

Neurorehabilitation therapy of patients with severe stroke based on functional electrical stimulation commanded by a brain computer interface

Carolina B Tabernig¹ , Camila A Lopez³, Lucía C Carrere¹,
Erika G Spaich² and Carlos H Ballario³

Abstract

Introduction: Brain computer interface is an emerging technology to treat the sequelae of stroke. The purpose of this study was to explore the motor imagery related desynchronization of sensorimotor rhythms of stroke patients and to assess the efficacy of an upper limb neurorehabilitation therapy based on functional electrical stimulation controlled by a brain computer interface.

Methods: Eight severe chronic stroke patients were recruited. The study consisted of two stages: screening and therapy. During screening, the ability of patients to desynchronize the contralateral oscillatory sensorimotor rhythms by motor imagery of the most affected hand was assessed. In the second stage, a therapeutic intervention was performed. It involved 20 sessions where an electrical stimulator was activated when the patient's cerebral activity related to motor imagery was detected. The upper limb was assessed, before and after the intervention, by the Fugl–Meyer score (primary outcome). Spasticity, motor activity, range of movement and quality of life were also evaluated (secondary outcomes).

Results: Desynchronization was identified in all screened patients. Significant post-treatment improvement ($p < 0.05$) was detected in the primary outcome measure and in the majority of secondary outcome scores.

Conclusions: The results suggest that the proposed therapy could be beneficial in the neurorehabilitation of stroke individuals.

Keywords

Brain computer interface, motor imagery, functional electrical stimulation, stroke, rehabilitation, EMOTIV Epop+, therapy

Date received: 5 October 2017; accepted: 21 June 2018

Introduction

Approximately 25% of men and 20% of women above 85 years of age will have a stroke, and between 25% and 40% of the survivors will develop significant sequelae.¹ Rehabilitation therapies seek to generate sensorimotor stimuli through the repetition of movements and their incorporation to activities of daily life, favoring the activity-dependent plasticity of the central nervous system.^{2–4} It is known that the type, shape, and synchrony of sensory feedback affects motor relearning.⁵ Current evidence suggests that the neural correlate which associates motor imagery generated in sensorimotor

cortical areas with activity produced by visual and proprioceptive feedback is a basic mechanism of motor learning.^{6,7}

¹Laboratorio de Ingeniería en Rehabilitación e Investigaciones Neuromusculares y Sensoriales (LIRINS), Facultad de Ingeniería, Universidad Nacional de Entre Ríos, Oro Verde, Argentina

²SMI[®], Department of Health Science and Technology, Aalborg University, Denmark

³Fundación Rosarina de Neuro-rehabilitación, Rosario, Argentina

Corresponding author:

Carolina B Tabernig, Laboratorio de Ingeniería en Rehabilitación e Investigaciones Neuromusculares y Sensoriales (LIRINS), Facultad de Ingeniería, Universidad Nacional de Entre Ríos, Oro Verde, Argentina.
Email: ctabernig@ingenieria.uner.edu.ar



Functional electrical stimulation (FES) is a neuro-rehabilitation therapy that assists the execution of repetitive functional movements commanded by the user while generating proprioceptive and visual feedback. To reconstitute the lost functionality of paralyzed limbs, a stimulator is activated at the moment of the realization of the desired motor function. In this sense, several signals have been proposed to control FES devices, among them heel switches, shoulder pads, pressure sensors, and brain computer interfaces (BCI).^{8,9,10}

A BCI is a device that records and processes brain signals to establish a communication channel between an individual and the outside environment.¹¹ One of the paradigms of BCI is based on the identification of the brain activity related to the motor imagery (MI). MI produces the desynchronization of the sensorimotor rhythms in the electroencephalogram (EEG). Sensorimotor rhythms refer to oscillations recorded on brain activity in somatic sensorimotor areas, concentrated in the frequency bands *mu* (8–12 Hz) and *beta* (12–30 Hz). This desynchronization is evidenced as a decrease in the power of the EEG signal related to rest. This event, which happens during MI, is called event-related desynchronization (ERD).^{12,13}

ERD can be observed on a specific EEG frequency band and with a spatial distribution in the sensorimotor cortex related to the MI task.¹⁴ It can be visualized through topographic maps in which the spatial distribution of an ERD indicator for a given EEG frequency is represented. The coefficient of determination r^2 is one of the indicators of brain activity related to MI. This coefficient takes real values between 0 and 1; values close to 1 indicate very good discrimination between rest and MI, while values close to 0 indicate that they are scarcely distinguishable.¹⁵

Recent works have reported topographic maps obtained during MI and movement of foot in healthy subjects,¹⁶ and of hands in people with stroke sequelae.^{17,18} They concluded that despite damage to the motor cortex due to stroke, it is feasible to detect the ERD associated with the MI of the affected limb. In addition, previous studies with BCI showed that correct training to generate the desynchronization of the electroencephalographic rhythm in patients with stroke by MI, could prove beneficial in their rehabilitation.^{19,20} In this sense, the ERD during MI for controlling a hand orthosis has been shown to be useful in facilitating motor relearning in both healthy subjects²¹ and stroke patients.²² Recently, researchers demonstrated the feasibility of continuously decoding the movement intention of paralysed limbs in stroke survivors from the ipsilateral unaffected motor cortex¹⁸ and the therapeutic potential of a BCI-driven neurorehabilitation approach using the unaffected hemisphere and an exoskeleton.²³ Some authors reported that, in isolated

cases, the application of BCI and FES to control paralyzed hand grasping was successful suggesting that this methodology could also generate favorable plastic changes at the cortical level.^{24,25} In addition, a recent study recommended that FES be kept active throughout the duration of MI.²⁶ However, the use of BCI and FES for therapeutic purposes in patients with sequelae of stroke is poor.

This article presents the results of a study whose objectives were to explore the ERD of stroke patients during MI and to evaluate the effects of a neurorehabilitation therapy based on BCI and FES (BCI-FES) for chronic patients with sequelae of ischemic stroke. It is sought to facilitate neuroplasticity through the activation of the cerebral cortex in the presence of MI (BCI-MI) and the sensory feedback produced by the movement of the most affected upper limb produced by FES.

Materials and methods

The study consisted of two stages. During both of them, patients were asked to imagine extending their most affected hand. In the first stage, the volunteers' ability to achieve ERD was assessed. The second stage consisted of 20 sessions using a BCI-FES System. During these sessions, when cortical activity related to MI was detected, the FES device was activated to assist contracting the wrist and finger extensor muscles of the most affected limb.

