Using EEG-based brain computer interface and neurofeedback targeting sensorimotor rhythms to improve motor skills: Theoretical background, applications and prospects

Camille Jeunet, Bertrand Glize, Aileen Mcgonigal, Jean-Marie Batail, Jean-Arthur Micoulaud-Franchi

[2]Using EEG-based Brain Computer Interface and Neurofeedback Targeting Sensorimotor Rhythms to Improve Motor Skills: Theoretical background, applications and prospects

Running title: Neurofeedback targeting sensorimotor rhythms

Camille JEUNET [a], Bertrand GLIZE [b, c], Aileen McGONIGAL [d, e], Jean-Marie BATAIL [f, g], Jean-Arthur MICOULAUD-FRANCHI [h, i] *

a - Laboratoire Cognition, Langues, Langage, Ergonomie (CLLE), CNRS / Univ. Toulouse Jean Jaurès, Toulouse, France
b - Physical and Rehabilitation Medicine Unit, EA4136, Bordeaux University Hospital, University of Bordeaux, F-33000 Bordeaux, France.
c - EA4136, University of Bordeaux, F-33000 Bordeaux, France; Physical and Rehabilitation Medicine Unit, Bordeaux University Hospital, Bordeaux, France
d - Aix Marseille Univ, Inserm, INS, Institut de Neurosciences des Systèmes, Marseille, France
e - Service de Neurophysiologie Clinique, Centre Hospitalo Universitaire de la Timone, 264, rue Saint-Pierre, 13005 Marseille, France.
f - Academic Psychiatry Department, Centre Hospitalier Guillaume Régnier, Rennes, France.
g - EA 4712 Behavior and Basal Ganglia, CHU Rennes, Rennes 1 University, France.
h - Service d'explorations fonctionnelles du système nerveux, Clinique du sommeil, CHU de Bordeaux, Place Amélie Raba-Léon, 33076 Bordeaux, France.
i - USR CNRS 3413 SANPSY, CHU Pellegrin, Université de Bordeaux, France.

* Corresponding author
Jean-Arthur MICOULAUD FRANCHI
Service d'explorations fonctionnelles du système nerveux, Clinique du sommeil
CHU de Bordeaux, Place Amélie Raba-Leon, 33076 Bordeaux
Tel : 06 22 36 40 19
E-mail : jarthur.micoulaud@gmail.com

Abstract

Many Brain Computer Interface (BCI) and neurofeedback studies have investigated the impact of sensorimotor rhythm (SMR) self-regulation training procedures on motor skills enhancement in healthy subjects and patients with motor disabilities. This critical review aims first to introduce the different definitions of SMR EEG target in BCI/Neurofeedback studies and to summarize the background from neurophysiological and neuroplasticity studies that led to SMR being considered as reliable and valid EEG targets to improve motor skills through BCI/neurofeedback procedures. The second objective of this review is to introduce the main findings regarding SMR BCI/neurofeedback in healthy subjects. Third, the main findings regarding BCI/neurofeedback efficiency in patients with hypokinetic activities (in particular, motor deficit following stroke) as well as in patients with hyperkinetic activities (in particular, Attention Deficit Hyperactivity Disorder, ADHD) will be introduced. Due to a range of limitations, a clear association between SMR BCI/neurofeedback training and enhanced motor skills has yet to be established. However, SMR BCI/neurofeedback appears promising, and highlights many important challenges for clinical neurophysiology with regards to therapeutic approaches using BCI/neurofeedback.

Key words

Neurofeedback; Motor ability; Brain Computer Interface; ADHD; Stroke; Closed loop.

INTRODUCTION

Neurofeedback is a neurophysiological technique that aims to teach users/patients to self-regulate targeted brain activity patterns in order to specifically enhance cognitive abilities or reduce clinical symptoms. The choice of target brain activity patterns is thus a key issue, in order for neurofeedback procedures to be efficient. From the multitude of EEG targets [61], sensorimotor rhythms (SMR) appear to be a very promising and interesting neurophysiological target to try to enhance motor skills. Many Brain Computer Interface (BCI) and neurofeedback studies have investigated the impact of SMR self-regulation training procedures on motor skills enhancement in healthy subjects and patients with motor disabilities. This critical review aims first to introduce the neurophysiological framework, in line with the motor imagery literature, which led to SMR being considered as a reliable and valid EEG target to improve motor skills through BCI/neurofeedback procedures. The different definitions of SMR target in BCI/neurofeedback studies will be introduced and the relationship between neuroplasticity, motor skills and SMR BCI/neurofeedback training discussed. The second objective of this review is to introduce the main findings regarding SMR BCI/neurofeedback in healthy subjects. The impact of such procedures on sport, acting and surgical skills will be analyzed. Third, the main findings regarding SMR BCI/neurofeedback efficiency in patients with hypokinetic activities (in particular motor deficit following stroke) as well as in patients with hyperkinetic activities (in particular Attention Deficit Hyperactivity Disorder, ADHD) will be introduced. This review is not meant to be a systematic, exhaustive review. Rather, it aims to propose a critical synthesis of the existing literature from a clinical neurophysiological point of view. Indeed, the opinions within the scientific and medical community are divided regarding the efficacy of BCI/neurofeedback. Most of the randomized clinical trials show significant weaknesses and do not enable us to clearly conclude on the efficacy of BCI/neurofeedback procedures, since the level of evidence remains too low. However, when compared to other potential EEG targets, SMR present the advantage of having a relatively well-identified neurophysiological relationship with motor imagery and motor skills. On the one hand, this characteristic results in the fact that SMR are considered as very interesting targets to better understand motor skills acquisition in various contexts. On the other hand, SMR also represent promising targets for the future development of innovative neurophysiological treatments.

BCI/NEUROFEEDBACK TARGETING SENSORIMOTOR RHYTHMS FOR ENHANCING NEUROPLASTICITY

Neuroplasticity and the acquisition of motor skills

Neuroplasticity is a normal ongoing state of the human brain. It refers to the ability of the latter to evolve its structure and function. This reorganization is observed from the molecular level to the behavioral level [41, 45, 46, 75]. One impressive example of neuroplasticity is the possibility of acquiring motor skills. This learning process involves and modifies the activity of specific brain areas such as the dorsolateral prefrontal cortex (DLPFC), the primary motor cortex (M1), the premotor cortex (PM), the pre-supplementary motor area (preSMA), the supplementary motor area (SMA), the primary somatosensory cortex (S1) and the posterior parietal cortex (PPC), striatum and cerebellum (for a review, see [25]). The progression from early to late stages of motor skill learning seems to be associated with an activation from anterior to more posterior regions of the brain [30], which reflects a progressive decrease in reliance on attentional resources and executive functions towards more automatic processes [45]. Proof of the plasticity induced by motor skill training and learning is visible both in structural (anatomic) and functional changes.

Anatomical changes are visible using magnetic resonance imaging (MRI) or diffusion tensor imaging (DTI). For instance, voxel-based morphometry (VBM) analyses suggest that musicians show higher grey matter density in the sensorimotor cortex and cerebellum than control subjects [39]. In addition, DTI analyses reveal higher fractional anisotropy in the internal capsule as well as plastic changes in the 3D morphology of the central sulcus in response to long-term motor skill training [39, 49]. Other studies investigating structural plasticity reported an increased volume of grey matter density in brain areas involved in the task. These changes seem to disappear when participants stop practicing, suggesting that structural plasticity is possible in all directions (for a review, see [16].

Functional changes are visible using transcranial magnetic stimulation (TMS), functional MRI or electroencephalography (EEG). For instance, the cortical representation of the hand, explored using TMS, is larger in professional racquetball players than in control participants [76]. Other findings suggest that this functional reorganisation is led by an enlargement or focused activation of the motor area involved in the control of the studied skill. Neuroplasticity also occurs in cognitive and perceptual domains associated with improved performances. For example, strong coupling of sensorimotor and auditory processing has been revealed in professional musicians (for a review, see [16]).

However, even though neuroplasticity is probably related to cellular and molecular mechanisms, one of the main challenges is to link human brain imaging findings to the underlying molecular events that have been well documented in animal models. These models report modulations of synaptic connections through long-term potentiation (LTP) and long-term depression (LTD) in rodents [83, 84]. In humans, learning to perform a motor task also seems to modulate LTP-like plasticity [87, 113], particularly in M1 via the monoaminergic modulation of motor systems (for a review, see [105]. Both in humans and animal models, brain derived neurotrophic factor (BDNF), a neurotrophin, also participates in this synaptic plasticity [1, 51]. These mechanisms are followed by other molecular and synaptic changes in order to induce automatic behaviours. For example, the involvement of neurons in the sensorimotor striatum during late stages of learning has been shown in animal models, probably via long lasting changes in glutamatergic neurotransmission. It might be partially part of a substrate that enables the acquisition of automatic behaviours [66, 111].

