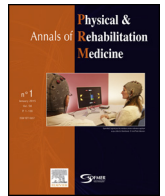




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Update article

# Brain computer interfaces for neurorehabilitation – its current status as a rehabilitation strategy post-stroke



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## ABSTRACT

The idea of using brain computer interfaces (BCI) for rehabilitation emerged relatively recently. Basically, BCI for neurorehabilitation involves the recording and decoding of local brain signals generated by the patient, as he/her tries to perform a particular task (even if imperfect), or during a mental imagery task. The main objective is to promote the recruitment of selected brain areas involved and to facilitate neural plasticity. The recorded signal can be used in several ways: (i) to objectify and strengthen motor imagery-based training, by providing the patient feedback on the imagined motor task, for example, in a virtual environment; (ii) to generate a desired motor task via functional electrical stimulation or rehabilitative robotic orthoses attached to the patient's limb – encouraging and optimizing task execution as well as “closing” the disrupted sensorimotor loop by giving the patient the appropriate sensory feedback; (iii) to understand cerebral reorganizations after lesion, in order to influence or even quantify plasticity-induced changes in brain networks. For example, applying cerebral stimulation to re-equilibrate inter-hemispheric imbalance as shown by functional recording of brain activity during movement may help recovery. Its potential usefulness for a patient population has been demonstrated on various levels and its diverseness in interface applications makes it adaptable to a large population. The position and status of these very new rehabilitation systems should now be considered with respect to our current and more or less validated traditional methods, as well as in the light of the wide range of possible brain damage. The heterogeneity in post-damage expression inevitably complicates the decoding of brain signals and thus their use in pathological conditions, asking for controlled clinical trials.

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## 1. Introduction

Sensorimotor rehabilitation forms an important part of the care provided after brain injury, aiming to restore the frequent loss of motor control and increase independence and quality of life. Stroke is the leading cause of acquired disability in adults, and as such occupies a special place amongst the different types of brain injuries. For those people surviving a stroke, up to 80% are left with a residual deficit in fine motor control of the upper limb [1].

In light of the heterogeneity of symptom expression post-stroke, a large toolbox of training-oriented rehabilitation techniques has been developed. The majority of these approaches are

based on theories of motor learning which assume that (a) motor re-learning is comparable to motor learning and (b) patients can learn [2]. The most fundamental law of motor learning is “practice”, encompassing skill acquisition, motor adaptation, and decision-making. Key-features of successful practice are high numbers of repetitions, high intensity, sensory priming, variable practice, and last but not least the provision of feedback [3–5]. Feedback facilitates the detailed appraisal of performance: it enforces the sensorial aspect in the sensorimotor loop. By highlighting the important features to the patient, it enhances active engagement as well as motivation. The latter is especially important, as no therapy will be effective when there is a lack of motivation to practice [4].

However, most of the common rehabilitation tools require a residual level of motor control to actually perform the required therapeutic tasks in order to have something to provide feedback on. For patients with severe deficits (little or no movement

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control), the current toolbox might therefore not be sufficient. Here, brain computer interfaces (BCI) hold promise for filling this gap. BCI records and decodes brain activity while performing or trying to perform motor and/or cognitive tasks. The BCI can therefore be configured such that it maps the decoded brain signals onto useful feedback on the performed task for both patient and therapist. This feedback can take many forms, including those of a visual, auditory or haptic nature. The decoded signal can even be used for the control of external devices that executed the intended movement, providing proprioceptive feedback. Consequently, one can consider BCI as a form of rehabilitation technology, which extends therapeutic possibilities to all patients regardless of the severity of paresis. When normal motor function is lost, the BCI may promote the recruitment of brain areas involved in the particular task, inducing neural plasticity required for recovery of function.

## 2. Neural plasticity

Neural plasticity is the ability of our nervous system to reorganize its structure, function and connections in response to training. The type and extent of neural plasticity is task-specific, highly time-sensitive and strongly influenced by environmental factors as well as motivation and attention [6]. By providing feedback on the intended movement and thereby restoring the “action–perception coupling”, BCI have already been shown to induce neural plasticity [7]. However, we know that not all plasticity is necessarily beneficial. Examples of maladaptive plasticity post-stroke are abnormal and non-functional movements, like syncinesia, chronic shoulder pain [8] or new onset epilepsy [9]. The goal of neurorehabilitation is therefore to simultaneously improve behaviour by driving adaptive changes in dysfunctional neuronal system, whilst avoiding maladaptive plasticity through carefully designed exercises in combination with (neuro)feedback.

