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SYMPOSIUM REPORT

Brain-computer interfaces as new brain output pathways

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Brain-computer interfaces (BCIs) can provide non-muscular communication and control for people with severe motor disabilities. Current BCIs use a variety of invasive and non-invasive methods to record brain signals and a variety of signal processing methods. Whatever the recording and processing methods used, BCI performance (e.g. the ability of a BCI to control movement of a computer cursor) is highly variable and, by the standards applied to neuromuscular control, could be described as ataxic. In an effort to understand this imperfection, this paper discusses the relevance of two principles that underlie the brain's normal motor outputs. The first principle is that motor outputs are normally produced by the combined activity of many CNS areas, from the cortex to the spinal cord. Together, these areas produce appropriate control of the spinal motoneurons that activate muscles. The second principle is that the acquisition and life-long preservation of motor skills depends on continual adaptive plasticity throughout the CNS. This plasticity optimizes the control of spinal motoneurons. In the light of these two principles, a BCI may be viewed as a system that changes the outcome of CNS activity from control of spinal motoneurons to, instead, control of the cortical (or other) area whose signals are used by the BCI to determine the user's intent. In essence, a BCI attempts to assign to cortical neurons the role normally performed by spinal motoneurons. Thus, a BCI requires that the many CNS areas involved in producing normal motor actions change their roles so as to optimize the control of cortical neurons rather than spinal motoneurons. The disconcerting variability of BCI performance may stem in large part from the challenge presented by the need for this unnatural adaptation. This difficulty might be reduced, and BCI development might thereby benefit, by adopting a 'goal-selection' rather than a 'process- control' strategy. In 'process control', a BCI manages all the intricate high-speed interactions involved in movement. In 'goal selection', by contrast, the BCI simply communicates the user's goal to software that handles the high-speed interactions needed to achieve the goal. Not only is 'goal selection' less demanding, but also, by delegating lower-level aspects of motor control to another structure (rather than requiring that the cortex do everything), it more closely resembles the distributed operation characteristic of normal motor control.

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Introduction

Brain–computer interfaces (BCIs) are a fundamentally new approach to restoring communication and control to people with severe motor disorders such as amyotrophic lateral sclerosis (ALS), brainstem stroke, spinal cord injury,

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muscular dystrophies, and cerebral palsy (Wolpaw et al. 2002; Wolpaw & Birbaumer, 2006 for review). All other assistive technology methods depend on the brain's natural output pathways of peripheral nerves and muscles (or peripheral nerves and glands; Wilhelm et al. 2006), and take outputs that the person still retains (e.g. vertical eye movement in a person with a brainstem stroke) and use these to replace missing functions (e.g. using gaze direction to select letters on a computer screen). In contrast, BCIs give the brain entirely new output pathways. They take electrophysiological or other measures of brain activity

and from these measures determine the person's wishes. Intent, which is normally achieved by speaking or by another motor action, is instead achieved by producing brain signals that encode the intent so that a computer can translate it into control of a device such as a computer cursor or a neuroprosthesis.

BCI research, which was confined to only three groups 20 years ago and only six to eight groups as recently as 10 years ago, is now a burgeoning enterprise, with over 100 groups throughout the world engaged in a broad spectrum of research and development efforts, and more entering the field every month. Up to now, this work has demonstrated that a variety of different brain signals, recorded in a variety of different ways and analysed with a variety of different algorithms, can support some degree of real-time communication and control (Vaughan & Wolpaw, 2006). As a result of this collective effort, two facts are becoming increasingly clear. One is encouraging, the other is sobering.

First, BCIs do offer a potentially valuable new option for restoring communication and control to people with severe disabilities; and practical dissemination of BCI technology has in fact begun. Second, however, the development of BCIs that are at once practical, reliable and capable of high-speed complex communication and control is an enormously difficult problem, and one that is far from solution. Furthermore, the origin of the difficulty is not clear – it is not simply a need for better recording methods or improved analysis algorithms – and thus the best route to its solution is also not clear. The origin of this

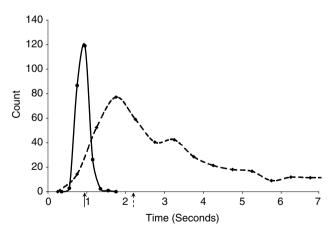


Figure 1. Distributions of times needed to move the cursor to the target in a centre-out task for a person using neurons in motor cortex (dashed line) and for three people using a joystick (continuous line)

The arrows indicate the median times for each distribution. The neuron control data are from 6 daily sessions, and include only the 73–95% (depending on the session) of the trials in which the cursor reached the target within 7 s. Even when the trials taking > 7 s are ignored, neural control is substantially slower and much more variable than normal muscle control. (From Hochberg *et al.* 2006; reprinted by permission from Macmillan Publishers Ltd: *Nature* vol. 442, pp. 164–171, ©2006.)

difficulty and how it might be at least circumvented and at best overcome are the topic of this article.