The acquisition of motor skills and motor imagery

A very interesting method that favors neuroplasticity processes for enabling the acquisition of motor skills is motor imagery. Indeed, "real" motor training, i.e., motor execution in an ecological context, is not always possible. On the other hand, motor imagery triggers brain structures sharing similar neural networks with motor execution, including motor-related regions and the inferior and superior parietal lobules [29]. Interestingly enough, visual and kinesthetic imagery seem to involve specific networks of sensory modalities, i.e., predominantly occipital regions and the superior parietal lobules for visual imagery, as well as motor-associated structures and the inferior parietal lobule for kinesthetic imagery [37], see **Figure 1.** The activation of these networks seems to induce changes similar to those obtained by motor execution, and might be led by the same molecular mechanisms. Indeed, motor imagery seems to induce LTP-like plasticity in M1, in the same way as motor execution does [7].

Post-stroke recovery provides a well-documented model of neuroplasticity and brain reorganisation following a focal lesion. Following the complex injury pathways that disrupt cerebral organisation, many mechanistic pathways enable the improvement of functional outcomes. Notably, both neuroplasticity and reinforcement of cortical representation areas have been described in animals [72] and in humans [50]. These results suggest a very plastic functional cortical representation [107] and have been hypothesized to involve various mechanisms, notably including vicariance. Vicariance is the theory that the cortical functions

of damaged areas can be managed by other, separate brain regions. Imaging studies have provided examples suggesting the occurrence of this mechanism in stroke recovery [40, 107]. Perilesional areas are also recruited and involved in recovery [69, 90, 106]. Underlying mechanisms include the functional use of pre-existing synaptic networks as well as structural changes, with the creation of new networks. All these phenomena might be enhanced by specific rehabilitation training procedures. Rehabilitation training and learning of skills consist of inducing recovery of impairments and disabilities in order to regain activities though specific and complex interventions, while adaptive strategies compensate for impaired body functions (for a review, see [48]). Thus, mental imagery –and motor imagery (MI) in particular– can be considered as a rehabilitation training procedure. MI practice has been shown to enable the improvement of motor skills. Nonetheless, it should be noted that MI abilities can be harmed in the case of motor impairment [44]. Motor imagery produces corticospinal facilitation of the specific muscles used to execute the imagined action [68] as well as in increases of hand representation in the motor map area over M1, as evoked by TMS, thus reducing inter-hemispheric imbalance [18]. In a similar way to healthy subjects, MI training has been shown to result in structural and functional modifications of the motor cortex in patients with stroke [50]. Similar modifications, including synaptic and cortical map plasticity, have been shown following action observation. Indeed, studies combining another rehabilitation approach to motor imagery have shown re-organization of cortical activation maps for the affected hand, using fMRI (for a review, see [33]. This improvement of motor function induced by MI seems to be partially related to prior MI skills. In other words, recovery of motor function after subcortical stroke seems to involve pre-existing cortical networks [92].

Another way to enhance neuroplasticity in post-stroke rehabilitation of upper-limb impairment is to provide motor-impaired patients with positive sensory feedback, using mirror therapy or muscle vibrations for example. The latter enables provision of haptic feedback and has been suggested to improve motor function, to reduce spasticity and to induce plastic effects on M1 in chronic stroke patients (e.g. increasing motor map areas and reducing resting motor threshold as measured using TMS) [53]. Regarding mirror therapy, patients are asked to attempt synchronous bilateral upper limb movements while observing, in a mirror, the reflection of the unaffected limb located in the same position as their affected limb. Mirror therapy has been suggested to significantly improve motor function in stroke patients [101]. TMS studies in healthy subjects revealed that a mirror visual feedback increased neuronal excitability in M1 [71] while fMRI studies suggested that this induced functional changes in the somatosensory areas, premotor cortex or higher-order visual regions like the superior temporal gyrus and the

superior occipital gyrus [32, 38, 54]. In chronic stroke patients, mirror therapy seems to induce cortical reorganization with a shift in activation balance within the primary motor cortex towards the affected hemisphere, as observed in fMRI [55]. In a study using MEG, Rossiter et al. found that mirror therapy normalized an asymmetrical pattern of movement-related beta desynchronisation in M1 during bilateral movements [88].

The latter study leaves open the opportunity to optimize the delivery of this feedback in order to enhance modifications of these cortical rhythms. The delivered visual or haptic feedback might not be temporally synchronized with the efferent cortical motor activity in both mirror of muscle and vibration therapies. Brain-computer interfaces (BCI) and neurofeedback, which are technologies that allow for the voluntary control of an external device (BCI) or of visual feedback, enable the detection of this efferent activity in order to produce the best time-matched feedback, and enhance the plastic effect induced by motor imagery in patients lacking motor control after a stroke or in healthy people. Hence, this tool might enable us to close the sensorimotor loop, from efferent motor activity to adapted and synchronized afferent sensorial feedback(s), see **Figure 2**. Indeed, recent findings suggest that training procedures combining motor imagery with a somatosensory input improves motor performance through M1 plasticity similarly to motor execution [11]. Hence, closing the loop with a sensory feedback might enhance the effects of motor imagery and provide robust changes in the brain.

Motor imagery and sensorimotor rhythms

As previously described, the effect of motor imagery (MI) on motor skill learning and neuroplasticity has been largely demonstrated in healthy subjects and patients with stroke. MI has been shown to activate the primary motor cortex (M1) as well as brain structures involved in the planning and control of voluntary movements. MI has been shown to be underlain by amplitude modulations of *Sensorimotor Rhythm* (SMR) [19, 26]. While SMR have been known for many decades, their functional role is still not completely understood. Nevertheless, SMR exhibit a good signal-to-noise ratio that can be measured using EEG, making them a relevant and reliable neurophysiological target for BCI and neurofeedback studies which aim at improving MI or motor abilities. Notably, many BCI and neurofeedback studies investigate the impact of SMR self-regulation training procedures on motor skills enhancement in healthy subjects and patients with motor disabilities (see below).

It should be noted however that the characteristics of the so-called “SMR”, especially temporal domain characteristics (i.e., frequency bands), vary quite extensively between studies. Broadly speaking, SMR have been defined as EEG rhythms in the central region, in particular two kinds

of EEG band activities: mu (7-11 Hz) and beta (12-30 Hz) [43]. Mu rhythms were described by Gastaut [34]. The clinical definition of mu rhythms [43] states that they are rhythms at 7–11 Hz, composed of arch-shaped waves occurring over the central or centro-parietal regions of the scalp during wakefulness. Their amplitude varies but is mostly below 50 mV. They are blocked or attenuated when a contralateral movement or a thought about movement is performed, as well as during readiness to move or tactile stimulation. From a frequency band standpoint, mu rhythms are part of the *Rhythmic Activity within the Alpha Band* (RAAB) [77].

It has been shown that it was possible to condition SMR in humans, in particular mu rhythms by Gastaut in 1952 [34] and low beta SMR by Jasper and Penfield in 1949 [42]. More specifically, they stated that it is possible for an individual to learn to self-regulate the amplitude of their SMR during/after MI tasks. Since these pioneering works, SMR have been broadly used for BCI and neurofeedback in order to improve motor skills. While SMR BCI studies generally consider a broad SMR EEG band including both mu (7-11 Hz), low beta (12-15 Hz or even 12-20 Hz) and high beta (20-30 Hz) frequency ranges, in most "SMR neurofeedback" studies, the so-called "SMR" do not include mu rhythms and are generally focused on "low beta" frequency range [56, 65].

SMR BCI experiments target two kinds of event-related patterns: event-related desynchronization and event-related synchronization patterns. During resting conditions, SMR activity in the mu frequency band is high. During motor imagery (as for voluntary movement), the amplitude of the mu rhythms decreases. The decrease of the EEG signal power is referred to as an event-related desynchronization. After the motor imagery stops, there is an increase in the high-beta rhythm (as is also the case for movement). This increase is referred to as an event-related synchronization. On the other hand, SMR neurofeedback studies dedicated to "SMR self-regulation" training procedures usually consider a narrower band, usually focussing on upregulation within the low-beta frequency range (12-15 Hz, although this range can vary depending on the study, and may sometimes not be specified). This can also be associated with training of simultaneous down-regulation of the theta band (around 4-8 Hz).

