. 13995-13999.
55. Rizzolatti, G., L. Fogassi, and V. Gallese, *Neurophysiological mechanisms underlying the understanding and imitation of action*. Nature Reviews Neuroscience, 2001. **2**(9): p. 661-670.
56. Ertelt, D., et al., *Action observation has a positive impact on rehabilitation of motor deficits after stroke*. NeuroImage, 2007. **36**, **Supplement 2**(0): p. T164-T173.
57. Carmichael, S.T. and M.F. Chesselet, *Synchronous neuronal activity is a signal for axonal sprouting after cortical lesions in the adult*. Journal of Neuroscience, 2002. **22**(14): p. 6062-6070.
58. Do, A.H., et al., *Brain-computer interface controlled functional electrical stimulation system for ankle movement*. J Neuroeng Rehabil, 2011. **8**: p. 49.
59. Do, A.H., et al. *Brain-computer interface controlled functional electrical stimulation device for foot drop due to stroke*. in *Engineering in Medicine and Biology Society (EMBC), 2012 Annual International Conference of the IEEE*. 2012.
60. Fei, M., et al. *BCI-FES training system design and implementation for rehabilitation of stroke patients*. in *Neural Networks, 2008. IJCNN 2008. (IEEE World Congress on Computational Intelligence)*. IEEE International Joint Conference on. 2008.
61. Daly, J.J., et al. *Development and Testing of Non-Invasive BCI + FES/Robot System For Use in Motor Re-Learning After Stroke*. in *Proceedings of the 13th Annual Conference of the International Functional Electrical Stimulation Society "From Movement to Mind"*. 2008. Freiburg, Germany.
62. Kubler, A., et al., *BCI meeting 2005-workshop on clinical issues and applications*. Neural Systems and Rehabilitation Engineering, IEEE Transactions on, 2006. **14**(2): p. 131-134.
63. Kübler, A., et al., *Brain-computer communication: Unlocking the locked in*. Psychological Bulletin, 2001. **127**(3): p. 358-375.