Limitations of current BCIs

BCI studies usually take place in highly controlled laboratory environments or in similarly constrained clinical situations. The BCI user, whether human or animal, typically assumes a specific posture in a simple stereotyped setting free of distractions and operates the BCI for brief periods under close supervision. In spite of these controlled conditions, one of the hallmarks of the results achieved is their variability. Users do much better on some days than others, and performance can vary widely even within a single session and from trial to trial. This high variability is perhaps best illustrated by BCI-based movement control. For example, Fig. 1 compares cursor movement times when the cursor is controlled by a joystick to cursor movement times when the cursor is controlled by a set of single neurons in motor cortex (Hochberg et al. 2006). BCI control is slower than joystick control and is also far more variable. Such variability appears to be a characteristic feature of all BCI approaches, whether non-invasive (e.g. EEG) or invasive (e.g. electrocorticographic (ECoG) or intracortical). In spite of prolonged practice and frequent recalibration of the algorithms that translate brain signals into output commands, variability in performance remains substantial. In contrast to the actions carried out by the brain's normal neuromuscular pathways, which are very consistent from trial to trial (e.g. Fig. 1), the actions carried out through BCIs display a disconcerting, and, up to now at least, ineradicable variability. This variability is likely to be even greater when BCIs are taken out of the protected settings in which they are now typically used and are applied to the day-to-day needs of people with severe disabilities.

Studies of multidimensional movement control are revealing another surprising feature of BCI performance. Although most researchers had assumed, and many still assume, that invasive methods that use single-neuron activity will provide far better control than non-invasive methods that use EEG, the results to date do not support this assumption. As Table 1 summarizes, the movement control obtained with scalp-recorded sensorimotor rhythms falls in the same range in terms of speed and precision as the control obtained with single neurons. The similarity is strikingly illustrated by comparing the videos available at http:// www.bciresearch.org/html/2d_control_8tn.html (Wolpaw & McFarland, 2004) and http://www.nature.com/nature/ journal/v442/n7099/suppinfo/nature04970.html (video 1) (Hochberg et al. 2006). Both show centre-out cursor control, one with EEG and one with single neurons.

Table 1. Comparison of BCI point-to-point movement control achieved with intracortical microelectrodes that record single neuron activity (Serruya *et al.* 2002; Taylor *et al.* 2002; Carmena *et al.* 2003) and EEG scalp electrodes that record sensorimotor rhythms (Wolpaw & McFarland, 2004)

Method	Reference	Movement time (s)	Movement precision (%)	Hit rate (%)
Intracortical implant	Serruya <i>et al.</i> (2002) Taylor <i>et al.</i> (2002) Carmena <i>et al.</i> (2003)	1.5–2.2	1.3–7.7	86–89
Scalp EEG	Wolpaw & McFarland (2004)	1.9	4.9	92

The ranges are based on each study's best user. Movement precisions are measured as target size as percentage of workspace and calculated from the dimensions of the targets, the cursors, and the workspaces. See Wolpaw & McFarland (2004) for details.

Even though one method has detailed knowledge of the behaviour of each of a substantial number of neurons directly involved in motor control and the other has only a few amplitudes of scalp-recorded EEG rhythms that reflect in a noisy and degraded fashion the combined activity of many millions of neurons and synapses, the methods do not differ markedly in their cursor control. Not only is their speed and accuracy similar, but for both the movements are similarly jerky, or in clinical terms, ataxic. They are similar to the cursor movements that might be produced by a joystick operated by a person with a severe cerebellar deficit. The fact that EEG and single neurons provide similarly defective control suggests that this problem is independent of the recording method.