Sensorimotor rhythm self-modulation and BCI/NF

To the best of our knowledge, there is no consensus with respect to the distinction between brain-computer interfaces (BCI) and neurofeedback (NF). Indeed, on the one hand, the functioning of both methods is in many ways comparable, and both are closed-loop systems. In other words, users/patients are asked to self-regulate some specific brain activity patterns, recorded using techniques such as EEG, functional near-infra red spectroscopy (fNIRS) or

fMRI. This brain-activity is then processed in order to provide users/patients with feedback on their ability to modulate the patterns of interest. For instance, users/patients can be provided with visual or haptic feedback that is temporally synchronized with the efferent cortical motor activity. Haptic feedback may have the advantage to improve the neuroplasticity effect related to the MI task. Users/patients should use the feedback in order to improve, i.e., to better self-regulate the patterns of interest. With that said, on the other hand, BCI and neurofeedback have been developed with fundamentally different objectives. Mainly, learning to self-regulate specific brain patterns is an *end* in neurofeedback while it is only a *means* in BCI.

- The goal of neurofeedback is to teach users/patients to self-regulate target brain activity patterns in order to specifically enhance cognitive abilities or reduce clinical symptoms. For instance, SMR neurofeedback training procedures, in which patients had to learn to increase their SMR, have proved effective in reducing ADHD symptoms [6].

- The goal of BCI, and more specifically of mental imagery-based BCI (MI BCI), which is the most commonly used BCI paradigm based generally on SMR-EEG recording, is to control an application without moving, using brain activity alone, through the completion of MI tasks such as motor imagery of the left vs. right hand. Performing each of these tasks will induce specific modulations of brain rhythms. For instance, a decrease in SMR amplitude over the contralateral sensorimotor cortex should occur when users perform unilateral hand motor imagery [78]. Since each task is associated with a specific control command, such as “turn the wheelchair towards the left” for left hand motor imagery, the system is able to determine which command the user intended to send from the modulation of their EEG activity. Consequently, BCI users should learn to self-regulate specific brain patterns in order to reliably control the application.

Beyond their divergent objectives, neurofeedback and BCI are also traditionally associated with different methods. In order to self-regulate their SMR for instance, users are usually asked to perform specific motor imagery tasks in BCI, while this is not the case in NF, in which they should usually find their own strategy. Moreover, in NF, the target pattern (location, frequency) is usually defined in advance. Then, users should find by themselves how to self-regulate this pattern, using the feedback they are provided with. This feedback usually simply reflects the amplitude of the target pattern. In BCI however, a machine learning approach is usually employed. Such an approach consists of using signal processing algorithms to determine the location and frequency of the target pattern that enable the best discrimination between the different tasks. The EEG feedback that users are provided with reflects their ability to produce EEG patterns specific to each task. In case of a BCI involving left vs. right-hand motor imagery tasks, these EEG patterns would theoretically correspond to modulations of SMR. However,

when a machine learning approach without any a priori on the location/frequency of the pattern is used, other EEG patterns could be selected.

NEUROFEEDBACK TARGETING SENSORIMOTOR RHYTHMS FOR ENHANCING MOTOR SKILLS IN HEALTHY SUBJECTS

The efficacy of neurofeedback to improve healthy subjects' performances has mainly been studied in three domains [104]: cognitive, sports and artistic activities. In this section, we focus on neurofeedback procedures dedicated to the improvement of motor performance, for which most of the studies have been carried out in the field of sport science. For more information regarding neurofeedback procedures dedicated to the improvement of cognitive and affective aspects of performance, please refer to [36].

Sport motor skills improvement

The first study evaluating neurofeedback efficiency for improving athletes' motor performance was led in 1991 by Landers et al. [47]. Three groups of archers were included in the study, including one passive-control group (no neurofeedback), one active-control group (neurofeedback with "incorrect feedback") and one experimental group (following a neurofeedback procedure based on the self-regulation of "low frequency EEG oscillations", although the exact EEG band was not further described in the paper). Participants in the experimental group significantly increased their performance from pre- to post-test (27 bow shots) while the active-control group showed a decrement in performance and the passive-control group showed no difference in performance between pre- and post-test. Nonetheless, the neurofeedback procedure was not associated with any clear EEG pattern changes. Following this study, several other neurofeedback experiments were conducted in the aim of enhancing athletes' performance in different sports, e.g., in golf [17, 82], swimming [28], dance [36, 81] or athleticism [63]. Mirifar et al. [65] proposed a systematic review of these neurofeedback studies. The authors included 14 studies, of which 6 investigated self-regulation of low beta SMR (12-15Hz on C3-C4 or Cz – up-regulation) and 2 investigated self-regulation of alpha power over the sensorimotor cortex (mu rhythm up-regulation). They concluded that, so far, a majority of published studies support the effectiveness of neurofeedback in improving athletes' performance. Nonetheless, the specificity of the neurofeedback effect remains to be demonstrated. Indeed, it happened that the same protocol had different effects within the same or similar task, and also that different protocols resulted in similar effects within a sport. Mirifar et al. stress the fact that the studies' quality was non-optimal. A similar conclusion was drawn

by Xiang et al. [110] following their meta-analysis of randomized controlled trials aimed at assessing the efficiency of neurofeedback procedures to improve sport performance. This meta-analysis, which included 10 studies of which 6 focuses on low beta SMR (12-15Hz), revealed a significant effect of neurofeedback on both athletes' sport performance and EEG self-regulation abilities. Nonetheless, it appeared that this effect was moderated by the control group design. In other words, neurofeedback effect on sport performance was not significantly different in experimental groups compared to active/placebo control groups in well-controlled experiments. The authors suggest that further studies, with better designed and organized trials, should be performed. Notably, as outlined by Park et al. [74] the mismatch between lab study conditions (both in terms of tasks, feedback and training environment) and real sporting conditions may, at least in part, explain the relatively small impact that these studies had on professional athletes. It may be hypothesized that ecological training procedures would favor both the acquisition and transfer of motor skills.

Acting skills improvement

Such an ecological neurofeedback procedure has been previously used in order to enhance acting performance in one study [35]. Participants had to up-regulate their low-beta SMR activity while down-regulating their theta and high-beta activities. One group performed neurofeedback while being immersed in a virtual reality environment, one group was provided with standard feedback on a computer screen and the last group was a passive-control group. Participants of both the neurofeedback groups exhibited improved acting skills compared to the passive-control group. Moreover, the virtual reality group reached the *neurofeedback performance asymptote* earlier than the standard computer screen group, reinforcing the hypothesis that ecological settings favor learning. In the same vein of artistic performance enhancement, Egner and Gruzelier [27] carried out two experiments that aimed to investigate neurofeedback effects on musical skills. The first experiment revealed that participants who followed neurofeedback training exhibited an improvement in musical performance. More specifically, participants who carried out not an SMR neurofeedback protocol, but an alpha/theta training procedure (which consisted of "increasing theta (5–8 Hz) over alpha (8–11 Hz) activity levels during a wakeful eyes-closed condition for the purpose of relaxation training" [27]) combined with weekly physical exercises and mental skills training exhibited a positive correlation between neurofeedback performance (ability to self-regulate alpha/beta ratio) and musical performance. These results suggest that slow wave neurofeedback training could be used to enhance artistic performance. Nonetheless, as stressed by Vernon [104] a

number of limitations related to the experimental protocol prevent firm conclusions with regards to the specificity of this improvement, i.e., the extent to which this improvement was due to the neurofeedback procedure itself or to confounding factors.

Surgical skills improvement

Furthermore, Ros et al. [85] proposed an SMR neurofeedback procedure in which participants had to *"elevate the low-beta SMR (12-15 Hz) while concurrently suppressing theta activity (4-7 Hz)"*. This training procedure enabled a significant improvement both in surgical technique and task completion time in microsurgeons in comparison to a passive-control group. In a more general/abstract context, Ros et al. [86] investigated the effects of a neurofeedback procedure of mu suppression over the right motor cortex on motor performance in a within-subject experimental design. Participants had to perform two serial reaction time tasks (SRTT), one immediately after the neurofeedback procedure, the other one either 7 days before or after the neurofeedback procedure. Performances at the SRTT improved significantly quicker during the task when the latter was performed just after a neurofeedback procedure than when it was performed 7 days before or after. This result suggests that a single neurofeedback session may be directly used to facilitate the early acquisition of a procedural motor task and that neurofeedback effects could be exploited immediately after this neurofeedback session.