Patients

Fourty-nine patients with unilateral ischemic stroke were contacted from September 2014 to April 2016, of whom eight were enrolled in the study after assessing the following criteria: at least one year of evolution since the ictus (average evolution: 36.8 ± 24.2 months, two females and six males, average age: 61.2 ± 19.0 years), with paralysis or marked weakness of the flexor-extensors of the fingers and the upper limb: modified Fugl-Meyer-Assessment (mFMA) with a score equal to or less than 25. Preservation of the cognitive functions necessary to understand the cues of the therapy and the informed consent, good sight, and minimal or null compromise of the sensitivity of the affected limb, were also required. The research was conducted following the Declaration of Helsinki. All of included patients expressed their written consent to participate in the study, which was approved by the Ethical Committee of the Fundación Rosarina de Neuro-rehabilitación, Rosario, province of Santa Fe, Argentina (RENIS No. IS001710).

Patients who had any psychiatric or neurological condition besides stroke, cerebellar syndrome, injuries

in the peripheral nervous system of the more affected limb, severe pain, spasticity grade 3 or higher on the modified Ashworth scale (mAsh), and/or taking high doses of medication that may cause inhibition of neuroplasticity were excluded. Table 1 shows the demographic characteristics of the patients at the start of the study, the location of their lesions, and the mFMA score with a maximum of 54 points.

Stage 1: Screening

Materials. For the assessment of the patients' ability to achieve ERD, eight monopolar EEG channels were recorded using a system consisting of the amplifier g.MOBILab+® (Guger Technologies, Austria, sampling frequency: 256 Hz, resolution: 16 bits, filters: 0.5–100 Hz, sensitivity: 500 μ V) and the BCI2000 software platform.²⁷ In the last one, a notch filter was used to suppress the 50 Hz power line interference and the signal was filtered using a bandpass filter between 0.5 Hz and 40 Hz.

As Figure 1 shows, the cap g.GAMMA® was used for the positioning of the passive electrodes (g.LADYbird®) on the scalp according to the extended version of the international 10-20 system. Taking into account the cortical areas of interest for the study, positions C3, C4, T7, T8, Pz, F3, F4, and Cz were selected. The ground and reference electrodes were placed on the right and left mastoids, respectively.

Experimental protocol. Each subject was asked to sit in a comfortable and relaxed position. During the experiment, subjects were instructed to avoid eye blinking and/or muscle movement as much as possible. EEG recordings consisted of three series with rest intervals between 1 and 2 min. Each series included three different tasks which involved the MI of the right hand, the left hand or both hands in response to an auditory cue.

Every task was repeated 10 times randomly during each series, separated by a 5 to 6 s random inter-trial interval. During the inter-trial intervals, subjects were asked to relax. At the end, 30 EEG recordings for each task were obtained, meanwhile the signals were visually examined by the operator.

EEG signal processing. The EEG recordings between 8 and 30 Hz were processed. This frequency range was divided in two frequency bands: *mu* rhythm and *beta* rhythm. The topographic maps of r^2 were computed using the “Offline Analysis” tool available in BCI2000 platform.²⁷ The most discriminative frequency of ERD (f_{ERD}) was determined as the one for which the spatial distribution of ERD in the cortical region related to the MI of the paretic upper limb (C3 or C4) was best and with the highest value of r^2 .

Stage 2: Therapy

Materials. The BCI-FES System was developed for an earlier study.¹⁰ It is a robust, fast-positioning system, which detects brain activity related to MI, and produces movement by FES. It consists of three blocks: the first is the BCI, made up of electrodes, amplifiers and EMOTIV Eloc+® software (EMOTIV Systems Inc., San Francisco, USA). The EEG was recorded with 128 Hz sampling rate and 14 bits resolution, filtered with a bandpass filter between 0.2 Hz and 45 Hz, and digital notch filters at 50 Hz and 60 Hz. The second is a microprocessor-based module that interconnects the other two blocks, and the third block is the FES stimulator (Flexicar, Buenos Aires, Argentina) which generates electrical stimulation pulses when the BCI sends the command signal (Figure 2). EEG signal was processed using Cognitiv™ Suite provided by EMOTIV Eloc+®,²⁸ which operation relies on ERD,²⁹

Table 1. Demographic and functional information of the eight stroke patients, evaluated by the modified upper limb Fugl–Meyer Assessment (mFMA).

Patient	Age	Gender	Evolution time since ictus (months)	Affected limb	Lesion location	mFMA
1	69	M	36	Left	Subcortical	06
2	76	M	12	Left	Cortical/subcortical	21
3	62	M	33	Right	Subcortical	19
4	65	M	60	Left	Subcortical	25
5	78	M	14	Left	Cortical/subcortical	03
6	18	F	12	Left	Subcortical	20
7	55	M	77	Left	Subcortical	23
8	67	F	50	Left	Cortical/subcortical	08

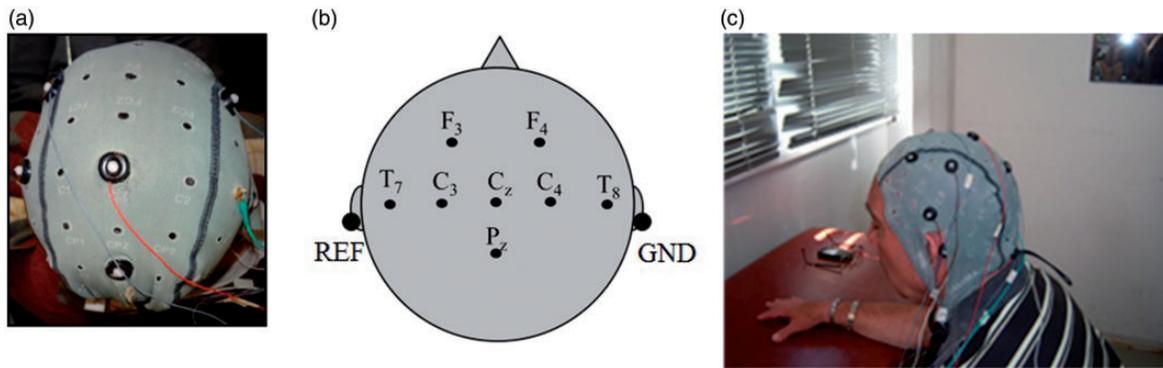


Figure 1. (a) Position of electrodes with gGAMMAcap[®], (b) EEG derivations, and (c) picture of a patient during motor imagination trials.

