

Keeping Our Eyes on the Prize; Are We Losing Sight of the ‘Why’ in BCI for Neurorehabilitation?



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*Technology is the answer. But what was the question?
Cedric Price (1966)*

Abstract Studies using BCIs based upon non-invasive, scalp recorded electroencephalography (EEG) have consistently demonstrated utility, both as scientific tools for neuromodulation and for clinical neurorehabilitation purposes. They are particularly appealing in clinical contexts where physical movement is impaired, for instance following stroke. The intrinsic advantage of Brain-Computer Interfaces (BCIs) over alternate rehabilitation strategies is that they work even when output at the behavioural level is non-existent. Patients exhibiting minimal or no residual limb movement after a stroke cannot partake in gold standard physiotherapy, but might still demonstrate brain activity patterns when attempting to move the impaired limb. These patterns can be targeted to enhance recovery. However, the role of BCI should evolve once behavioural output is available. We must not be seduced by the allure of cutting-edge technology at the expense of targeting the specific neurophysiological features that are most likely to drive recovery. At the most basic mechanistic level, the majority of BCIs are driven by neural signals generated by imagination of movement. We need to revisit the question—could motor imagery alone could achieve the same outcomes, or what is the added clinical benefit of the BCI? Accordingly, what is the minimum required intervention using BCI (in terms of time and hardware) to establish a habit of good quality motor imagery that could then sustain rehabilitation without the technology? Motor imagery is free,

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available to every person and at any time. Using technology to harness its virtues while not compromising its simplicity is the ultimate challenge for the field.

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Studies using BCIs based upon non-invasive, scalp recorded electroencephalography (EEG) have consistently demonstrated utility, both as scientific tools for neuromodulation and for clinical neurorehabilitation purposes. They are particularly appealing in clinical contexts where physical movement is impaired, for instance following stroke. Using a BCI where on-screen avatars are driven by neural activation in motor regions encourages the patient to engage in imagined or attempted movements. By providing tangible visual feedback and rewarding desirable neural features, activity in motor pathways is maintained. This may promote use-dependent plasticity and rewiring for recovery of function. However, clinical adoption of the approach has been limited. This is due mainly to difficulties with implementation in non-research settings, as training to achieve neural control of the BCI requires lengthy sessions over multiple days or weeks [1]. Human participants typically use imagined movements or scenarios to achieve BCI control that are associated with distinct scalp-detectable patterns of neural activity. The lack of spatial sensitivity of EEG to distinguish between different imagined (or even executed) movements from different muscles makes decoding and classifying the neural activity challenging, especially in the early days of training.

TMS-NF is a novel approach to provide richer, more muscle-specific feedback in a BCI [2]. In this closed loop system, the size of Motor Evoked Potentials (MEPs) in response to Transcranial Magnetic Stimulation (TMS) are incorporated into the NF signal, such that users can learn how to facilitate or inhibit their brain-muscle pathways by engaging mental strategies to make the MEP larger or smaller (Fig. 1). This typically results in a much faster (i.e. within one training session) grasp of how to execute distinct mental strategies in order to control the game, compared to those reported for EEG BCI. This also produces more spatially distinct and temporally stable neural signatures when the same mental strategies are later executed during simultaneous EEG recording [3]. TMS-NF would not be a practical long-term approach for neurorehabilitation due to the expense and size of the required apparatus, but if it could be used in the early phase of training while still in hospital, the learned strategies may transfer well to an EEG BCI that could be used by patients in their own homes (e.g. see Simon and Ruddy [4], and Fig. 1).

Stroke is one of the leading causes of death and disability worldwide, and incidence is rising at an alarming rate [5]. There have been substantial improvements to emergency stroke care, with advances in thrombolytic therapy leading to a 25% reduction in stroke related deaths. While this is undoubtedly a positive advance, the more worrying implication is that there is now an increasing number of survivors left with significant disabilities as a result of the brain damage, preventing them from leading independent lives. A major unsolved problem is getting the paralysed upper limb functional again. This is one of the key obstacles preventing independence in