BCI/NEUROFEEDBACK TARGETING SENSORIMOTOR RHYTHMS FOR ENHANCING MOTOR SKILLS IN PATIENTS WITH BRAIN AND MENTAL DISORDERS

Motor abilities can be affected in case of brain or mental disorders. In this section, we focus on SMR BCI/neurofeedback procedures dedicated to the improvement of motor skills in brain and mental disorders for which most of the studies have been conducted. Concerning brain disorders, we focus on stroke. In this disorder, SMR BCI/neurofeedback training procedures aim to reduce hypokinetic activity by training to down-regulate mu rhythm or low beta SMR activity (enhance SMR event-related desynchronization) or to up-regulate high beta SMR activity (enhance SMR event-related synchronization) by performing MI. Such an application of BCIs based on MI results from the literature on the benefits of MI for post-stroke rehabilitation. Concerning mental disorders, we focus on ADHD. In this disorder, neurofeedback aims to reduce hyperkinetic activity by training to up-regulate low beta SMR activity during an attentional resting condition (no MI / motor inhibition). For a general review of neurofeedback and mental and brain disorder, please refer to [61].

Reducing hypokinetic activity: the case of stroke

BCI methods have been used according to two strategies for post-stroke neurorehabilitation [24, 94, 102]. The first strategy consists of using BCI approaches as "assistive technologies", i.e., as substitution for a lost motor ability [20]. The second strategy consists of using BCI as "rehabilitative/restorative technologies", by using neurofeedback procedures, in order to facilitate brain plasticity and motor recovery [26]. Both these techniques have been largely developed by Birbaumer's and Pfurtscheller's teams.

Assistive BCI were initially used for patients with tetraplegia in order to translate some specific EEG brain patterns into a selection of letters or words on a computer screen [9, 10] or to control a prosthetic limb [20]. However, the reliability and performance of such non-invasive EEG BCI are not high enough for these technologies to be used in daily life as assistive technology. Further researches are currently being conducted with invasive BCI or hybrid BCI (EEG with other physiological signals such as electrooculograms (EOG) or electromyograms (EMG) [64]. Rehabilitative BCI training procedures are very close to neurofeedback procedures. Nonetheless, in the field of stroke rehabilitation, the term BCI is more often used than the term neurofeedback. Both these procedures rely on the fact that SMR modulations in the hemisphere ispilateral to the stroke lesion can benefit the motor recovery [94]. In order to maximize the brain plasticity effect, the feedback is integrated into an orthotic device that assists the desired motor movement of the paralyzed hand [9, 14]. The hypothesis behind such a closed loop neural interface is that re-establishing the contingency loop between the ipsilateral cortical activity related to motor imagery (motor planning or attempted execution in relation with the measured SMR activity) and proprioceptive feedback (induced by the haptic effect of the orthotic device) would provide a somatosensory feedback to the primary motor cortex (M1), via the somatosensory cortex S1 and direct thalamic input. This would therefore induce simultaneous activation of presynaptic inputs to M1 with postsynaptic M1 activation that could result in Hebbian potentiation, improve motor learning and brain plasticity [26], and thus maximize the effect of the physical therapy applied after the stimulation with SMR training [19], see **Figure 2.**

The first case study investigating the use of SMR neurofeedback (reward production of low beta activity (15-21 Hz) and down-regulation of production of theta activity (4-8 Hz) in a patient with a stroke was published in 1995, and suggested a possible beneficial effect of neurofeedback on motor recovery [89]. However, the protocol was not specifically designed in line with the literature on MI in post-stroke. In 2007, Birbaumer et al. [9] developed a specific SMR BCI/neurofeedback training procedure that enabled a stroke patient suffering from a hand

motor deficit to control a hand orthotic device (open and close commands, based on MI). In 2008, it was shown that a majority of patients with stroke could use such a technology by learning to down-regulate their mu rhythm (i.e., 9-12 Hz oscillations in central areas), thus enhancing SMR event-related desynchronization, in the hemisphere ipsilateral to the stroke lesion [14]. This study thus suggests that patients with a lesion (due to stroke) in the motor cortex may still be able to perform motor imagery and motor attempts of the paretic hand. Nevertheless, this study did not reveal any functional improvement related to the BCI/neurofeedback training procedure. This may be due to the fact that the training was not associated with a goal-directed physical therapy that could enable transfer and generalization of the skills into daily life activities. In 2009-2010, two case studies (down-regulation of mu rhythm, here defined as 8-15 Hz frequency band, occurring during MI [13], and high beta SMR (21-24 Hz) up-regulation occurring after MI [23]) suggested a possible beneficial effect on motor recovery of the association of ipsilateral SMR BCI/neurofeedback training procedure and goal-directed physical therapy [13, 23]. Moreover, fMRI analysis showed that clinical improvement was associated with increased activation of the hemisphere ipsilateral to the stroke lesion [15], which suggests a specific effect of the SMR training procedure on brain plasticity and recovery after stroke.

A 2013 randomized double blind controlled study included 32 patients with stroke without residual finger movements [80]. The 16 patients of the active group performed 20 sessions of SMR BCI/neurofeedback training (the exact beta EEG band in central areas was not described in the paper) associated with a goal-directed physical therapy. The other 16 patients of the sham group performed 20 sessions of random SMR BCI/neurofeedback training, also associated with a goal-directed physical therapy. The active group exhibited a higher clinical hand motor recovery. This clinical improvement correlated with fMRI results showing increased activation of the hemisphere ipsilateral to the stroke lesion [80], which was confirmed in other neuroimaging and electrophysiological studies [79, 103, 112]. Interestingly, the efficacy of the SMR EEG BCI/neurofeedback training was related to the integrity of descending and ascending cortico-spinal pathways [12]. This result strengthens the importance of the motor-somatosensory loop to induce Hebbian potentiation and thus brain plasticity [94]. Lastly, it has been shown that stroke recovery was higher with haptic than with visual feedback [73].

The efficacy of SMR BCI/neurofeedback training has been consistently suggested in less well-controlled studies. For a recent systematic review, see [67]. Interestingly, Thibault et al. [100] highlighted the fact that only one neurofeedback randomized double blind controlled study demonstrated a clinical superiority of neurofeedback over sham neurofeedback [80] . This study

is therefore important in the current debate regarding the efficacy of neurofeedback [57]. Nonetheless, the characteristics of the population were not detailed in this study, which may reduce its legitimacy to generalize the results to the entire stroke population. Further studies are thus needed to establish well-defined stroke criteria (severity, localization: cortical vs subcortical, type: ischemic vs hemorrhagic, temporal evolution, etc.) that could be associated with predictive factors of response to such neurofeedback therapies.

Reducing hyperkinetic activity: the case of ADHD

In order to reduce pathological excessive motor activity, it has been proposed that patients could be trained to voluntary self-modulate their SMR brain oscillations through neurofeedback procedures. The neurophysiological rational for such protocol did not come from MI literature, but largely from the literature by Sterman's team. In the 1960s, Sterman showed that operant conditioning of SMR through neurofeedback procedures could be applied on cats, which were trained to modulate their SMR brain oscillation [109]. Their results suggested that the cats trained to enhance their SMR activity were more resistant to a drug that induced epileptic seizures [96]. In 1972, the same team published the first case study showing a possible beneficial effect of low-beta SMR up-regulation neurofeedback (i.e., 11-13 Hz oscillations in central areas) on the frequency of generalized motor epileptic seizure [98]. Many open-label studies and a few more controlled trials on the topic have been published since; for a review see [60]. Their hypothesis according to which it would be useful to use SMR training procedures to control seizure activity was based on intracerebral recordings in animals [97, 108]. During neurofeedback training, the subject is trained to increase their SMR rhythm and to decrease motor activities in the sensorimotor cortex (S1) in a vigilant state of alertness and motor relaxation [61]. It would decrease the activity of motor efferences in the posterior ventrolateral nucleus (VLP) of the ventrobasal (VB) thalamic complex as well as in the red nucleus (NR) of the brainstem, leading to a reduction in muscle tension and myotatic reflex [97]. The reduction of muscular activity would in turn decrease the activity of somatic afferent paths, which would favour a transition from rapid non-rhythmic activity to rhythmic oscillatory activity between the VLP and the reticular nucleus (NRT) of the thalamus [97]. These oscillatory activities would spread through the thalamo-cortical loops at S1 and give rise to the SMR rhythm synchronization recorded in EEG**.** The mechanisms of action of neurofeedback on SMR rhythms would thus consist in reducing the activity of efferences and afferences in the sensorimotor system, leading to a decrease in cortical neuronal excitability and an increase in the epileptogenic threshold [97]. It should be noted that SMR share similarities with sleep

spindle activities and that training to increase SMR in waking states increases the number of spindles during stage 2 slow sleep states [99]. Therefore, SMR neurofeedback training procedures have been applied to patients with insomnia [31, 91]. Moreover, as it has been clinically shown that SMR neurofeedback induces a decrease of motor activity as well as an improvement of the vigilant state of alertness related to attention capacities, it has been suggested to use such a training for Attentional Deficit Hyperactivity Disorder (ADHD) (previously called hyperkinetic disorder) therapies [58]. In 1976 [52], Lubar's team published the first case study showing a possible beneficial effect of neurofeedback on hyperkinetic activity in a child with ADHD treated with low-beta SMR neurofeedback ("*production of 12-14-Hz activity in the absence of 4-7 Hz slow-wave activity*"). This study is very interesting because: i) training (during a single session) and learning (across different sessions) effects during the neurofeedback procedure were controlled, and ii) training procedure and feedback presentation were reversed (trained to decrease the amplitude of SMR) in order to investigate the specificity of the effect on motor inhibition [52].