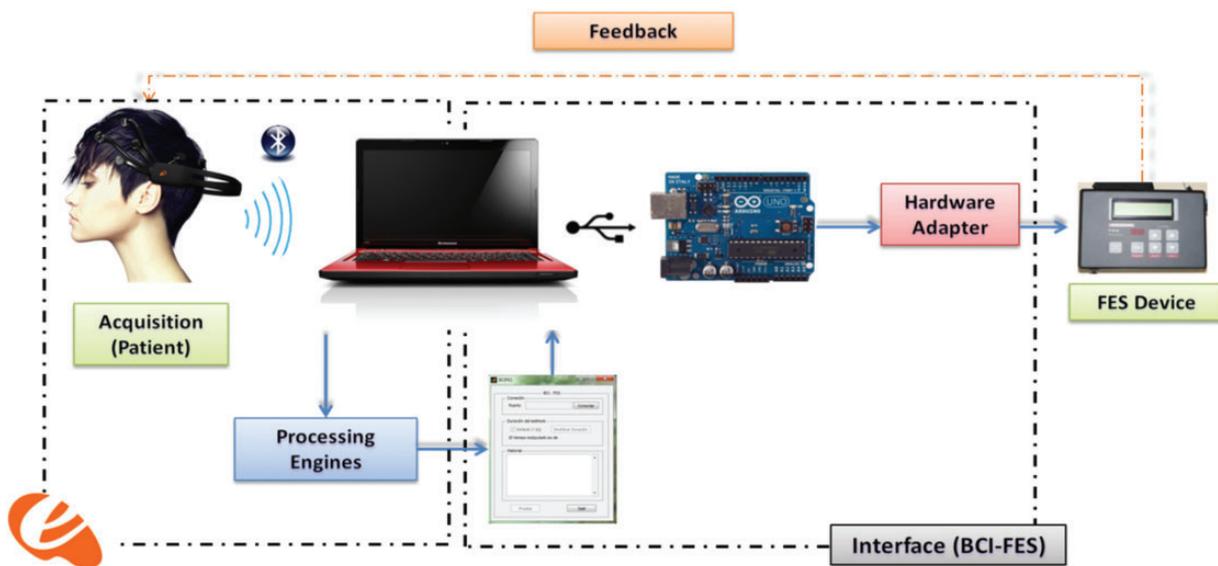


Figure 2. Components of the *Emotiv_BCI-FES Systems* employed in the therapy: the headset for EEG signal acquisition; the processing engines where the BCI and interface software run; the microprocessor-based module with the hardware adapter, and the FES device. The movement assisted by FES gives the patient proprioceptive and visual feedback.

detected on the recorded EEG signals within the range of frequencies between 0.2 and 43 Hz. The *Emotiv_BCI-FES System* presented an average accuracy of 92.7% and an average true positive rate (TPR) of 85.4% when it was evaluated in a stroke patient during two sessions of use in which the BCI was disabled during the resting trials (to avoid false FES activation to patient).

The stimulator generates biphasic rectangular pulses of 0.2 ms duration, a frequency of 25 pps and a maximal current intensity of 40 mA. These parameters were set for each patient prior to use and allowed them to obtain full joint movement.

BCI-FES intervention. The intervention consisted of four weekly sessions of 60 min duration (including the setup

time), for 5 consecutive weeks (20 sessions in total). In a neuro-rehabilitation context, it is very important to respect the necessity and daily state of patients. For this reason, the amount of MI trials and resting periods and its duration varied in each session and depended on the patient's capability, but ranged between 20 and 30 MI trials. MI and rest trials were executed consecutively. During the sessions, the therapist gave the patient the same MI instruction (functional cue) as in the first stage "imagine extending your paretic hand to grasp the glass in front of you". The MI of the affected hand should produce an ERD in cortical areas and consequently activates the FES device.

The threshold to initiate FES was determined for each patient during a previous training period according to the instructions in the User's Manual of

EMOTIV Epcoc.²⁸ The training process involved recording of EEG signals and consisted of two steps. Each step was done in 8 s trials and repeated 5 times, in order to construct a personalized pattern for the MI of the most affected hand. The first step was the training of a neutral state. During it, patients relaxed and remained still. The second step was the training of a cognitive state while patients performed the MI task. To test patient's training, the therapist used a virtual cube supplied by Emotiv. The therapist classified a trial as correct if the patient followed the instruction and the cube did not move during the neutral state and moved when the patient performed the MI task.

The hold time and trigger delay time of the EMOTIV System were set to null in order to command the FES device when the threshold was reached. If patients, also or instead of imaging, intended to move their limbs, the therapist asked them to relax and to be quiet in order to avoid muscle artefacts. Besides, the EEG signal was examined by visual observation by the therapist. When the patient activated the FES device, electrical stimulation was delivered during 5 s. To avoid false positives, the BCI was disabled during the resting trials and periods.

Evaluation. The patients were evaluated 30 days and one day before starting the intervention in order to confirm that they were in the chronic stage of the ictus. To ensure stability in the evolution of the stroke, they were required to present a variation of the mFMA score equal to or less than two points between both dates; otherwise, they were excluded from the study. Patients were also evaluated one day after the therapy finished.

- A. Primary outcome measure: The mFMA used to assess upper limb motor function was based on the FMA scale (total 66 points). The coordination and speed (6 points) scores were excluded since patients were not able to execute this part of the test. The reflex scores (6 points) were also excluded because reflexes are not relevant for this rehabilitation application. The maximum score in the mFMA scale was 54 points. A higher score indicates improvement in the evaluated function.
- B. Secondary outcome measures: The mAsh scale was used to evaluate spasticity in the following muscle groups: finger, wrist, and elbow flexors and shoulder abductors (5 points for each joint, maximum score: 20). A lower score indicates improvement. The Amount of Use (AU) and Quality of Movement (QM) were evaluated using the modified Motor Activity Log (mMAL).^{30,31} The MAL is a measure of self-perceived upper extremity participation. It uses a semi-structured interview to assess how much and how well patients use their affected arm for activities of daily living. The final score is the average of the

score (between 0 and 5) obtained in each of the questions answered by the patient (maximum score: 5). A higher score indicates improvement.

Changes in quality of life were assessed using a Visual Analog Scale (VAS) subscale of the EQoL-5D (Euro Quality of Life) scale.^{32,33} The scores are between 0 and 10 (maximum score: 10). A higher score implies perception of improvement in the patient's quality of life.

Finally, the active Range of Movement (RoM) of shoulder abduction and elbow, wrist, and fingers flexion and extension was assessed.

Statistical processing

A Wilcoxon signed rank test was performed to compare the scores obtained when applying the primary and secondary assessment measures before and after treatment, because data were not normally distributed or were ordinal. The statistical processing was run in SPSS® v.23. A significance level of $p < 0.05$ was used.

Results

Stage 1: Screening

Figure 3 shows the topographic maps of the eight patients for the most discriminative f_{ERD} . Each map is a representation of the cerebral cortex seen from above where the recording channels (in black spots) are identified and the value of the coefficient of determination r^2 in each cortical area is represented (in color coding). In all the maps, desynchronization in cortical areas associated to upper limb movement are evidenced through a high value of r^2 . It is also observed that f_{ERD} is presented in both sensorimotor rhythms: *mu* and *beta*.