Further incremental refinements of recording and analysis techniques can probably reduce variability to some extent and increase performance for both invasive and non-invasive methods. Nevertheless, the results to date suggest that, without a fundamental change in how BCI development is conceived and pursued, variability will remain a prominent feature of BCI operation, and the surprising similarity in the capacities of invasive and non-invasive methods is also likely to persist. Solving these problems and thereby realizing the full potential of BCI development may be facilitated by further consideration of the fact that BCIs attempt to establish entirely new output pathways for the brain, that is they demand that the brain do something entirely new. The implications of this demand become clear when BCI development is viewed in terms of what the brain normally does and how it normally does it.

Normal brain functions are widely distributed and undergo continual adaptation

Until less than 200 years ago, the function of the central nervous system (CNS) was not clear: on the one hand, the CNS was thought to provide an interface between a person's immortal soul and the material world, while at the same time it was thought to manage low-level reflex interactions between the organism and its environment (Wolpaw, 2002). In the early 19th century,

philosophical developments and experimental discoveries led to the formulation and widespread acceptance of the sensorimotor hypothesis, the hypothesis that the entire function of the CNS is to convert sensory inputs into appropriate motor outputs. This hypothesis sets the agenda of neuroscience: to understand the physiological, anatomical, genetic, developmental, metabolic, hormonal and environmental factors that shape and control this conversion, as well as the pathological processes that can damage or disrupt it.

Because it seeks to establish new output pathways for the brain, new ways of acting on the world, BCI research is a departure from, or an addition to, this agenda. Nevertheless, it depends on the same brain structures and processes that have evolved to control the brain's standard output pathways, and thus it is likely to be governed by the same principles that apply to standard outputs. The research of the past 150 years, and especially of the past several decades, has revealed two basic principles concerning how the brain converts sensory inputs into motor outputs.

First, the task of creating motor outputs is distributed throughout the CNS from the cerebral cortex to the spinal cord. No single area is wholly responsible for an action. As summarized on the left side of Fig. 2, the selection, formulation, and reliable execution of actions such as walking, speaking, or playing the piano are accomplished by collaboration among cortical areas, basal ganglia, thalamic nuclei, cerebellum, brainstem nuclei, and spinal cord interneurons and motoneurons. For example, the high-speed real-time interactions needed to ensure precise and coordinated movements are handled in considerable part by spinal cord reflex pathways. The product of this widely distributed brain activity is appropriate excitation of the spinal cord motoneurons that activate muscles and thereby produce actions. While activity in a variety of brain areas correlates with motor action, the activity in any one area may vary substantially even in highly constrained settings. This variability contrasts with the trial-to-trial consistency of the motor action itself.

Second, the actions that accomplish a person's intent, whether it be to walk across a room, speak specific words,

or play a particular piece on the piano, are mastered and maintained by initial and continuing adaptive changes in brain function. In early development and throughout later life, neurons and synapses throughout the CNS change continually to master new skills and to maintain those already mastered (Mendell, 1984; Wolpaw & Lee, 1989; Cohen et al. 1997; Thompson et al. 1997; Lieb & Frost, 1997; Whelan & Pearson, 1997; Lisberger, 1998; Garcia et al. 1999; Medina et al. 2000, 2002; Hansel et al. 2001; King et al. 2001; Wolpaw & Tennissen, 2001; van Alphen & De Zeeuw, 2002; Wolpaw, 2002; Carey & Lisberger, 2002; Blazquez *et al.* 2002). This adaptive plasticity is responsible for basic skills such as walking and talking and for more specialized skills such as ballet, and is guided by the results produced. For example, as muscle strength, limb length and body weight change with growth and ageing, CNS plasticity modifies motoneuron control so as to maintain motor skills. Furthermore, the basic anatomy and physiology of the CNS on which this adaptation operates are the result of evolution guided by the need to produce appropriate actions, that is to produce appropriate control of the spinal motoneurons that activate the muscles. In the light of these two principles, BCI development presents a unique and difficult challenge.