Since then, many studies investigating the efficacy of neurofeedback as a potential therapy for ADHD have been published. In most studies, neurofeedback training protocols correspond to low beta SMR neurofeedback, which in the field of ADHD is conventionally called a Theta/Beta Ratio (TBR) training (on EEG recorded from Cz or C3-C4). Indeed, TBR training procedures consist of rewarding low beta activity (around 16-20 Hz) while down-regulating the theta activity (around 4-8 Hz), in order to decrease the Theta/Beta Ratio. ADHD clinical applications have received a lot of attention both from non-specialist, general public sources [2] and from research groups [3]. Nevertheless, the methodological quality of these studies is very variable, and the results of the different meta-analyses tend to swing back and forth [62]. Four meta-analyses investigated the therapeutic usefulness of EEG neurofeedback in ADHD [5, 21, 56, 95]. All these meta-analyses concluded that: i) EEG neurofeedback could be more effective on the inattention dimension than in the hyperactivity dimension of ADHD, and ii) neurofeedback is more effective in randomized open trials than in randomized blinded trials, for which the size effect remains non-significant in two meta-analyses [21, 95]. The discrepancy between these meta-analyses can be explained by the selection of the studies included and the difference regarding the training procedure [62]. Moreover, from a neurophysiological standpoint, it can be questioned whether the chosen EEG targets are valid targets for ADHD children. Indeed, the level of evidence regarding the relationship between SMR activity and the hyperactivity and inattention dimensions of ADHD remains poor [4]. Therefore, an important and timely field of research consists of determining better, i.e. more reliable and specific, EEG

targets related to hyperkinetic activity [22], but also to the inattention dimension in ADHD. This will enable more relevant and efficient training to be provided to patients [59], which should ensure that the EEG target is modified during the neurofeedback procedure.

CONCLUSION

In this critical review, we first described and discussed the relationship between neuroplasticity, motor skills and SMR BCI/neurofeedback training in line with the MI literature. More precisely, we argued that BCI/neurofeedback could be used to train healthy subjects and patients to voluntarily self-regulate their SMR in order to trigger neuroplasticity phenomena and enable the acquisition of motor skills. Based on this theoretical background, we introduce the literature in which such procedures have been tested and evaluated. Mainly, we describe studies in which SMR BCI/neurofeedback demonstrated efficiency in improving sport performance as well as acting and surgical skills. BCI/Neurofeedback training seems to be very promising for improving healthy subjects' motor skills. Nonetheless, due to a range of limitations (e.g., selection and design for the control group, varied number of sessions, non-ecological training procedures, non-optimal feedback, absence of recordings of changes in baseline EEG activity) we agree with previous authors that "a clear association between BCI/neurofeedback training and enhanced performance [both in terms of EEG self-regulation and motor skills] has yet to be established" [104]. We also present the literature in which the efficiency of these BCI/neurofeedback techniques to improve the clinical symptoms of patients showing hyperkinetic (ADHD) or hypokinetic (stroke) activities was assessed. While these first results are promising, further investigations are also required, especially in order to determine the specificity of the effects observed: is the clinical improvement due to neuroplasticity phenomena? To which extent? What is the influence of the placebo effect and the mechanisms underlying the latter? What is the impact of the training procedure and which variables should be controlled for? In the context of stroke studies, Ramos-Murguiaday et al. [80] highlight the challenges to be addressed in order to ensure the efficiency of BCI/neurofeedback techniques:

i. It is possible to assess the clinical efficacy of BCI/neurofeedback through a well-controlled study (with adequate size of study population, randomized and blinded protocol, adequate control group, and high quality of EEG BCI/neurofeedback sessions),
ii. It is of the utmost importance to determine reliable, valid and well specified (particularly in terms of spatial and temporal characteristics) EEG targets, related to the clinical

parameter of efficacy, to underlying pathophysiological mechanisms of the disorder and also mechanisms of neuroplastic modulation,

iii. It is also necessary to control for learning, training and plasticity effects by designing and implementing an appropriate BCI/neurofeedback protocol design (with optimized quality of signal recordings, signal processing, threshold, feedback reinforcements, duration and number of sessions, transfer/generalization methods) [3].

These challenges appear relevant and could be applied to other pathologies. Regarding clinical aspects, this review has mainly focused on SMR BCI/neurofeedback procedures in stroke and ADHD. Nevertheless, motor skills are also altered in various other neurological and psychiatric disorders. In particular, motor disabilities are core manifestations in depression and schizophrenia; some studies suggest a relationship with SMR alterations [70, 93]. Here as well, as highlighted by Ramos-Murguiaday et al. [80], further neurophysiological studies are required to better investigate the relationship between specific motor manifestations and SMR activities in these disorders. If such relationships were demonstrated, SMR BCI/neurofeedback could be of great interest to reduce the symptoms of motor disabilities, which are currently under-investigated and under-treated in psychiatry [8].

Disclosure of potential conflicts of interest:

The authors declare that they have no conflict of interest.

Figure 1: Neural processes shared between real and imagined movements, which impact the brain through neuroplasticity. These plastic effects occur at different levels: molecular, functional and structural changes induced by visual and/or haptic feedback. *LTP = Long-Term Potentiation*

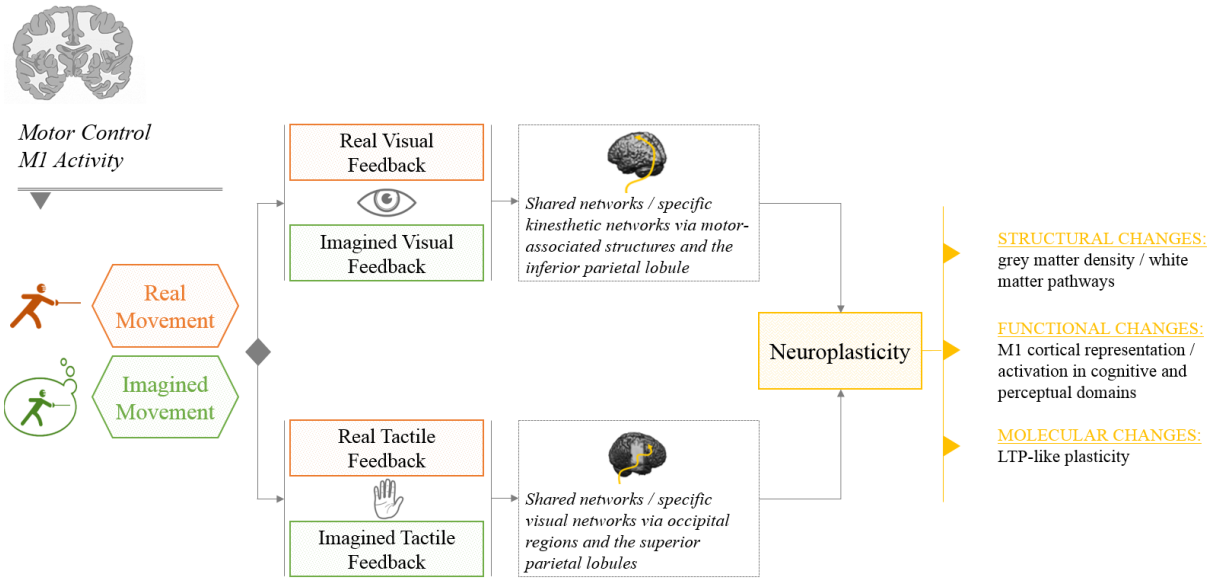
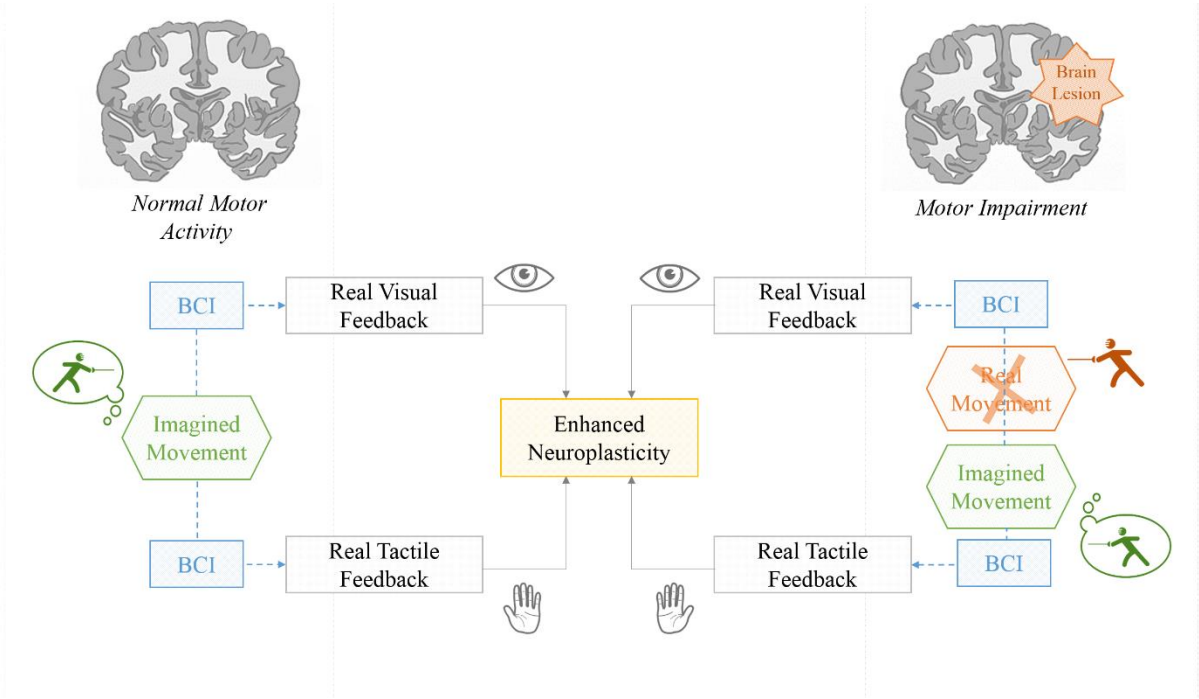