Stage 2: Therapy

Figure 4 shows a picture of the therapist next to a patient during the intervention. The *Emotiv_BCI-FES System* and the glass in front of the patient can also be seen.

The mFMA scores for one day and 30 days prior to intervention were identical for all patients (15.62 ± 8.55). The difference in the mFMA score for each patient was null, which indicates that the upper limb motor function of each patient remained stable during that month, evidencing the chronic stage of stroke (Figure 5).

Significant post-treatment improvement was detected in mFMA ($z = -2.546$; $p = 0.011$) and in active RoM for elbow ($z = -2.060$; $p = 0.039$) and wrist ($z = -2.041$; $p = 0.041$) flexions (Figure 5). In addition, significant improvements were observed in QM mMAL

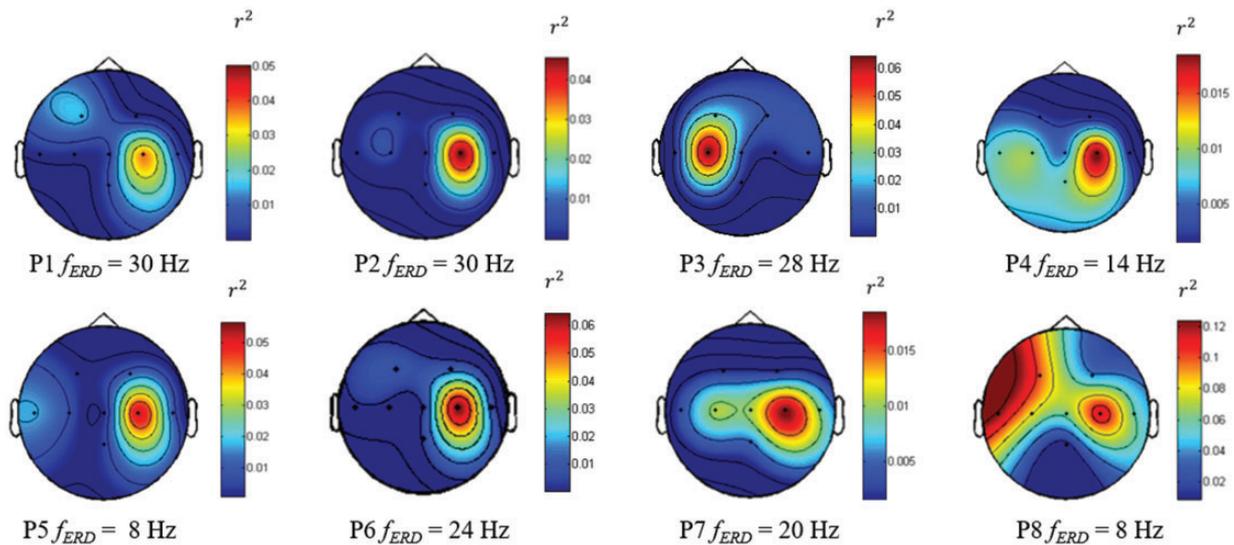


Figure 3. Topographic maps during imagery motor tasks of the paretic upper limbs for the selected f_{ERD} for each of the eight patients. The color scale of r^2 for each map is shown at the right of the map.

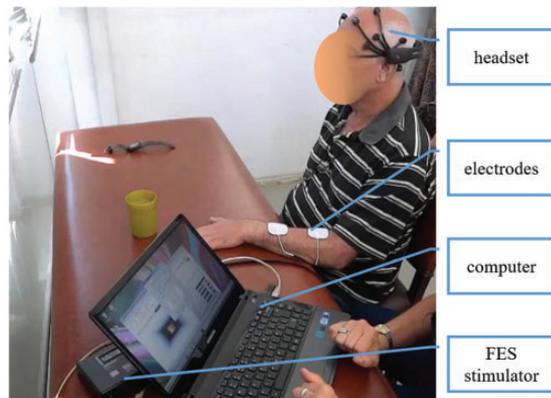


Figure 4. A patient using the *Emotiv_BCI-FES System*. The different elements of the system are visible in the picture: the headset for EEG signal acquisition; the computer where the software for the BCI and the interface run; the FES device and the electrical stimulation electrodes placed on the extensors of the wrist.

($z = -2.524$; $p = 0.012$), AU mMAL ($z = -2.546$; $p = 0.011$), and VAS scores ($z = -2.546$; $p = 0.011$) (Figure 6). Regarding the spasticity, significant reduction was observed in the mAsh score for shoulder abductors ($z = -2.251$; $p = 0.024$) and for wrist ($z = -2.236$; $p = 0.025$), elbow ($z = -2.460$; $p = 0.014$), and finger ($z = -2.271$; $p = 0.023$) flexors (Figure 7). As it can be observed in Figures 5 to 7, all of outcome measures reflected that no patient worsened their condition.

No significant changes were observed in RoM for shoulder abduction and finger flexion and extension.

Discussion

The main findings of this study are that all of the involved stroke patients were able to desynchronize their ipsilesional sensorimotor rhythms during the MI of their affected hand and that significant post-treatment improvement was detected in mFMA and in the majority of the secondary outcome scores, when they were treated with 20 sessions of therapy based on FES triggered by BCI.

Characteristics of the ERD in stroke patients

ERD was observed in relation to the MI of the paretic arm. The cortical topographic maps were different across patients with respect the value of r^2 , the spatial localization, and the frequency bands for the ERD.

The location of the ERD matched generally the sensorimotor cortex for the upper limb^{13,14}, however, the values of r^2 differed across patients. Patients 2 and 6 presented ERD well located in the contralateral sensorimotor cortex (close to the C4 electrode). They showed also the highest r^2 together with high mFMA scores and the least chronicity (12 months), which might be related. On the other hand, patients 4 and 7 with high mFMA scores showed the lowest r^2 ; these patients had the longest chronicity (60 and 77 months respectively), suggesting that the time after stroke might influence the ability to desynchronize. Very severe patients (1, 5 and 8), with the lowest mFMA, obtained r^2 values close to 0.05, which are similar to those reported by Antelis et al.¹⁸ Thus, there does not seem to be an evident relationship between the

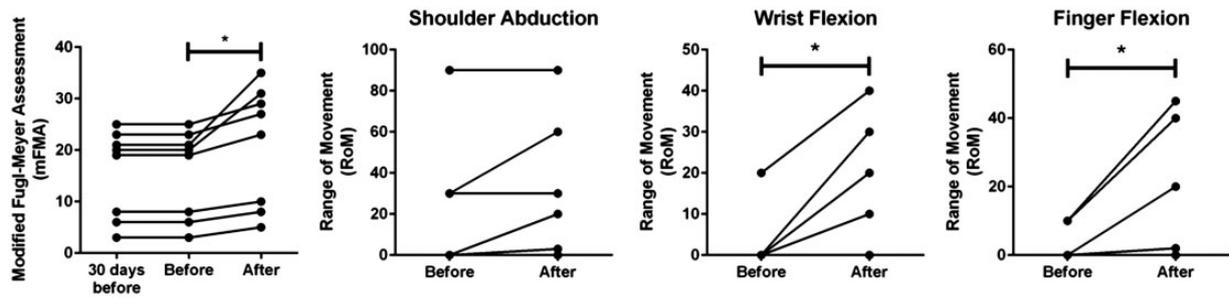


Figure 5. mFMA and active RoM measures for each patient ($n = 8$). The asterisk indicates a statistically significant change ($p < 0.05$).