The processes of learning how to operate a BCI device depend on the existence of neural plasticity and are suspected to follow the similar principles as conventional learning processes (Daly et al., 2008). Various studies have shown that we are not only able to reorganize brain connections, but also to modulate our brain activity by training. Especially this modulating brain activity is used to control BCI. Wolpaw et al. demonstrated in 1991 that humans are able to control a cursor on a computer screen by modulating the sensorimotor rhythm amplitude, in the absence of actual movement or sensation [10]. More recently, Ramos-Murguialday showed that patients post-stroke are able to learn how to control the sensorimotor rhythm desynchronization, especially when contingent feedback is provided [11].

## 3. Brain computer interfaces

Brain computer interfaces translate, as described above, the patterns of local brain activation into a desired action, when our motor system is lacking the capacity to perform the action. It forms a bridge between our desired or imagined movements and reality. The common aim of BCI systems post-brain injury is to restore the lost motor function by helping the patient learn to produce normal brain activity and/or to use the brain activity to operate training devices. By doing so, BCI integrates a bottom-up (inducing changes at the neural level by acting on the periphery of the body) with top-down (neurological intervention to alter peripheral behaviour) approaches.

Currently, there are several non-invasive methods available for the recording of brain activity in a way that is useful for BCI applications. These methods include electroencephalography (EEG) [12], magnetoencephalography (MEG) [13], functional

near-infrared spectroscopy (fNIRS) [14] and functional magnetic resonance imaging (fMRI) [15]. The selection of methods is mainly dependent on the trade-off between ease of use, resolution of states, and cost of the device. Based on their relative portable nature and low costs, EEG and fNIRS seem to be the best potential candidates for usage in post-brain injury rehabilitation.

Beyond the choice of measurement modality used for recording brain activity, there are numerous signal features, which have the capacity to convey information regarding underlying brain dynamics. Frequently used features in EEG, for example include the amplitudes of a particular evoked potential (e.g. P300), the composition of slow cortical potentials (SCP) or spectral features, such as the (de)synchronisation of the sensorimotor rhythm (SMR). The latter especially has been used in motor rehabilitation due to its robust association with motor area activation during real and imagined movement, a fact exploited in the exploration of the recovering stroke-damaged brain [16]. When there is no motor activity – the sensorimotor brain areas are at rest or inhibited – the amplitude of the SMR is high (SMR synchronisation), reflecting an “idling” state. When motor information is processed, a decrease of SMR amplitude can be observed (SMR desynchronisation). These pattern changes in SMR amplitude can be used to trigger an external device in order to display real-time sensory feedback or to execute the intended action.

In the following sections, we will focus on several applications of BCI systems to restore motor function in three domains:

- real-time neurobiological feedback during motor imagery;
- representation of the performed action in virtual realities;
- activation of external devices inducing actual movement by means of an orthosis or by functional electrical stimulation (FES).

## 4. BCI and motor imagery

Motor imagery (MI) can be described as a dynamic state during which a subject mentally repeats a specific movement (sequence), without any overt motor output [17]. It shares many of the same neural mechanisms with actual movement execution, with an emphasis on the prefrontal cortex, which is responsible for the creation and maintenance of an explicit representation used in thought and action [18]. MI can be either kinaesthetic (you “feel” the movement in your mind) or visual (you “see” the movement in your mind) from an internal (first person) perspective or an external (third person) perspective, each of which are linked with different neuronal subsystems that can be activated simultaneously and seem inherently tied to each other [19]. For motor recovery, an internal kinaesthetic imagery seems optimal as it activates the motor network of the brain [20]. However, before the development of BCI systems, it was difficult for a therapist to monitor whether patients were indeed performing kinaesthetic MI. By coupling MI to BCI, MI can be visualized, providing feedback to both the patient and the therapist on the strategy used, thus, ameliorating both motor learning and therapy engagement alongside.