The challenge of BCI development

Unlike all normal motor actions, which are produced by spinal motoneurons, BCI outputs are produced by brain signals that reflect activity in one or more brain areas. In normal life, the brain activity responsible for these signals simply contributes to motoneuron control. In contrast, when these signals operate a BCI, the brain activity responsible for them becomes the output of the CNS. Figure 2 illustrates this fundamental change. The neurons that produce the brain signals assume the role normally performed by spinal motoneurons; their activity becomes the final product, the output, of the entire CNS. How well they can perform in this new role depends on how well the many brain areas that normally collaborate to control spinal motoneurons can adapt to control instead the neurons that are producing the crucial brain signals. Can they adapt to optimize the brain signals produced by cortical neurons instead of the muscle contractions produced by spinal motoneurons? For example, can the cerebellum, which normally ensures that spinal motoneurons activate muscles so that movement is smooth, rapid, and accurate, change its role to ensure that cortical neurons produce brain signals that move a cursor (or a neuroprosthesis) smoothly, rapidly, and accurately? On the answers to these and related questions depend the ultimate capacities and practical usefulness of BCIs.

The studies to date indicate that the adaptation necessary to control cortical neurons rather than spinal motoneurons is possible but as yet imperfect. As Fig. 1 and the videos referenced above illustrate, trial-to-trial variability is high, and the cursor movements produced

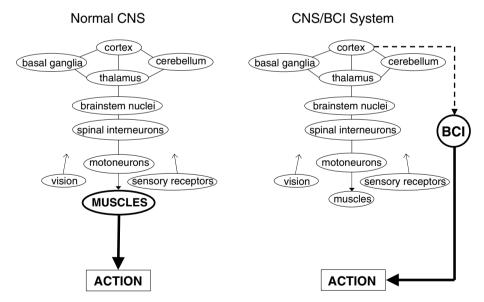


Figure 2. Comparison of CNS production of normal motor actions and CNS production of a BCI-mediated action

The vastly oversimplified diagram on the left shows the production of normal motor action by the many CNS areas that collaborate to control spinal motoneurons and thereby activate muscles. The diagram on the right shows the production of a BCI-mediated action by the same CNS areas collaborating to control the cortical area that produces the brain signals the BCI uses to determine intent. A BCI assigns to cortical neurons the output role normally performed by spinal motoneurons, and thereby requires that the CNS adapt to optimize this entirely new kind of output.

are nowhere near as smooth, rapid and accurate as normal limb movements. Furthermore, these imperfections seem to be similarly prominent whether the brain signals used for control are the activity of individual cortical neurons or the amplitudes of EEG rhythms. Thus, the control deficits cannot be readily ascribed to the recording method.

While future refinements in recording and analysis methods and in training algorithms are likely to improve control to some degree, the extent and nature of the control deficits so prominent in the work to date suggest that substantial progress requires a more realistic strategy that recognizes the unique challenge of BCI usage for the CNS. A realistic strategy should minimize the difficulty of the challenge, and should make the challenge as similar as possible to the demands of normal muscle-based control.

Process control versus goal selection

BCIs provide new output pathways for the brain. A BCI output pathway can function in two different ways: it can control a process or it can select a goal. These two options are shown in Fig. 3. A BCI output pathway can, like spinal motoneurons, control all the details of the process that accomplishes the user's intent. For example, it can specify each of the sequence of individual movements that bring the output device, whether a cursor or a neuroprosthesis, to its target. To do this effectively, it must manage intricate high-speed interactions with the device as the movement proceeds. Alternatively, the new output pathway provided by a BCI can simply communicate the goal (e.g. the target to which the cursor should move) to software that then manages the high-speed interactive process that moves the cursor to the target. Up to the present, many noninvasive and almost all invasive BCI studies have adopted the process-control strategy (e.g. Table 1), while non-invasive BCI studies using the P300 evoked potential (e.g. Farwell & Donchin, 1988) and a few invasive studies using cortical neuron activity (e.g. Musallam et al. 2004) have adopted the goal-selection strategy.

Process control places greater demands on the BCI than does goal selection. Process control requires effective management of the complex high-speed interactions between the BCI output to the device and the sensory inputs indicating the moment-to-moment state of the process. Thus, for example, process control requires that the cortex provide the rapid responses to position-, velocity- and acceleration-related inputs that are normally provided by spinal cord reflex pathways. Goal selection is easier. It requires only that the BCI provide the one part of the action that the software alone cannot provide: the goal, that is, the user's intent. Once that is communicated, the software can itself manage the high-speed real-time interactions that ensure that the goal is achieved rapidly and reliably. Thus, in light of the currently primitive

state of BCI development, goal selection appears to be a more realistic strategy. While the limited invasive data available at present differ too much in protocol to allow a clear comparison of the two strategies, current non-invasive studies suggest that a spelling protocol that uses a goal-selection approach (i.e. P300-based letter selection) may be faster and more reliable than a spelling protocol that uses a process-control approach (i.e. sensorimotor rhythm-based movement to letters) (E. W. Sellers & T. M. Vaughan, personal communication).