Figure 6. Scores obtained in QM mMAL, AU mMAL and VAS measures for each patient ($n = 8$). The asterisk indicates a statistically significant change ($p < 0.05$).

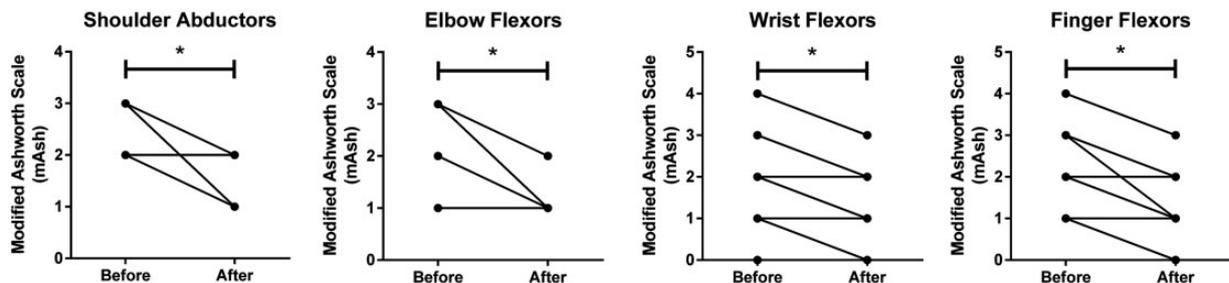


Figure 7. Scores obtained in mAsh measures for each patient ($n = 8$). The asterisk indicates a statistically significant change ($p < 0.05$).

functional sequelae measured by mFMA and the obtained r^2 for the ipsilesional hemisphere during MI. Kaiser et al.³⁴ found no significant relationship between the degree of impairment and ERD during motor execution of the most affected hand. But, they also reported that patients with lower spasticity showed weaker ERD in the ipsilesional hemisphere during MI of the affected hand.

Six of the eight patients showed desynchronization of the *beta* rhythm, while the two remaining participants evidenced ERD in *mu* rhythm. These results coincide with those reported by McFarland et al.³⁵ for healthy people, where they demonstrated that there is

a desynchronization of the rhythms *mu* or *beta*, both during movement and MI.

The spatial localization of ERD was slightly different in all cases, but mostly focused on the contralateral sensorimotor cortex, even though it was lesioned. In the patients included in the present study, ipsilateral ERD was not found during MI of the most affected hand, like other authors did.^{34,18} Kaiser et al.³⁴ reported that during MI, more impaired patients showed higher ERD in the contralesional (ipsilateral) hemisphere as compared with less impaired patients. Antelis et al.¹⁸ reported similar observations during the attempt and execution of movement. They found significant cortical

activation on the uninjured motor cortex when moving or attempting to move either of the two arms. They attributed this ipsilateral activation to interconnecting circuits between both hemispheres. Stepień et al.³⁶ reported that stroke people changed the amplitude dynamics of oscillations in both hemispheres and that their ipsilateral ERD was stronger than the contralateral ERD when moving the paretic hand. Activation of other areas was, however, observed for instance in patients 1 and 8, who presented a high r^2 with a well-located upper limb ERD but also some values of r^2 in frontal and temporal lobes due to eye blink artifacts as confirmed by further processing of the EEG signals.

The ERD pattern, which consists of f_{ERD} and its cortical spatial localization, changes between sessions, due to several issues, among them motor learning and plasticity.³⁷ Many BCI Systems used it as a characteristic for classification. However, in this study the f_{ERD} was only used in one session of Stage I to identify the patients' ability to desynchronize. As reported by Scherer et al.,³⁸ there is no evidence of a common ERD pattern in patients with stroke, which suggests the need for calibration of BCI systems through a study of individual ERD. Then, in future steps, it would be interesting to employ a BCI System which considers these issues for MI detection.

Improvements due to the BCI-FES therapy

In the second stage of this study, the efficacy of the *Emotiv_BCI-FES System* to induce motor functional recovery in chronic severe stroke patients was investigated. Command signals were generated from the perilesional area which was structurally intact but functionally altered. Significant improvement was obtained in the main outcome measures, which reflected clinical and functional recovery after the intervention.

Reports about BCI-based rehabilitation of individuals with stroke are emerging and with promising results.^{22,23,39,40} Systems based on a BCI-MI paradigm to detect ERD from ipsilesional²² or contralesional²³ hemisphere, or to detect the peak negative of movement-related cortical potentials,³⁹ or to control other devices⁴⁰ have been reported; but in all cases, the mechanisms by which the use of BCI facilitates cortical reorganization in stroke patients are still being discussed. Additionally, the alone contribution of FES to cortical reorganization is not clear either.⁴¹

The primary outcome measure (mFMA) showed significant improvement after treatment. The mean mFMA difference was 5.37 points reflecting clinically important changes for functional recovery for stroke patients.⁴² This improvement was larger than that shown earlier for an intervention based on a BCI-MI-activated orthoses plus physiotherapy, where a mean

difference pre and post treatment of 3.41 points was reported.²² The reason for this improvement is not clear; it could perhaps be related to the activation of the motor cortex during BCI-MI, the FES, the type of feedback or a combination of them.

The almost simultaneous neuronal activation provoked by the ERD and by the sensory inputs from the kinetic, proprioceptive, and visual feedback generated by FES, could have facilitated the functional recovery. This happened perhaps by integration of the proprioceptive and the visuo-motor inputs associated with the realization and observation of the movement in the severely impaired paretic hand.^{43,44} This sensory feedback might reactivate the cortical representation of the movement in the sensorimotor cortex, which would be reinforced for the next MI. The feedback might facilitate hereby motor learning.⁴⁵ Assessment of the time elapsed between the neuronal activation and the feedback generated by FES would be needed to clarify how these were paired.