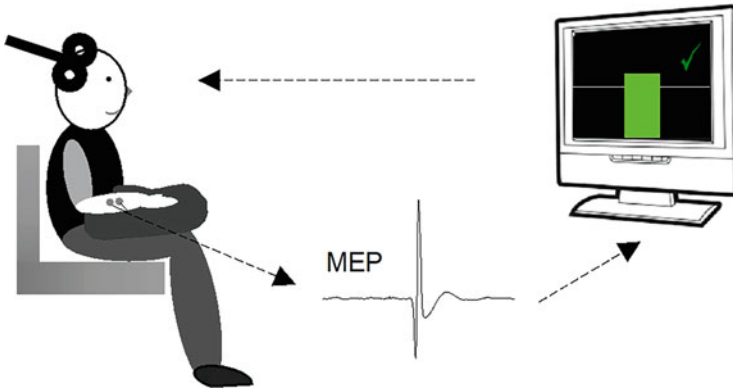


Fig. 1 TMS Neurofeedback protocol used in Ruddy et al. [2]. The peak-peak amplitude of the motor evoked potential (MEP) following TMS is calculated in real-time and displayed to the participant. The height of the rectangle on the screen represents the amplitude of the participant’s MEP. In UP training, participants are rewarded for exceeding their baseline amplitude (white horizontal line). In DOWN trials, they are rewarded for keeping amplitudes small, below the baseline. In a successful trial, when the baseline is exceeded, the bar turns green and a positive soundbite is played. In an unsuccessful trial, the bar turns red and a discouraging soundbite is played

stroke survivors, as without the use of one limb, they are unable to perform the most basic activities of daily living, such as dressing, preparing food, and personal care. As the brain-muscle pathways that previously controlled the upper limb are permanently damaged, recovery of function may only occur due to growth and development of new neural connections. In this field of research, novel, theory driven, innovative methods to promote this re-wiring of neural pathways are urgently needed.

BCIs take a wide range of different formats, providing user feedback from a variety of different neural signals. Some constitute assistive technology, circumventing the damaged nervous system to translate an intention to move into remote control of an external device. Others work upon harnessing the power of motor imagery to activate brain circuits involved in movement in order to promote an optimal neurochemical environment for neuroplastic processes to occur, and prevent further deterioration of unused pathways. The aforementioned are two very different approaches—one with a focus on compensation, finding a new way to achieve the desired task, and the other with a focus on restitution—regaining the capacity for the brain to control the appropriate muscles by reliance on rewiring and forming new neural connections to take on the function of the damaged neurons. Here we aim to more specifically demarcate the clinical instances in which the benefits of BCI are likely to supersede those of other approaches, with a view towards equipping researchers (and ultimately clinicians) with tools to choose the right BCI approach at the right time for the right patients.

First and foremost, we need to develop a clearer understanding of the underlying mechanisms—the neural elements that are being altered by the BCI—in order to provide clear medical justification, and a more standardised, scalable application of

brain-based physiotherapy. There is a wide heterogeneity in BCI design, slowing its clinical deployment [6]. Yet, a more pressing challenge is our limited understanding of the mechanisms that drive BCI control and BCI initiated recovery processes [1].

The myriad of proteins, cells, synapses, structural and functional networks that make up the brain, and the way they interact to produce measurable signals at the scalp, are yet to be consolidated into a comprehensive framework of brain health [7–9]. Instead of resorting to increasingly complex and expensive technology [10], it is crucial to devise innovative but minimalist ways to interact with the injured brain.

1 Identification of Appropriate Target Neural Signal

Any form of brain signal, ranging from protein-level fluctuations to network activities and oscillations, can be utilized for BCI. It is also valuable to consider the potential applications where brain-derived signals, such as motor evoked potentials from electromyography [2, 3], can be leveraged as inputs to inform a BCI [11, 12]. Here, we will focus predominantly on Electroencephalography (EEG) BCI, as the majority of BCIs capture brain activity through EEG [13].

For a BCI with a goal involving neurorehabilitation, the primary objective is to restore functional movement in the user. This distinguishes it from efforts to achieve the best possible control over the avatars/actuators in the BCI, which is often the focus from a bioengineering perspective. Rehabilitative BCI can target at least three separate dimensions for brain signal analysis: The signal will originate from a specific location, it will exhibit a distinct temporal development, and it will propagate itself spatiotemporally with an oscillation [14]. Researchers have successfully targeted all three dimensions for controlling BCI [10, 13, 15, 16]. In the spatial dimension, post-stroke BCI for rehabilitation may bring about functional change by enhancing activity dependant plasticity in motor regions [17, 18]. In the temporal dimension, the aim may be to augment conduction speed between the brain's motor areas [19, 20]. From a neural oscillations perspective, a target mechanism may be to bias neural oscillatory behaviour towards more 'normal' patterns than those typically detected from the post-stroke brain [21].

Rehabilitation contexts introduce issues that do not exist when testing with healthy controls: Firstly, signals recorded from the injured brain are often complex and idiosyncratic, and secondly, the chosen brain signal can be anticipated to evolve as the patient recovers. To deal with these complexities, we suggest a multi-phase BCI approach. Akin to physiotherapy, a multi-phase BCI may start targeting a specific brain signal during the acute phase of a brain injury, and progressively address patient needs until another BCI phase begins that may target another brain signal during the chronic phase of a brain injury. Ultimately, the best method to accomplish this depends on the specific rehabilitative objectives pursued.