Furthermore, the goal-selection strategy has the potential to provide more natural control, that is control closer to normal neuromuscular control. As discussed above and illustrated in Fig. 2, normal neuromuscular control is a product of the combined activity of multiple areas from the cortex to the spinal cord. The cortex alone does not control the motoneurons, and, for some important aspects of movement, has relatively little influence. Much of the process of movement control is delegated to subcortical and spinal areas. In a much cruder but qualitatively similar approach, BCI goal selection obtains intent alone from the cortex and delegates actual control of the process to downstream

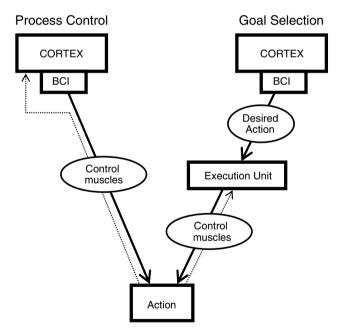


Figure 3. The process-control and goal-selection strategies of BCI development

In the process-control approach, the cortical (or other) brain area that produces the signals used by the BCI handles all the complex high-speed interactions required for rapid smooth and accurate movement. In the goal-selection approach, the BCI simply determines intent, and the process of movement is accomplished by software. Goal selection is much less demanding than process control, and, because it distributes the production of action, is more similar to normal motor control. (While in this example the BCIs control muscles, the same considerations apply to control of a cursor or a device such as a robotic arm or a wheelchair.)

hardware and software. Thus, with further development, including refinement and elaboration of feedback from the downstream apparatus to the CNS, the goal-selection strategy has the potential to emulate with increasing fidelity the brain's normal output pathways. In contrast, process-control BCI methods that vest control entirely in the cortex are likely to remain an artificial and fundamentally unnatural approach.

Conclusion

A BCI changes the final product of CNS activity from spinal motoneuron control to control of the brain area responsible for the signals that the BCI uses to determine the user's intent. Thus, BCI usage presents a unique challenge. It requires that the many CNS areas normally involved in producing motor actions adapt so as to optimize cortical neuron control rather than spinal motoneuron control. The variability characteristic of current BCI performance may stem largely from the difficulty presented by the need for this new and unnatural adaptation. The difficulty might be decreased by switching from a process-control strategy in which the BCI handles all the complex high-speed interactions involved in movement, to a less demanding goal-selection strategy in which the BCI simply communicates the user's goal to software that itself handles the high-speed interactions that achieve the goal. In addition, by assigning lower-level aspects of motor control to an artificial structure (rather than requiring that cortex do everything), the goal-selection strategy imitates the distributed operation typical of normal motor control and may thus provide BCI function that users find more similar to normal motor function.

References

- Blazquez PM, Hirata Y, Heiney SA, Green AM & Highstein SM (2002). Cerebellar signatures of vestibulo-ocular reflex motor learning. *J Neurosci* 23, 9742–9751.
- Carey MR & Lisberger SG (2002). Embarrassed, but not depressed: Eye opening lessons for cerebellar learning. *Neuron* **35**, 223–226.
- Carmena JM, Lebedev M, Crist RE, O'Doherty JE, Santucci DM, Dimitrov DF, Patil PG, Henriquez CS & Nicolelis MAL (2003). Learning to control a brain–machine interface for reaching and grasping by primates. *Plos Biol* 1, 1–16.
- Cohen TE, Kaplan SW, Kandel ER & Hawkins RD (1997). A simplified preparation for relating cellular events to behavior: mechanisms contributing to habituation, dishabituation, and sensitization of the *Aplysia* gill-withdrawal reflex. *J Neurosci* 17, 2886–2899.
- Farwell LA & Donchin E (1988). Talking off the top of your head: toward a mental prosthesis utilizing event-related brain potentials. *Electroencephalogr Clin Neurophysiol* **70**, 510–523.
- Garcia KS, Steele PM & Mauk MD (1999). Cerebellar cortex lesions prevent acquisition of conditioned eyelid responses. *J Neurosci* **19**, 10940–10947.