Regarding the BCI-FES therapy, Chung et al.⁴⁶ found that BCI-FES training may be more effective in stimulating brain activation than only FES training for dorsiflexion in post-stroke patients. Corbet et al.⁴⁷ reported that the connectivity in the lesioned hemisphere significantly increased in patients who used BCI-FES therapy compared to those who used only FES. Then, in the present study, the FES-assisted wrist extension commanded by BCI-MI might have contributed significantly to the increased mFMA score.

Significant reduction was obtained in mASH scores in all tested muscles. The effect of FES on spasticity is not conclusive. Some studies reported a decrease in spasticity, while others did not find a reduction in spasticity of the stimulated muscle (for a review see Quandt and Hummel⁴¹). Then, it is unclear what the cause of the reduction of spasticity in all tested muscles was. On the other hand, there is evidence that patients learn to modulate their sensorimotor rhythms³⁷ and that the increased activation could probably reflect reorganization of the cortical motor system.⁴⁸ The reduction of the spasticity of the flexors (Figure 7) might have influenced the significant improvement in the active RoM of wrist flexion (Figure 5). Besides, no significant improvement was found in the RoM for wrist extension, which could be likely attributed to a lack of muscle force in the wrist extensors. This is needed to counteract the flexor spasticity and could be built with help of, for example, FES training.⁴⁹ The 20 sessions provided in this study were probably not enough to result on increased force.

The difference in the means of QM mMAL and AU mMAL scores was higher than one point, which reflects an improvement in self-perceived upper extremity participation.⁵⁰ Regarding VAS scores, three points of

difference were detected before-after the intervention, which is bigger than Morone et al. reported in a BCI study for hospitalized post-stroke patients.³³ These measures show that patients perceive an improvement in their quality of life and motivation, which is probably associated with the changes measured with the mFMA scores.

Regarding the dynamic during the therapy session, it is very important that patients are focused during the therapy. It is known that stroke patients can present a deficit of concentration;⁵¹ therefore, the functional cue given by the therapist to the patient is very important to improve the patients' participation during the BCI-FES session. This aspect also contributes to the efficacy of the intervention, as suggested by Jeunet et al.⁵²

The patients were in a chronic and stable stage and during the period of this intervention, they did not change their daily routine other than incorporating the BCI-FES therapy (assessed by means of an interview performed by the therapist). Therefore, it is likely that the observed improvements might be attributed to the BCI-FES intervention. Besides, in the chronic stage, there are modifications in the neural networks, with an interhemispheric imbalance, in which for instance the unaffected hemisphere inhibits perilesional areas.⁵³ This imbalance, measured as the index of laterality,⁵⁴ could have conditioned the intended cortical reorganization with the present intervention. A study in sub-acute stroke patients could help elucidate this issue.

Methodological considerations

There were some differences between the EEG acquisition systems used during the screening and therapy stages. In the first stage, a portable research grade amplifiers and electrodes with wet gel applications were used. In the therapy stage, a more economically accessible device, the EMOTIV Epoc+[®] System, to ease the daily use in a physical therapy environment was used. The later system has electrodes with saline-soaked sponges on the contacts. Regarding the quality of these EEG signals, Ekanayake reported that the EMOTIV system captures actual EEG but that the quality of these signals is not as good as those used for diagnosis in medical equipment.⁵⁵ However, this system was employed earlier to successfully record EEG.^{56,57} Then, and taking into account that the aim of the second stage of this study was therapeutic (not diagnosis), the quality of the EEG recordings from the EMOTIV system was regarded appropriate.

As it was described in the material and methods section, a preliminary performance study of the *Emotiv_BCI-FES System*, evaluated in two sessions by a stroke patient, showed an average accuracy of

92.7% and an average TPR of 85.4%. This average accuracy was larger than 75% (the chance level for this kind of protocol of BCI). These results were similar to those reported by other authors, such as Darvishi et al.⁵⁸ who reported an average accuracy of 83% of a BCI-MI System which provided intrinsic visual and proprioceptive feedback by an orthosis in eight healthy subjects. Muñoz et al.⁵⁹ reported a BCI system based on the Emotiv EPOC and the open source software OpenViBe for the MI-based experiment implementation. This system was evaluated in eight healthy subjects showing an average accuracy of the best classifier of 96.7%. The average TPR of the *Emotiv_BCI-FES System* used for this intervention is within the ranges reported by other authors. Pichiorri et al.⁶⁰ reported, also in healthy subjects, an average TPR ranging from 53% to 96% for a BCI based on ERD. Using the movement related cortical potentials to detect the MI, Niazi et al.⁶¹ reported a TPR of $64.5 \pm 5.33\%$ for motor imagination in healthy subjects and $55.01 \pm 12.01\%$ for motor attempt in patients with stroke, whereas Aliakbaryhosseinabadi et al.⁶² reported a TPR of $75.3 \pm 5.5\%$ in healthy volunteers. Then, these preliminary results of the *Emotiv_BCI-FES System* performance demonstrate that BCI control was actually achieved by the user.

Even though the electrodes of the EMOTIV Epoc+[®] headset are not placed on the primary motor cortex, this BCI allowed recording EEG signals related to the motor cue because it can identify the attempt of the user to perform different physical actions.²⁸ Further analysis of EEG signals recorded during the therapy stage would be needed to understand how this BCI-FES therapy works. On the other hand, for motor recovery purposes, it is important to register EEG from the sensorimotor cortex for the upper limb, although the area of the motor cortex is often displaced in stroke patients.⁶³ Therefore, in future studies, other EEG acquisition systems to register and process the EEG to generate the command signal from the upper limb sensorimotor cortex during MI should be used.

The small sample size and the lack of a control condition are regarded as limitations of this study that prevent drawing any definitive conclusions about the efficacy of the proposed intervention, thus limiting the current study to a preliminary study. Although other studies have shown functional improvements in chronic stroke people after interventions such as robotic therapy,⁶⁴ constraint-induced movement therapy,⁶⁵ BCI-driven orthosis^{22,23} or standard physical therapy,⁶⁶ the patients included in the present study did not take part in any other rehabilitation intervention during the BCI-FES therapy. Then, this experimental design, despite lacking a control group, resulted in evidence that represent an important step towards developing and

translating into clinics BCI–FES-driven rehabilitation protocols for chronic stroke individuals. A randomized controlled trial to study the efficacy of this type of treatment would be the next step to take.

Conclusions

In this study, it was possible to verify the ability to desynchronize the sensorimotor rhythms in the damaged motor cortex of the eight studied patients, although they had no previous experience modulating them. Besides, it was shown that a therapeutic intervention based on *Emotiv_BCI–FES System* improved the motor function of the upper limb of severe, chronic stroke patients. The data suggested that this BCI–FES therapy is promising for the rehabilitation of post-stroke individuals.