Figure 2: Impact of the brain lesion. Due to the lesion and motor impairment, only imagined movement might have an impact on plasticity, involving networks and mechanisms which enhance neuroplasticity, particularly using brain computer interfaces (BCI) that enable their users to be provided with visual and/or haptic feedback



References

[1] Akaneya Y, Tsumoto T, Kinoshita S, Hatanaka H. Brain-derived neurotrophic factor enhances long-term potentiation in rat visual cortex. Journal of Neuroscience 1997; 17: 6707-6716.

[2] Arns M. A NExT Step for neurofeedback in France. Encephale 2017; 43: 97-98.

[3] Arns M, Batail JM, Bioulac S, Congedo M, Daudet C, Drapier D, et al. Neurofeedback: One of today's techniques in psychiatry? Encephale 2017; 43: 135-145.

[4] Arns M, Conners CK, Kraemer HC. A decade of EEG Theta/Beta Ratio Research in ADHD: a meta-analysis. J Atten Disord 2013; 17: 374-83.

[5] Arns M, de Ridder S, Strehl U, Breteler M, Coenen A. Efficacy of neurofeedback treatment in ADHD: the effects on inattention, impulsivity and hyperactivity: a meta-analysis. Clin EEG Neurosci 2009; 40: 180-9.

[6] Arns M, Heinrich H, Strehl U. Evaluation of neurofeedback in ADHD: The long and winding road. Biol Psychol 2014; 95: 108-15.

[7] Avanzino L, Gueugneau N, Bisio A, Ruggeri P, Papaxanthis C, Bove M. Motor cortical plasticity induced by motor learning through mental practice. Frontiers in behavioral neuroscience 2015; 9.

[8] Bernard JA, Mittal VA. Updating the research domain criteria: the utility of a motor dimension. Psychol Med 2015; 45: 2685-9.

[9] Birbaumer N, Cohen LG. Brain-computer interfaces: communication and restoration of movement in paralysis. J Physiol 2007; 579: 621-36.

[10] Birbaumer N, Ghanayim N, Hinterberger T, Iversen I, Kotchoubey B, Kubler A, et al. A spelling device for the paralysed. Nature 1999; 398: 297-8.

[11] Bonassi G, Biggio M, Bisio A, Ruggeri P, Bove M, Avanzino L. Provision of somatosensory inputs during motor imagery enhances learning-induced plasticity in human motor cortex. Scientific Reports 2017; 7: 9300.

[12] Brasil F, Curado MR, Witkowski M, Garcia E, Broetz D, Birbaumer N, et al. MEP predicts motor recovery in chronic stroke patients undergoing 4-weeks of daily physical therapy. Human Brain Mapping Annual Meeting 2012; Beijing.

[13] Broetz D, Braun C, Weber C, Soekadar SR, Caria A, Birbaumer N. Combination of brain-computer interface training and goal-directed physical therapy in chronic stroke: a case report. Neurorehabil Neural Repair 2010; 24: 674-9.

[14] Buch E, Weber C, Cohen LG, Braun C, Dimyan MA, Ard T, et al. Think to move: a neuromagnetic brain-computer interface (BCI) system for chronic stroke. Stroke 2008; 39: 910-7.

[15] Caria A, Weber C, Brotz D, Ramos A, Ticini LF, Gharabaghi A, et al. Chronic stroke recovery after combined BCI training and physiotherapy: a case report. Psychophysiology 2011; 48: 578-82.

[16] Chang Y. Reorganization and plastic changes of the human brain associated with skill learning and expertise. Frontiers in human neuroscience 2014; 8.

[17] Cheng MY, Huang CJ, Chang YK, Koester D, Schack T, Hung TM. Sensorimotor Rhythm Neurofeedback Enhances Golf Putting Performance. J Sport Exerc Psychol 2015; 37: 626-36.

[18] Cicinelli P, Marconi B, Zaccagnini M, Pasqualetti P, Filippi MM, Rossini PM. Imagery-induced cortical excitability changes in stroke: a transcranial magnetic stimulation study. Cerebral Cortex 2005; 16: 247-253.

[19] Claflin ES, Krishnan C, Khot SP. Emerging treatments for motor rehabilitation after stroke. Neurohospitalist 2015; 5: 77-88.
[20] Collinger JL, Wodlinger B, Downey JE, Wang W, Tyler-Kabara EC, Weber DJ, et al. High-performance neuroprosthetic control by an individual with tetraplegia. Lancet 2013; 381: 557-64.
[21] Cortese S, Ferrin M, Brandeis D, Holtmann M, Aggensteiner P, Daley D, et al. Neurofeedback for Attention-Deficit/Hyperactivity Disorder: Meta-Analysis of Clinical and Neuropsychological Outcomes From Randomized Controlled Trials. J Am Acad Child Adolesc Psychiatry 2016; 55: 444-55.
[22] Dahan A, Ryder CH, Reiner M. Components of motor deficiencies in ADHD and possible interventions. Neuroscience 2017.
[23] Daly JJ, Cheng R, Rogers J, Litinas K, Hrovat K, Dohring M. Feasibility of a new application of noninvasive Brain Computer Interface (BCI): a case study of training for recovery of volitional motor control after stroke. J Neurol Phys Ther 2009; 33: 203-11.
[24] Daly JJ, Wolpaw JR. Brain-computer interfaces in neurological rehabilitation. Lancet Neurol 2008; 7: 1032-43.
[25] Dayan E, Cohen LG. Neuroplasticity subserving motor skill learning. Neuron 2011; 72: 443-54.
[26] Dobkin BH. Brain-computer interface technology as a tool to augment plasticity and outcomes for neurological rehabilitation. J Physiol 2007; 579: 637-42.
[27] Egner T, Gruzelier JH. Ecological validity of neurofeedback: modulation of slow wave EEG enhances musical performance. Neuroreport 2003; 14: 1221-4.
[28] Faridnia M, Shojaei M, Rahimi A. The effect of neurofeedback training on the anxiety of elite female swimmers. Annals of Biological Research 2012; 3: 1020–1028.
[29] Filgueiras A, Conde EFQ, Hall CR. The neural basis of kinesthetic and visual imagery in sports: an ALE meta− analysis. Brain imaging and behavior 2017: 1-11.
[30] Floyer-Lea A, Matthews PM. Distinguishable brain activation networks for short-and long-term motor skill learning. Journal of neurophysiology 2005; 94: 512-518.
[31] Fovet T, Micoulaud-Franchi JA, Vialatte FB, Lotte F, Daudet C, Batail JM, et al. On assessing neurofeedback effects: should double-blind replace neurophysiological mechanisms? Brain 2017; 140: e63.
[32] Fritzsch C, Wang J, dos Santos LF, Mauritz K-H, Brunetti M, Dohle C. Different effects of the mirror illusion on motor and somatosensory processing. Restorative neurology and neuroscience 2014; 32: 269-280.
[33] Garrison KA, Winstein CJ, Aziz-Zadeh L. The mirror neuron system: a neural substrate for methods in stroke rehabilitation. Neurorehabilitation and neural repair 2010; 24: 404-412.
[34] Gastaut H. Etude électroencéphalographique de la réactivité des rythmes rolandiques. Rev Neurol 1952; 87: 175-82.
[35] Gruzelier J, Inoue A, Smart R, Steed A, Steffert T. Acting performance and flow state enhanced with sensory-motor rhythm neurofeedback comparing ecologically valid immersive VR and training screen scenarios. Neurosci Lett 2010; 480: 112-6.
[36] Gruzelier JH, Thompson T, Redding E, Brandt R, Steffert T. Application of alpha/theta neurofeedback and heart rate variability training to young contemporary dancers: state anxiety and creativity. Int J Psychophysiol 2014; 93: 105-11.
[37] Guillot A, Collet C, Nguyen VA, Malouin F, Richards C, Doyon J. Brain activity during visual versus kinesthetic imagery: an fMRI study. Human brain mapping 2009; 30: 2157-2172.