Prasad et al. in 2010 [21] integrated an EEG-based BCI for MI within a rehabilitation protocol combining physical practice with MI. The MI consisted of imagining the performance of motor sequences and kinaesthetic sensations associated with it, while holding the upper limb still. In each training session participants (5 chronic patients post-stroke) first performed/tried to execute the movement physically, followed by the MI of the same movement. This was done for the non-impaired and impaired upper limb respectively. The neurofeedback of MI performance was provided by means of a simple visual representation called the “ball-basket” game, in which a ball falls with constant speed from the top of the screen. The ball has to be placed in a target basket

appearing on either the left or the right bottom of the screen, using MI of the respective limb movement. The trajectory of the ball was defined as a result of the patient's MI, confirming patient engagement online. After six weeks of training, with two sessions per week, all participants tended to improve their motor function of the impaired arm around the minimally clinical important difference on the Action Research Arm Test. Therefore, the authors concluded that BCI supported MI is a feasible intervention as part of a post-stroke protocol combining both physical practice and MI. However, it still needs to be verified whether the improvement was due to the neurofeedback, as studies with only MI have also shown functional improvements post-stroke [22].

Mihara et al. [23,24] attempted to clarify this question in two steps. Using an fNIRS based BCI system, they first asked 21 healthy participants to kinaesthetically imagine finger flexion and extension alternated with rest periods. The associated brain activity was visualized by means of a vertical bar. Participants were told that the bar was higher when they achieved good kinaesthetic MI during the task period and were more relaxed during rest periods. One group received "relevant feedback" that was contingent with the MI task – reflecting the true kinaesthetic imagery performance. The other group received "sham-feedback", meaning that the size of the bar was unrelated to the brain activity measured. Contingent and thus relevant neurofeedback induced significantly greater activation of the contralateral premotor cortex as well as higher self-assessment scores for kinaesthetic motor imagery. The premotor cortex is crucial for both motor control and the generation of MI [25]. In contrast, sham-feedback was related to activations of the parietal association cortex. The parietal association cortex is rather linked to memory related visuospatial imagery [26]. These results demonstrate the importance of task contingent feedback when targeting plasticity in the motor network. To verify whether feedback contingent training indeed leads to motor improvement post-stroke, Mihara et al. (2013) subsequently repeated the protocol in a training design with 20 patients post-subcortical stroke. Participants received 6 training sessions with BCI driven MI of distal upper limb control in addition to standard rehabilitation. Patients were randomly allocated to a contingent or a sham-feedback based group. As expected, the cortical activation of the premotor area in relation to MI was greater in the contingent feedback group. Also, it was associated with a greater functional gain on the hand/finger subscale of the Fugl–Meyer Assessment; even in participants with severe motor deficits. Together these results clearly indicate that only contingent feedback on kinaesthetic motor imagery leads to activations in the targeted motor regions. It facilitates adaptive neural plasticity to improve motor functioning post-stroke, emphasizing the promise of BCI-MI as a rehabilitation strategy post-stroke.

## 5. BCI and motor imagery in conjunction with virtual reality environments

In contrast to the simple visual representation described above, virtual reality (VR) representations allow for three-dimensional (3D) feedback of MI. The complexity of this 3D environment can thereby vary from very simple to highly complex. With 3D representation, a deeper immersion in the virtual environment is suspected, which on its turn increases the motivation and potentially the engagement of the patient-player. While playing, the therapeutic aspect becomes less evident and motor learning becomes more intrinsic with the attention focussed on exploring the environment rather than on training/imagining paretic movement [27]. Leeb et al. proposed a BCI whereby the control signal is used to navigate within a virtual environment, by turning left (left hand MI) or right (right hand MI). In their pilot study, they demonstrated the importance of virtual feedback being as real as

possible. For example, when the turning angles in the virtual environment were too large compared to physical capacities, subjects lost the feeling of performing real movements. Based on these results, the researchers here emphasized that feedback that behaves in an unknown or unpredicted way could disturb the focused attention and interfere with the sense of immersion provided, decreasing the motor learning potential [28].

Subsequently, knowing that people post-stroke are able to perceive motor characteristics in virtual environments [29], VR also opens doors to observational learning of performed movement. It is well established that the observation of movement activates, just like imagery does, the same neural networks as during overt movement execution [30]. The movements perceived are thought to be mapped onto the observers' motor repertory, inducing "motor resonance" [31]. The motor resonance following observation may thus facilitate plasticity when the observed action is directly matching the internal simulated action. [32] demonstrated by combining observation of daily actions with concomitant physical training of the observed actions, that stroke patients are also able to learn from action–observation and that it had a positive impact on rehabilitation of motor deficits post-stroke.