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: This work was supported by the Fundacion Rosarina de Neuro-rehabilitación (FRN) and by the Universidad Nacional de Entre Rios (UNER) [PID 6163]; Argentina. During the execution of this project, CL and CB were employed at FRN; CT and LC were employed at UNER and ES was employed at Aalborg University.

Guarantor

CBT

Contributorship

CHB and CBT researched literature and conceived the study. CHB was involved in protocol development, gaining ethical approval, patient recruitment. LCC performed the screening stage and CL the second stage. All authors were involved in data analysis. CBT wrote the first draft of the manuscript. EGS collaborated with the discussion of this article and with the overall manuscript. All authors reviewed and edited the manuscript and approved the final version of the manuscript.

ORCID iD

Carolina B Tabernig  <http://orcid.org/0000-0001-5122-5080>

References

- Langhorne P, Coupar F and Pollock A. Motor recovery after stroke: a systematic review. *Lancet Neurol* 2009; 8: 741–54.
- Young J and Forster A. Review of stroke rehabilitation. *BMJ* 2007; 334: 86–90.
- O'Dell M, Chi-Chang D and Harrison V. Stroke rehabilitation: strategies to enhance motor recovery. *Annu Rev Med* 2009; 60: 55–68.
- Malouin F and Richards C. Mental practice for relearning locomotor skills. *J Acute Care Phys Ther* 2010; 90: 240–251.
- Levin M, Sveistrup H and Subramanian S. Feedback and virtual environments for motor learning and rehabilitation. *Schedae* 2010; 1: 19–36.
- Moritz C, Perlmutter S and Fetz E. Direct control of paralysed muscles by cortical Neuros. *Nature* 2008; 456: 639–642.
- Legenstein R, Chase S, Schwartz A, et al. A reward-modulated Hebbian learning rule can explain experimentally observed network reorganization in a brain control task. *J Neuroscience* 2010; 30: 8400–8410.
- Schiaffino L and Tabernig CB. Position control with PID regulation for a FES system: preliminary results. *J Phys Conf Ser* 2016; 705: 012058.
- Arguissain F, Giménez D and Tabernig C. Diseño y Desarrollo de una Interfaz ICC-FES como Herramienta de Rehabilitación Neurológica. *Revista argentina de Bioingeniería* 2010; 16: 31–41.
- Jure F, Carrere L, Gentiletti G, et al. BCI-FES system for neuro-rehabilitation of stroke patients. *J Phys Conf Ser* 2016; 705: 012058.
- Birbaumer N. Breaking the silence: brain-computer interfaces (BCI) for communication and motor control. *Psychophysiology* 2006; 6: 517–532.
- Wang W, Collinger J, Perez M, et al. Neural interface technology for rehabilitation: exploiting and promoting neuroplasticity. In: Dicciano C and Cooper R (eds) *Phys Med Rehabil Clin N Am* 2010; 21: 157–178.
- Pfurtscheller G and Lopes da Silva FH. *Electroencephalography: basic principles, clinical applications, and related fields*. Philadelphia, PA: Lippincott Williams & Wilkins, 2005, pp.1003–1016.
- Pfurtscheller G. *BCIs that use sensorimotor rhythms. Brain-computer interfaces: principles and practice*. New York: Oxford University Press, 2013, pp.227–241.
- Aldea R and Eva OD. Detecting sensorimotor rhythms from the EEG signals using the independent component analysis and the coefficient of determination. In: *IEEE Int Symp on Signals, Circuits and Systems (ISSCS) Proc*, Iasi, Romania, 11–12 July 2013, pp.1–4.
- Carrere C and Tabernig C. Detection of foot motor imagery using the coefficient of determination for neurorehabilitation based on BCI technology. *IFMBE Proc* 2015; 49: 944–947.
- Tabernig C, Carrere L, Lopez C, et al. EEG Event-Related Desynchronization of patients with stroke during motor imagery of hand movement. *J Phys Conf Ser* 2016; 705: 012058.
- Antelis JM, Montesano L, Ramos-Murguialday A, et al. Decoding of upper limb movement intention from EEG measurements of the contralesional motor cortex in chronic stroke patients. *IEEE Trans Biom Eng* 2017; 64: 99–111.
- Birbaumer N and Cohen L. Brain-computer interfaces: communication and restoration of movement in paralysis. *J Physiol* 2007; 579: 621–636.