[38] Hamzei F, Läppchen CH, Glauche V, Mader I, Rijntjes M, Weiller C. Functional plasticity induced by mirror training: the mirror as the element connecting both hands to one hemisphere. Neurorehabilitation and neural repair 2012; 26: 484-496.
[39] Han Y, Yang H, Lv Y-T, Zhu C-Z, He Y, Tang H-H, et al. Gray matter density and white matter integrity in pianists' brain: a combined structural and diffusion tensor MRI study. Neuroscience letters 2009; 459: 3-6.
[40] Jaillard A, Martin CD, Garambois K, Lebas JF, Hommel M. Vicarious function within the human primary motor cortex? A longitudinal fMRI stroke study. Brain 2005; 128: 1122-1138.
[41] Jäncke L. The plastic human brain. Restorative neurology and neuroscience 2009; 27: 521-538.
[42] Jasper H, Penfield W. Electrocorticograms in man: Effect of volontary movement upon the electrical activity of the precentral gyrus. Arch. für Psych. und Zeits. Neurol 1949; 183: 163-174.
[43] Kane N, Acharya J, Benickzy S, Caboclo L, Finnigan S, Kaplan PW, et al. A revised glossary of terms most commonly used by clinical electroencephalographers and updated proposal for the report format of the EEG findings. Revision 2017. Clin Neurophysiol Pract 2017; 2: 170-185.
[44] Kashuk S, Williams J, Thorpe G, Wilson P, Egan G. Diminished motor imagery capability in adults with motor impairment: An fMRI mental rotation study. Behavioural brain research 2017; 334: 86-96.
[45] Kelly AC, Garavan H. Human functional neuroimaging of brain changes associated with practice. Cerebral Cortex 2004; 15: 1089-1102.
[46] Kolb B, Whishaw IQ. Brain plasticity and behavior. Annual review of psychology 1998; 49: 43-64.
[47] Landers DM, Petruzzello SJ, Salazar W, Crews DJ, Kubitz KA, Gannon TL, et al. The influence of electrocortical biofeedback on performance in pre-elite archers. Med Sci Sports Exerc 1991; 23: 123-9.
[48] Langhorne P, Bernhardt J, Kwakkel G. Stroke rehabilitation. Lancet 2011; 377: 1693-702.
[49] Li S, Han Y, Wang D, Yang H, Fan Y, Lv Y, et al. Mapping surface variability of the central sulcus in musicians. Cerebral Cortex 2009; 20: 25-33.
[50] Liepert J, Graef S, Uhde I, Leidner O, Weiller C. Training-induced changes of motor cortex representations in stroke patients. Acta neurologica scandinavica 2000; 101: 321-326.
[51] Lu B. BDNF and activity-dependent synaptic modulation. Learning & memory 2003; 10: 86-98.
[52] Lubar JF, Shouse MN. EEG and behavioral changes in a hyperkinetic child concurrent with training of the sensorimotor rhythm (SMR): a preliminary report. Biofeedback Self Regul 1976; 1: 293-306.
[53] Marconi B, Filippi GM, Koch G, Giacobbe V, Pecchioli C, Versace V, et al. Long-term effects on cortical excitability and motor recovery induced by repeated muscle vibration in chronic stroke patients. Neurorehabilitation and neural repair 2011; 25: 48-60.
[54] Matthys K, Smits M, Van der Geest JN, Van der Lugt A, Seurinck R, Stam HJ, et al. Mirror-induced visual illusion of hand movements: a functional magnetic resonance imaging study. Archives of physical medicine and rehabilitation 2009; 90: 675-681.
[55] Michielsen ME, Selles RW, van der Geest JN, Eckhardt M, Yavuzer G, Stam HJ, et al. Motor recovery and cortical reorganization after mirror therapy in chronic stroke

patients: a phase II randomized controlled trial. Neurorehabilitation and neural repair 2011; 25: 223-233.
[56] Micoulaud Franchi J, Geoffroy P, Fond G, Lopez R, Bioulac S, Philip P. EEG Neurofeedback treatments in children with ADHD: An updated meta-analysis of Randomized Controlled Trials. Front Hum Neurosc. 2014; doi: 10.3389/fnhum.2014.00906.
[57] Micoulaud Franchi JA, Fovet T. Neurofeedback: time needed for a promising non-pharmacological therapeutic method. Lancet Psychiatry 2016; 3: e16.
[58] Micoulaud-Franchi JA, Bat-Pitault F, Cermolaccce M, Vion-Dury J. Neurofeedback dans le trouble déficit de l'attention avec hyperactivité : de l'efficacité à la spécificité de l'effet neurophysiologique. Annales Medico Psychologiques 2011; 169: 200-208.
[59] Micoulaud-Franchi JA, Fovet T. Neurofeedback: time needed for a promising non-pharmacological therapeutic method. Lancet Psychiatry 2016; 3: e16.
[60] Micoulaud-Franchi JA, Lanteaume L, Pallanca O, Vion-Dury J, Bartolomei F. [Biofeedback and drug-resistant epilepsy: back to an earlier treatment?]. Rev Neurol (Paris) 2014; 170: 187-96.
[61] Micoulaud-Franchi JA, McGonigal A, Lopez R, Daudet C, Kotwas I, Bartolomei F. Electroencephalographic neurofeedback: Level of evidence in mental and brain disorders and suggestions for good clinical practice. Neurophysiol Clin 2015; 45: 423-33.
[62] Micoulaud-Franchi JA, Salvo F, Bioulac S, Fovet T. Neurofeedback in Attention-Deficit/Hyperactivity Disorder: Efficacy. J Am Acad Child Adolesc Psychiatry 2017; 55: 1091-1092.
[63] Mikicin M. The autotelic involvement of attention induced by eeg neurofeedback training improves the performance of an athlete's mind. Biomedical Human Kinetics 2015; 7.
[64] Millan JD, Rupp R, Muller-Putz GR, Murray-Smith R, Giugliemma C, Tangermann M, et al. Combining Brain-Computer Interfaces and Assistive Technologies: State-of-the-Art and Challenges. Front Neurosci 2010; 4.
[65] Mirifar A, Beckmann J, Ehrlenspiel F. Neurofeedback as supplementary training for optimizing athletes' performance: A systematic review with implications for future research. Neurosci Biobehav Rev 2017; 75: 419-432.
[66] Miyachi S, Hikosaka O, Lu X. Differential activation of monkey striatal neurons in the early and late stages of procedural learning. Experimental brain research 2002; 146: 122-126.
[67] Monge-Pereira E, Ibanez-Pereda J, Alguacil-Diego IM, Serrano JI, Spottorno-Rubio MP, Molina-Rueda F. Use of Electroencephalography Brain-Computer Interface Systems as a Rehabilitative Approach for Upper Limb Function After a Stroke: A Systematic Review. PM R 2017; 9: 918-932.
[68] Munzert J, Lorey B, Zentgraf K. Cognitive motor processes: the role of motor imagery in the study of motor representations. Brain research reviews 2009; 60: 306-326.
[69] Murase N, Duque J, Mazzocchio R, Cohen LG. Influence of interhemispheric interactions on motor function in chronic stroke. Annals of neurology 2004; 55: 400-409.
[70] Nieber D, Schlegel S. Relationships between psychomotor retardation and EEG power spectrum in major depression. Neuropsychobiology 1992; 25: 20-3.
[71] Nojima I, Mima T, Koganemaru S, Thabit MN, Fukuyama H, Kawamata T. Human motor plasticity induced by mirror visual feedback. Journal of Neuroscience 2012; 32: 1293-1300.