A first step towards applying action–observation in BCI has been made by Holper et al. [33], who observed brain activity during coupled imagery and observation: participants had to imagine that a movement presented in VR was their own movement. The VR presentation was from a first person perspective – as if the participant was watching their own movements. This double condition led to stronger brain activations in the sensorimotor network. The next step envisaged for that work is to control the movement shown in the virtual environment based on the brain activity measured with the BCI system, increasing the coupling between imagination, observation and back to imagination [33].

## 6. BCI and motor imagery for movement

VR provides strong visual feedback of the imagined movement. By means of external devices like hand orthoses or functional electric stimulation (FES) systems, the imagined movement can be turned into overt action, providing haptic as well as proprioceptive feedback.

### 6.1. Orthosis

In 2008, Buch et al. coupled a hand orthosis to a MEG-based BCI-MI system. Eight post-stroke patients without residual finger movement were trained to volitionally control their SMR amplitude. First, feedback was provided by a simple visual system, showing cursor displacement on a computer screen: downward movement of the cursor reflected activity towards SMR desynchronization, upward movement reflected activity towards SMR synchronization. Second, when SMR desynchronization was successful, as indicated by the cursor hitting a target displayed on the lower edge of the screen, haptic and proprioceptive feedback was provided by the opening/closing of an orthosis attached to the paralyzed hand. Over 13–22 training sessions, participants successfully learned to control their SMR amplitude. However, functional outcome on the Medical Research Council scale showed no change in finger strength [34]. Interestingly, a serial case study with 8 chronic post-stroke patients and similar set-up as Buch et al. in 2008 by Shindo et al. in 2011 [35] did show an increase in voluntary electromyographic activity in four participants with little to no function, and functional improvement in two participants, with mild finger function. This was combined with a greater suppression of SMR rhythm over both hemispheres as well as with an increased cortical excitability in the attained hemisphere.

The limited or even lack of functional improvement in both studies might be explained by the lack of concomitant active physical training, as Prasad et al. [21] only showed a beneficial effect of MI training when it was combined with conventional physical rehabilitation.

Birbaumer et al. performed a controlled EEG-based BCI plus orthoses training study in 2013 ([11], see also [36] – in this special issue for more information on their work on brain machine interfaces in paralysis). They assigned 32 chronic post-stroke patients with little to no residual hand control to two matched groups. In the experimental group, successful MI-induced SMR desynchronization activated contingent online movements of the hand and arm orthoses. In the control group, movement of the orthoses occurred randomly. Both groups received behavioural physiotherapy directly after the BCI training session. After around 18 days of training, a significant group  $\times$  time effect was observed: the Fugl-Meyer Assessment score improved more in the experimental group (from 11.16 to 14.56) compared to the control group (from 13.29 to 13.64). However, no difference in functional capacity was observed on the Goal Attainment Scaling and Motor Activity Log. The improvement in motricity coincided with a shift of movement related brain activity over the motor and premotor cortex towards the ipsilesional hemisphere. These results further confirm that the combination of BCI-MI plus orthosis with physical training may help to improve upper limb motor control post-stroke.

All together, task and time-contingent proprioceptive feedback seems essential to close the sensorimotor loop between movement related neural activity and its associated feedback provided by the orthosis driven movement. This may actually prime the ipsilesional sensorimotor networks for action related neural plasticity, facilitating motor learning and thus improving the effects of actual motor training directly after the BCI-MI training.

## 6.2. Functional electrical stimulation

Functional electric stimulation is based on the principle that one can artificially compensate for the loss of voluntary motor control by means of stimulating the paralyzed muscles of the affected limb. The short electrical pulses elicit action potentials in the efferent nerves, inducing contractions of the underlying muscles [37]. Initially, FES was applied in a bottom-up approach: inducing plasticity of the brain by association of peripheral stimuli. By coupling FES to a BCI system, contraction of the muscles becomes a direct result of the users' intention, changing it into a coupled top-down/bottom-up loop.