20. Buch E, Schanечи A, Fourkas A, et al. Parietofrontal integrity determines neural modulation associated with grasping imagery after stroke. *Brain* 2012; 135: 596–614.
21. Ramos-Murguialday A, Schürholz M, et al. Proprioceptive feedback and brain computer interface (BCI) based neuroprostheses. *PLoS ONE* 2012; 7: e47048.
22. Ramos-Murguialday A, Broetz D, et al. Brain-machine-interface in chronic stroke rehabilitation: a controlled study. *Ann Neurol* 2013; 74: 100–108.
23. Bundy DT, Souders L, Baranyai K, et al. Contralesional brain–computer interface control of a powered exoskeleton for motor recovery in chronic stroke survivors. *Stroke* 2017; 48: 1908–1915.
24. Pfurtscheller G, Müller G, Pfurtscheller J, et al. Thought–control of functional electrical stimulation to restore hand grasp in a patient with tetraplegia. *Neurosci Lett* 2003; 351: 33–36.
25. Müller-Putz G, Scherer R, Pfurtscheller G, et al. EEG-based neuroprosthesis control: a step towards clinical practice. *Neurosci Lett* 2005; 382: 169–174.
26. Reynolds C, Osuagwu B and Vuckovic A. Influence of motor imagination on cortical activation during functional electrical stimulation. *Clin Neurophysiol* 2015; 126: 1360–1369.
27. Schalk G and Mellinger J. *General-purpose software for brain–computer interface research, data acquisition, stimulus presentation, and brain monitoring*. London: Springer-Verlag London Limited, 2010, pp.9–35.
28. EMOTIV. EMOTIV user manual, https://emotiv.zen-desk.com/hc/en-US/article_attachments/200343895/EPOCUserManual2014.pdf (2014, accessed 16 February 2018).
29. Lang, M. Investigating the EMOTIV EPOC for cognitive control in limited training time. Honors Report. Department of Computer Science, University of Canterbury, NZ, 2012.
30. Taub E, McCulloch K, Uswatte G, et al. *Motor activity log manual*, https://www.uab.edu/citherapy/images/pdf_files/CIT_Training_MAL_manual.pdf (2011, accessed January 2015).
31. Uswatte G, Taub E, Morris D, et al. Reliability and validity of the upper extremity motor activity log. *Stroke* 2005; 36: 2493–2496.
32. Herdmana M, Badiab X, Berra C, et al. El EuroQol-5D: una alternativa sencilla para la medición de la calidad de vida relacionada con la salud en atención primaria. *Aten Primaria* 2001; 28: 425–429.
33. Morone M, Pisotta I, Pichiorri F, et al. Proof of principle of a brain-computer interface approach to support post-stroke arm rehabilitation in hospitalized patients: design, acceptability and usability. *Arch Phys Med Rehabil* 2015; 96: S71–S78.
34. Kaiser V, Daly I, Pichiorri F, et al. Relationship between electrical brain responses to motor imagery and motor impairment in stroke. *Stroke* 2012; 43: 2735–2740.
35. McFarland D, Miner L, Vaughan T, et al. Mu and beta rhythm topographies during motor imagery and actual movements. *Brain Topogr* 2000; 12: 177–186.
36. Stepień M, Conradi J, Waterstraat G, et al. Event-related desynchronization of sensorimotor EEG rhythms in hemiparetic patients with acute stroke. *Neurosci Lett* 2011; 488: 17–21.
37. McFarland D, Sarnacki W, Vaughan T, et al. Brain-computer interface (BCI) operation: signal and noise during early training sessions. *Clin Neurophysiol* 2005; 116: 56–62.
38. Scherer R, Mohapp A, Grieshofer P, et al. Sensorimotor EEG patterns during motor imagery in hemiparetic stroke patients. *Int J Bioelectromagn* 2007; 9: 155–162.
39. Mrachacz-Kersting N, Jiang N, Stevenson A, et al. Efficient neuroplasticity induction in chronic stroke patients by an associative brain-computer interface. *J Neurophysiol* 2016; 115: 1410–1421.
40. Monge-Pereira E, Ibañez-Pereda J, et al. 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.
41. Quandt F and Hummel F. The influence of functional electrical stimulation on hand motor recovery in stroke patients: a review. *Exp Transl Stroke Med* 2014; 21: 6–9.
42. Page S, Fulk G and Boyne P. Clinically important differences for the upper-extremity Fugl–Meyer Scale in people with minimal to moderate impairment due to chronic stroke. *Physical therapy* 2012; 92: 791–798.
43. Buch E, Shanchechi A, Fourkas A, et al. Parietofrontal integrity determines neural modulation associated with grasp imagery after stroke. *Brain* 2012; 135: 596–614.
44. Melvyn A and Goodale. Visuomotor control: where does vision end and action begin?. *Curr Biol* 1998; 8: 489–491.
45. Sigrist R, Rauter G, Riener R, et al. Augmented visual, auditory, haptic, and multimodal feedback in motor learning: a review. *Psychonomic Bull Rev* 2013; 20: 21–53.
46. Chung E, Kim J, et al. Effects of brain-computer interface-based functional electrical stimulation on brain activation in stroke patients: a pilot randomized controlled trial. *J Phys Ther Sci* 2015; 27: 559–562.
47. Corbet T, Leeb R, et al. BCI-NMES therapy enhances effective connectivity in the damaged hemisphere in stroke patients. In: *Proceedings of the 6th international brain–computer interface meeting*, CA, USA, 30 May–3 June 2016.
48. Koritnik B, Azam S, et al. Functional changes of the cortical motor system in hereditary spastic paraparesis. *Acta Neurol Scand* 2009; 120: 182–190.
49. Elbasiouny S, Moroz D, Bakr M, et al. Management of spasticity after spinal cord injury: current techniques and future directions. *Neurorehabil Neural Repair* 2010; 24: 23–33.
50. Lang C, Edwards D, Birkenmeier R, et al. Estimating minimal clinically important differences of upper-extremity measures early after stroke. *Archive Phys Med Rehabil* 2008; 89: 1693–1700.

51. Cicerone K. Attention deficits and dual task demands after mild traumatic brain injury. *Brain Injury* 1996; 10: 79–90.
52. Jeunet C, N’Kaoua B and Lotte F. Advances in user-training for mental-imagery-based BCI control: Psychological and cognitive factors and their neural correlates. *Progr Brain Res* 2016; 228: 3–35.
53. Koralek AC, Jin X, Long JD, et al. Corticostriatal plasticity is necessary for learning intentional neuroprosthetic skills. *Nature* 2012; 483: 331–335.
54. Stinear CM, Barber PA, Coxon JP, et al. Priming the motor system enhances the effects of upperlimb therapy in chronic stroke. *Brain* 2008; 131: 1381–1390.
55. Ekanayake H. P300 and Emotiv EPOC: does Emotiv EPOC capture real EEG?, <http://neurofeedback.visaduma.info/P300nEmotiv.pdf> (2010, accessed 16 February 2018).
56. Esfahani ET and Sundararajan V. Classification of primitive shapes using brain–computer interfaces. *Comput-Aided Des* 2012; 44: 1011–1019.
57. Badcock NA, Mousikou P, Mahajan Y, et al. Validation of the Emotiv EPOC® EEG gaming system for measuring research quality auditory ERPs. *Peer J* 2013; 1: e38.
58. Darvishi S, Ridding MC, Abbott D, et al. Does feedback modality affect performance of brain computer interfaces? In: *NER, 7th International IEEE/EMBS conference on*, Montpellier, France, 22–24 April 2015, pp.232–235.
59. Muñoz JE, Ríos L and Henao O. Low cost implementation of a motor imagery experiment with BCI system and its use in neurorehabilitation. In: *Conference proceedings of the IEEE Engineering Medicine and Biology Society*, Chicago, Illinois, USA, 26–30 August 2014, pp.1230–1233.
60. Pichiorri F, Fallani FDV, Cincotti F, et al. Sensorimotor rhythm-based brain–computer interface training: the impact on motor cortical responsiveness. *J Neural Eng* 2011; 8: 025020.
61. Niazi IK, Jiang N, Tiberghien O, et al. Detection of movement intention from single-trial movement-related cortical potentials. *J Neural Eng* 2011; 8: 066009.
62. Aliakbarhosseinabadi S, Jiang N, Vuckovic A, et al. Detection of movement intention from single-trial movement-related cortical potentials using random and non-random paradigms. *Brain-Computer Interfaces* 2015; 2: 29–39.
63. Harrison T, Silasi G, Boyd J, et al. Displacement of sensory maps and disorganization of motor cortex after targeted stroke in mice. *Stroke* 2013; 44: 2300–2306.
64. Fasoli SE, Krebs HI, Stein J, et al. Effects of robotic therapy on motor impairment and recovery in chronic stroke. *Arch Phys Med Rehabil* 2003; 84: 477–482.
65. Page SJ, Sisto S, Levine P, et al. Efficacy of modified constraint-induced movement therapy in chronic stroke: a single-blinded randomized controlled trial. *Arch Phys Med Rehabil* 2004; 85: 14–18.
66. Winstein CJ, Stein J, Arena R, et al. Guidelines for adult stroke rehabilitation and recovery: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke* 2016; 47: e98–e169.