2 Identifying Therapeutic Goals

The intrinsic advantage of Brain-Computer Interfaces (BCIs) over alternate rehabilitation strategies is that they work even when output at the behavioral level is non-existent. Patients exhibiting minimal or no residual limb movement after a stroke cannot partake in gold standard physiotherapy [22], but might still demonstrate brain activity patterns when attempting to move the impaired limb. These patterns can be targeted to enhance recovery [1]. However, the role of BCIs should evolve once behavioral output is available. Uncertainty about how BCI can engage neural recovery mechanisms in the brain means that standalone BCI therapy is unlikely to produce better results than conventional physiotherapy in cases where behavioural output is available. In this context, the role of the BCI may transition from being the primary feedback and training mechanism for a patient to take on a more complementary role in the recovery process.

3 Identifying the Most Appropriate Technology to Improve Function

In BCI research for neurorehabilitation, the primary objective is to facilitate neural recovery. Achieving accurate BCI control is secondary. As such, rehabilitative BCI is not so much a competition to employ the most cutting-edge methods for the best possible BCI control, but rather a race to identify the most clinically relevant aspects of healthy or injured brains.

So-called black box machine learning methods, where the result is uninterpretable to humans, are not recommended as BCI components [23]. While they may have advantages over more traditional methods, many require large datasets, which are generally unsustainable in both the academic and medical fields. Furthermore, since researchers or clinicians are not able to oversee the results, these methods carry risks such as overfitting and negative adaptation, rendering them ethically questionable as well as impractical [24, 25]. As a result, theory-led methods are preferable.

In situations where there are few or no constraints imposed on the data by the chosen brain signal or the rehabilitative objective, unbiased data processing methods can provide benefits. Unbiased methods take all available data and determine for themselves what is important and what is not, without referring to predetermined goals. They can offer greater flexibility in identifying optimal solutions for BCI control, including adaptations to signal changes over time, adaptations to patient idiosyncrasies, and the exploration of potential solutions not previously considered by researchers. However, unbiased processes may lack the necessary methodological power to validate BCI mechanisms and are potentially more susceptible to noise.

Based on the qualities of the brain signal and the requirements dictated by the rehabilitative objective, most BCI designs will gravitate towards a specific technological solution. If these qualities or the rehabilitation objective change during the

rehabilitation process, the technology employed should adapt correspondingly. While this multimodal approach may initially appear more complex, it is likely to yield superior results and more standardized protocols.

4 Thinking Outside the (Black) Box

The presented steps are intended to help BCI design by encouraging innovative solutions. For example, multimodal and multiphasic BCIs may also incorporate phases or modes where the brain is not the signal generator but rather a signal processor. The brain could be the receiver of a stimulus such as transcranial magnetic stimulation or a sensory stimulus. This could enhance the specificity of the generated brain signal along various dimensions, making it easier to design a rehabilitative objective around it.

For this purpose, we have developed a multimodal and multiphasic BCI using a TMS-BCI in the initial phase and an EEG-BCI in the subsequent phase. Preliminary results suggest that the multimodal approach was successful in facilitating BCI control compared to a unimodal, single-phase group (2-Phase BCI).

Alternatively, the brain signal could be augmented with additional behavioural data. For example, wearable devices could provide a BCI with an additional signal dimension, enabling the BCI to make more complex decisions. Such multimodal and multiphasic approaches may allow for the targeting of different aspects of rehabilitation during the same treatment or the application of different BCI strengths simultaneously.

A multiphasic approach to rehabilitative BCI could also contribute to its success. To achieve success, BCIs must not only be mechanistically sound and effective but also scalable on a grand scale, ideally allowing patients to use them with minimal clinical supervision. This has yet to be fully realized as researchers continue to strive to find simple and effective solutions. However, a multiphasic approach may help BCIs have a short, intensive acute care phase, followed by a long-term easy solution for at-home use.

In an experiment we designed [4], we developed a clinically relevant but minimal BCI setup. This setup was dispatched to participants' homes, and they were instructed to set it up and train using online guidance. The results affirmed the feasibility of this approach.

5 Conclusion

Brain-Computer Interfaces (BCIs) continue to gain momentum as an appealing method for restoring motor function in a neurorehabilitation context. However, we must not be seduced by the allure of cutting edge technology at the expense of targeting the specific neurophysiological features that are most likely to drive

recovery. At the most basic mechanistic level, the majority of BCIs are driven by neural signals generated by imagination of movement. We need to revisit the question—could motor imagery alone could achieve the same outcomes, or what is the added clinical benefit of the BCI? Accordingly, what is the minimum required intervention using BCI (in terms of time and hardware) to establish a habit of good quality motor imagery that could then sustain rehabilitation without the technology? Motor imagery is free, available to every person and at any time. Using technology to harness its virtues while not compromising its simplicity is the ultimate challenge for the field.

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