- Hansel C, Linden DJ & D'Angelo E (2001). Beyond parallel fiber LTD: the diversity of synaptic and non-synaptic plasticity in the cerebellum. *Nat Neurosci* **4**, 467–475.
- Hochberg LR, Serruya MD, Friehs GM, Mukand JA, Saleh M, Caplan AH, Branner A, Chen D, Penn RD & Donoghue JP (2006). Neuronal ensemble control of prosthetic devices by a human with tetraplegia. *Nature* **442**, 164–171.
- King DAT, Krupa DJ, Foy MR & Thompson RF (2001). Mechanisms of neuronal conditioning. *Int Rev Neurobiol* 45, 313–337.
- Lieb JR & Frost WN (1997). Realistic simulation of the *Aplysia* siphon-withdrawal reflex circuit: roles of circuit elements in producing motor output. *J Neurophysiol* 77, 1249–1268.
- Lisberger SG (1998). Physiologic basis for motor learning in the vestibulo-ocular reflex. *Otolaryng Head Neck Surg* **119**, 43–48.
- Medina JF, Nores WL, Ohyama T & Mauk MD (2000). Mechanisms of cerebellar learning suggested by eyelid conditioning. *Curr Opin Neurobiol* **10**, 717–724.
- Medina JF, Repa JC, Mauk MD & LeDoux JE (2002). Parallels between cerebellum- and amygdala-dependent conditioning. *Nat Rev Neurosci* **3**, 122–131.
- Mendell LM (1984). Modifiability of spinal synapses. *Physiol Rev* **64**, 260–324.
- Musallam S, Corneil BD, Greger B, Scherberger H & Andersen RA (2004). Cognitive control signals for neural prosthetics. *Science* **305**, 258–262.
- Serruya MD, Hatsopoulos NG, Paminski L, Fellows MR & Donoghue JP (2002). Instant neural control of a movement signal. *Nature* **416**, 141–142.
- Taylor DA, Helms Tillery SI & Schwartz AB (2002). Direct cortical control of 3D neuroprosthetic devices. *Science* 296, 1829–1832.
- Thompson RF, Bao S, Chen L, Cipriano BD, Grethe JS, Kim JJ, Thompson JK, Tracy JA, Weninger MS & Krupa DJ (1997). Associative learning. *Int Rev Neurobiol* **41**, 151–189.
- van Alphen AM & De Zeeuw CI (2002). Cerebellar LTD facilitates but is not essential for long-term adaptation of the vestibulo-ocular reflex. *Eur J Neurosci* **16**, 486–490.
- Vaughan TM & Wolpaw JR (ed.) (2006). The Third International Meeting on brain–computer interface technology: Making a difference. *IEEE Trans Neural Syst Rehabil Eng*, vol. 14.
- Whelan P & Pearson KG (1997). Plasticity in reflex pathways controlling stepping in the cat. *J Neurophysiol* **78**, 1643–1650.
- Wilhelm B, Jordan M & Birbaumer N (2006). Communication in locked-in syndrome: effects of imagery on salivary pH. *Neurology* **67**, 534–535.
- Wolpaw JR (2002). Memory in neuroscience: rhetoric versus reality. *Behav Cog Neurosci Rev* 1, 130–163.
- Wolpaw JR & Birbaumer N (2006). Brain–computer interfaces for communication and control. In *Textbook of Neural Repair and Rehabilitation; Neural Repair and Plasticity*, ed. Selzer ME, Clarke S, Cohen LG, Duncan P & Gage FH, pp. 602–614. Cambridge University Press, Cambridge.
- Wolpaw JR, Birbaumer N, McFarland DJ, Pfurtscheller G & Vaughan TM (2002). Brain–computer interfaces for communication and control. *Clin Neurophysiol* **113**, 767–791.

- Wolpaw JR & Lee CL (1989). Memory traces in primate spinal cord produced by operant conditioning of H-reflex. *J Neurophysiol* **61**, 563–572.
- Wolpaw JR & McFarland DJ (2004). Control of a two-dimensional movement signal by a noninvasive brain–computer interface in humans. *Proc Natl Acad Sci U S A* **101**, 17849–17854.
- Wolpaw JR & Tennissen AM (2001). Activity-dependent spinal cord plasticity in health and disease. *Annu Rev Neurosci* **24**, 807–843.

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