Meng et al. verified the feasibility of an EEG-based BCI-FES system in chronic post-stroke patients. They asked two post-stroke participants to imagine repetitive wrist extension/flexion. When subjects successfully imagined this movement, which was reflected by a cursor moving towards and hitting a target on a computer screen in front of the participant, the FES system was activated. The size of target was dependent on the imagery performance of the participant, with smaller targets for better imagery encouraging them to achieve better levels of neural control. After 10 training session, the error rate of the BCI control became less than 20%, showing that chronic patients post-stroke could learn to improve their motor imagery-based on the closed loop sensorimotor control via the BCI-FES system [38]. Subsequently, a case study of a 43-year-old woman chronic post-stroke by Daly et al. showed that after three weeks of frequent training with an EEG-based BCI-FES system, the woman regained volitional isolated index finger extension [39]. These studies together indicate that the neural plasticity-induced by the BCI-FES training not only may improve motor imagery, but that these changes may lead to motor improvements.

## 7. Additional advantages of brain activation monitoring during rehabilitation

When using a BCI system, the activation level of the brain is automatically analysed. Aside from using the system to induce movement or provide feedback on motor imagery and/or intention, it can also be used to monitor (i) the global level of attention directed towards the tasks and (ii) the level of inter-hemispheric (dis)balance.

An important issue in motor learning is the amount of mental workload, or “how hard the brain is working to meet task demands” [40–42]. Mandrick et al. showed that NIRS measured activity over the prefrontal cortex (PFC) could discriminate between low and moderate levels of workload [41,42], with a plateau effect towards higher levels of workload. In addition, NIRS has been shown to be sensitive to attention decrement regardless of task duration [43]. These results suggest that it may be worthwhile to monitor changes in attention during BCI training, to avoid mental overloading and so as to ensure better attention focus towards the task at hand.

Subsequently, it has been widely described that after stroke the interaction between hemispheres is marked by an imbalance. The damaged hemisphere lacks the capacity to inhibit the healthy hemisphere, leading to an excessive inhibition of the afflicted hemisphere by the healthy one. Better motor recovery post-stroke is often linked to a restoration of the inter-hemispheric balance [44]. Automatically monitoring the (change in) inter-hemispheric interactions during BCI training could provide important information on treatment strategies, by adding for instance repetitive transcranial magnetic stimulation before training in the case of such hemispheric asymmetry [45] or by modulating the choice of exercises depending on the kind of brain activation observed.