[72] Nudo RJ, Milliken GW. Reorganization of movement representations in primary motor cortex following focal ischemic infarcts in adult squirrel monkeys. Journal of neurophysiology 1996; 75: 2144-2149.
[73] Ono T, Shindo K, Kawashima K, Ota N, Ito M, Ota T, et al. Brain-computer interface with somatosensory feedback improves functional recovery from severe hemiplegia due to chronic stroke. Front Neuroeng 2014; 7: 19.
[74] Park JL, Fairweather MM, Donaldson DI. Making the case for mobile cognition: EEG and sports performance. Neurosci Biobehav Rev 2015; 52: 117-30.
[75] Pascual-Leone A, Amedi A, Fregni F, Merabet LB. The plastic human brain cortex. Annu. Rev. Neurosci. 2005; 28: 377-401.
[76] Pearce A, Thickbroom G, Byrnes M, Mastaglia F. The corticomotor representation of elite racquet sport athletes. Exp Brain Res 2000; 130: 238-243.
[77] Pfurtscheller G, Aranibar A. Event-related cortical desynchronization detected by power measurements of scalp EEG. Electroencephalogr Clin Neurophysiol 1977; 42: 817-26.
[78] Pfurtscheller G, Neuper C. Motor Imagery and Direct Brain-Computer Communication. Proceedings of the IEEE 2001; 89: 1123–1134.
[79] Pichiorri F, Morone G, Petti M, Toppi J, Pisotta I, Molinari M, et al. Brain-computer interface boosts motor imagery practice during stroke recovery. Ann Neurol 2015; 77: 851-65.
[80] Ramos-Murguialday A, Broetz D, Rea M, Laer L, Yilmaz O, Brasil FL, et al. Brain-machine interface in chronic stroke rehabilitation: a controlled study. Ann Neurol 2013; 74: 100-8.
[81] Raymond J, Sajid I, Parkinson LA, Gruzelier JH. Biofeedback and dance performance: a preliminary investigation. Appl Psychophysiol Biofeedback 2005; 30: 64-73.
[82] Ring C, Cooke A, Kavussanu M, McIntyre D, Masters R. Investigating the efficacy of neurofeedback training for expediting expertise and excellence in sport. Psychology of sport and exercise 2015; 16: 118–127.
[83] Rioult-Pedotti M-S, Friedman D, Donoghue JP. Learning-induced LTP in neocortex. Science 2000; 290: 533-536.
[84] Rioult-Pedotti M-S, Friedman D, Hess G, Donoghue JP. Strengthening of horizontal cortical connections following skill learning. Nature neuroscience 1998; 1: 230-234.
[85] Ros T, Moseley MJ, Bloom PA, Benjamin L, Parkinson LA, Gruzelier JH. Optimizing microsurgical skills with EEG neurofeedback. BMC Neurosci 2009; 10: 87.
[86] Ros T, Munneke MA, Parkinson LA, Gruzelier JH. Neurofeedback facilitation of implicit motor learning. Biol Psychol 2014; 95: 54-8.
[87] Rosenkranz K, Kacar A, Rothwell JC. Differential modulation of motor cortical plasticity and excitability in early and late phases of human motor learning. Journal of Neuroscience 2007; 27: 12058-12066.
[88] Rossiter HE, Borrelli MR, Borchert RJ, Bradbury D, Ward NS. Cortical mechanisms of mirror therapy after stroke. Neurorehabilitation and neural repair 2015; 29: 444-452.
[89] Rozelle GR, Budzynski TH. Neurotherapy for stroke rehabilitation: a single case study. Biofeedback Self Regul 1995; 20: 211-28.
[90] Saur D, Lange R, Baumgaertner A, Schraknepper V, Willmes K, Rijntjes M, et al. Dynamics of language reorganization after stroke. Brain 2006; 129: 1371-1384.
[91] Schabus M, Griessenberger H, Gnjezda MT, Heib DPJ, Wislowska M, Hoedlmoser K. Better than sham? A double-blind placebo-controlled neurofeedback study in primary insomnia. Brain 2017; 140: 1041-1052.

[92] Sharma N, Baron J-C. Motor Recovery After Subcortical Stroke Depends on Modulation of Extant Motor Networks. Frontiers in neurology 2015; 6.
[93] Singh F, Pineda J, Cadenhead KS. Association of impaired EEG mu wave suppression, negative symptoms and social functioning in biological motion processing in first episode of psychosis. Schizophr Res 2011; 130: 182-6.
[94] Soekadar SR, Birbaumer N, Slutzky MW, Cohen LG. Brain-machine interfaces in neurorehabilitation of stroke. Neurobiol Dis 2015; 83: 172-9.
[95] Sonuga-Barke EJ, Brandeis D, Cortese S, Daley D, Ferrin M, Holtmann M, et al. Nonpharmacological interventions for ADHD: systematic review and meta-analyses of randomized controlled trials of dietary and psychological treatments. Am J Psychiatry 2013; 170: 275-89.
[96] Sterman M, LoPresti R, Fairchild M. Electroencephalographic and behavioral studies of monomethyl hydrazine toxicity in the cat. Aerospace Medical Research Laboratory 1969; AMRL-TR-69-3: 1-8.
[97] Sterman MB. Basic concepts and clinical findings in the treatment of seizure disorders with EEG operant conditioning. Clin Electroencephalogr 2000; 31: 45-55.
[98] Sterman MB, Friar L. Suppression of seizures in an epileptic following sensorimotor EEG feedback training. Electroencephalogr Clin Neurophysiol 1972; 33: 89-95.
[99] Sterman MB, Howe RC, Macdonald LR. Facilitation of spindle-burst sleep by conditioning of electroencephalographic activity while awake. Science 1970; 167: 1146-8.
[100] Thibault RT, Raz A. When can neurofeedback join the clinical armamentarium? Lancet Psychiatry 2016; 3: 497-8.
[101] Thieme H, Mehrholz J, Pohl M, Behrens J, Dohle C. Mirror therapy for improving motor function after stroke. Stroke 2013; 44: e1-e2.
[102] van Dokkum LE, Ward T, Laffont I. Brain computer interfaces for neurorehabilitation - its current status as a rehabilitation strategy post-stroke. Ann Phys Rehabil Med 2015; 58: 3-8.
[103] Varkuti B, Guan C, Pan Y, Phua KS, Ang KK, Kuah CW, et al. Resting state changes in functional connectivity correlate with movement recovery for BCI and robot-assisted upper-extremity training after stroke. Neurorehabil Neural Repair 2013; 27: 53-62.
[104] Vernon D. Can neurofeedback training enhance performance? An evaluation of the evidence with implications for future research. Applied psychophysiology and biofeedback 2005; 30: 347.
[105] Vitrac C, Benoit-Marand M. Monoaminergic Modulation of Motor Cortex Function. Frontiers in neural circuits 2017; 11: 72.
[106] Warburton E, Price CJ, Swinburn K, Wise RJ. Mechanisms of recovery from aphasia: evidence from positron emission tomography studies. Journal of Neurology, Neurosurgery & Psychiatry 1999; 66: 155-161.
[107] Ward N. Future perspectives in functional neuroimaging in stroke recovery. Europa medicophysica 2007; 43: 285-294.
[108] Wyrwicka W, Sterman MB. Instrumental Conditioning of Sensorimotor Cortex EEG Spindles in the Waking Cat. Physiol Behav 1968; 3: 703-707.
[109] Wyrwicka W, Sterman MB, Clemente CD. Conditioning of induced electroencephalographic sleep patterns in the cat. Science 1962; 137: 616-8.
[110] Xiang MQ, Hou XH, Liao BG, Liao JW, Hu M. The effect of neurofeedback training for sport performance in athletes: A meta-analysis. Psychology of Sport and Exercise 2018.

[111] Yin HH, Mulcare SP, Hilário MR, Clouse E, Holloway T, Davis MI, et al. Dynamic reorganization of striatal circuits during the acquisition and consolidation of a skill. Nature neuroscience 2009; 12: 333-341.
[112] Young BM, Nigogosyan Z, Remsik A, Walton LM, Song J, Nair VA, et al. Changes in functional connectivity correlate with behavioral gains in stroke patients after therapy using a brain-computer interface device. Front Neuroeng 2014; 7: 25.
[113] Ziemann U, Iliać TV, Pauli C, Meintzschel F, Ruge D. Learning modifies subsequent induction of long-term potentiation-like and long-term depression-like plasticity in human motor cortex. Journal of Neuroscience 2004; 24: 1666-1672.