## 8. Future challenges

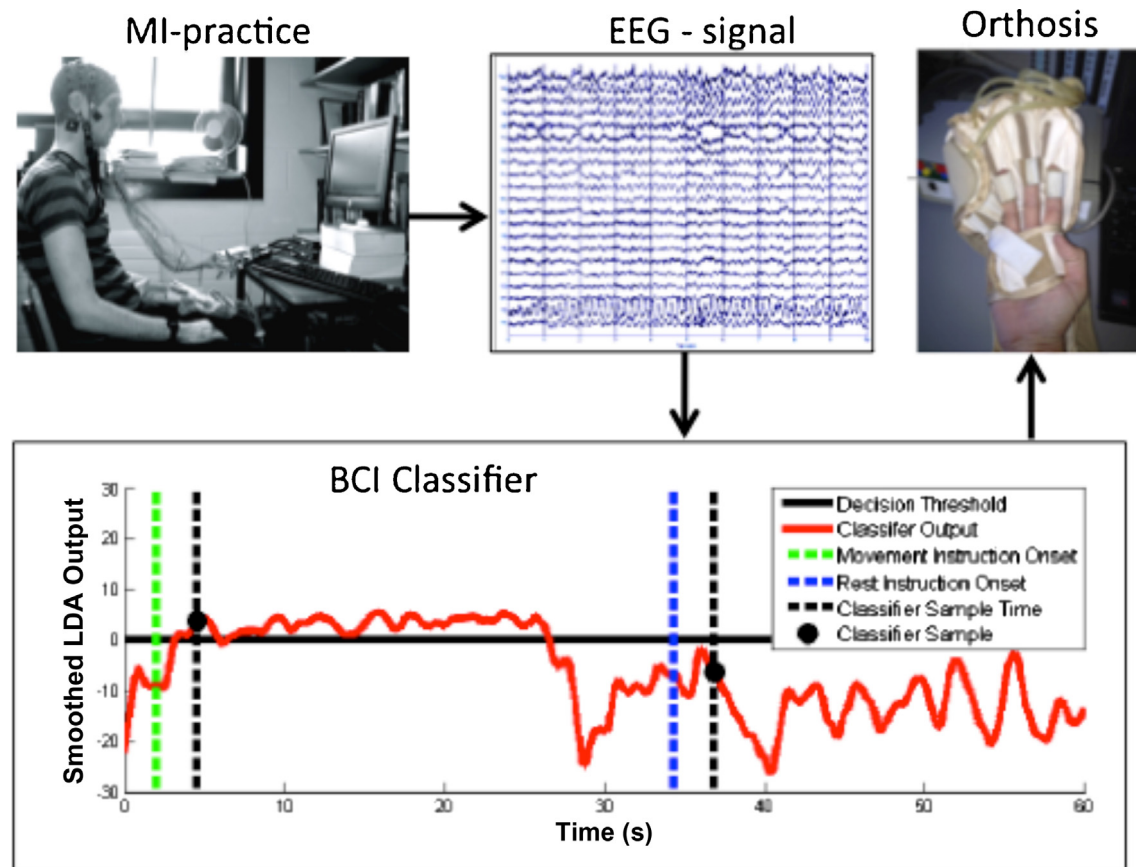
So far, based on preliminary findings with small patient groups, BCI appears a promising rehabilitation tool after brain damage. With better understanding of neuro-dynamics during brain recovery, it may be expected to enter standard rehabilitation practice. However, low-cost, non-invasive and easy installable BCI should be developed to assure implementation in clinical practice. An interesting example of such a BCI has been shown by Coffey and colleagues who developed an EEG-based BCI with an inflatable glove, training finger and wrist extension (see Figs. 1 and 2). Using simple Velcro to attach the glove, the participant himself can easily put it on and as the system is lightweight it may even be useful for home-based rehabilitation [46].

Nevertheless, in order to change its status from “promising tool” to simply “tool”, several issues can be identified that require further clarification. First, we need to define how BCI can be integrated with and complete existing (more or less validated) rehabilitation methods, like task oriented rehabilitation, high intensity and repetitive exercises, mirror therapy, constrained-induced therapy, mechanized or robotic rehabilitation, serious games, modulation of sensory afferents, etc. Once integrated, its comparative efficiency should be evaluated in relation to targeted group of patients from complete paresis to mild functioning. Second, BCI needs to be refined in the light of the wide spectrum of brain damage. The heterogeneity in post-damage expression inevitably complicates the decoding of brain signals, imposing the question of what features in the brain encode the most relevant output to induce beneficial plasticity. For instance, one may wonder whether it would be beneficial to focus on the activations observed when stroke patients try to move their paretic side since those activations may include irrelevant regions of the brain.





**Fig. 1.** A non-invasive BCI platform developed by [46]: (a) deflated pneumatic glove, (b) maximal conflated pneumatic glove; (c) air pump and valve to con/deflate the glove.



**Fig. 2.** The coupling between EEG and pneumatic glove by classifying the EEG signal to induce movement by thought or intention.

Should one therefore focus on the resemblance with activations of the non-paretic side? Or on activations associated with imagined movement that are used frequently but are lacking the motor execution component? Third, what are the most effective BCI paradigms to not only induce plasticity but also improve motor function? Will using external devices have a larger impact on motor function than motor imagery, virtual realities or other forms of feedback? Or does it depend on the post-injury treatment window? This last remark brings us to the final point: time. When should BCI be applied to gain most plasticity? At which moment in time post-injury or at what stage of “natural” or “training-induced” plasticity is its application the most beneficial? And what is the best timing between BCI training combined with more conventional movement-based physiotherapy?

## 9. Conclusion

Overall, we might conclude that BCI systems are a promising tool to add to the (post-stroke) motor rehabilitation toolbox. Its potential usefulness for a patient population has been shown on

various levels and its diverseness in interface applications makes it adaptable to a large population [23,24,44]. We can look forward to discovering the results of clinical trials based on a controlled design to validate the impact of BCI on motor and functional recovery, as well as quality of life post-stroke.

## Disclosure of interest

The authors declare that they have no conflicts of interest concerning this article.

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