Feasibility of a New Application of Noninvasive Brain Computer Interface (BCI): A Case Study of Training for Recovery of Volitional Motor Control After Stroke

Janis J. Daly, MSPT, PhD, Roger Cheng, BME, Jean Rogers, PT, Krisanne Litinas, MS, BME, Kenneth Hrovat, MS, BME, and Mark Dohring, PhD

Background/Purpose: A large proportion of individuals with stroke have persistent deficits for which current interventions have not restored normal motor behavior. Noninvasive brain computer interfaces (BCIs) have potential advantages for restoration of function. There are also potential advantages for combining BCI with functional electrical stimulation (FES). We tested the feasibility of combined BCI + FES for motor learning after stroke.

Case Description: The participant was a 43-year-old woman who was 10 months post-stroke. She was unable to produce isolated movement of any of the digits of her involved hand. With effort she exhibited simultaneous mass hyperextension of metacarpal phalangeal joints of all four fingers and thumb with simultaneous flexion of proximal interphalangeal and distal interphalangeal joints of all fingers.

Intervention: Brain signals from the lesioned hemisphere were used to trigger FES for movement practice. The BCI + FES intervention consisted of trials of either attempted finger movement and relax conditions or imagined finger movement and relax conditions. The training was performed three times per week for three weeks (nine sessions total).

Outcome: The participant exhibited highly accurate control of brain signal in the first session for attempted movement (97%), imagined movement (83%), and some difficulties with attempted relaxation (65%). By session 6, control of relaxation (deactivation of brain signal) improved to >80%. After nine sessions (three per week) of BCI + FES intervention, the participant demonstrated recovery of volitional isolated index finger extension.

Discussion: BCI + FES training for motor learning after stroke was feasible. A highly accurate brain signal control was achieved, and this signal could be reliably used to trigger the FES device for isolated index finger extension. With training, volitional control of isolated finger extension was attained in a small number of sessions. The source of motor recovery could be attributable to BCI, FES, combined BCI + FES, or whole arm or hand motor task practice.

Key words: *coordination, motor learning, motor control, functional electrical stimulation, FES, neuromuscular electrical stimulation stroke, NMES*

(*JNPT* 2009;33: 203–211)

INTRODUCTION

After brain injury and persistent motor deficits caused by stroke, methods for motor recovery use either an externally generated electrical or magnetic field sent to the brain (eg, transcranial magnetic stimulation)[1] or treatment targeted at the periphery (ie, upper or lower limb). Treatments targeted at the upper and lower limbs are expected to restore motor control through a change in brain function.[2–4] Although promising, there is a large proportion of individuals with stroke for whom none of these methods has restored functional motor control. Therefore, it is important to investigate new methods that have potential for success in facilitating the recovery of brain function that will result in the recovery of more normal motor control.

Brain computer interface (BCI) technology may prove useful in rehabilitation and motor recovery after neural disease or neural injury. There are a number of different types of BCIs. Some invasive systems use cortical recordings (electrocorticography-based BCIs) and some use recordings of neuronal action potentials or local field potentials from within the brain (intracortical BCIs).[5] In contrast, this article describes an application of noninvasive BCIs that uses electroencephaolographic (EEG) recordings from the surface of the scalp. For the remainder of this article, BCI will refer exclusively to noninvasive, EEG-based BCIs.

Noninvasive BCIs can be used to record and analyze brain signals that can then be used to determine a BCI user's intention. During the past 15 years, noninvasive, EEG-based BCIs have been developed and tested for use in improving communication and device control for those who are severely

Cognitive and Motor Learning Research Program, (J.J.D., R.C., J.R., K.L., K.H., M.D.), Louis Stokes Cleveland Department of Veterans Affairs Medical Center, Ohio; and Professor, Department of Neurology, (J.J.D.), Case Western Reserve University School of Medicine, Cleveland Ohio.

Supported by the Department of Veterans Affairs, Office of Rehabilitation Research and Development (grants B3388R and B508S) and NIH (grant R01 NS-063275).

None of the authors of this manuscript have any competing financial conflicts of interest.

Address correspondence to: Janis J. Daly, E-mail: jjd17@case.edu

Supplemental digital content is available for this article. Direct URL citations appear in the printed text and are provided in the HTML and PDF versions of this article on the journal's Web site (www.jnpt.org).

ISSN: 1557-0576/09/3304-0203
DOI: 10.1097/NPT.0b013e3181c1fc0b

paralyzed.[5] The BCI system conducts the following steps: signal processing to extract and classify a brain signal feature that can be used as control signal; and delivery of online feedback to the user regarding how the brain signal was classified (ie, whether the signal was classified according to the user's intention). For these applications of device control or communication, there was no expectation that there would be any recovery of motor control. However, there are a number of BCI features that suggest potential usefulness during rehabilitation for motor recovery after stroke. The first is the potential to engage the brain's own neural cells, without imposing an externally generated electrical or magnetic field into the brain. The second feature is that BCI can engage central nervous system neural function directly, rather than exclusively focusing at the periphery of the body, on upper or lower limb movements. Finally, the use of the BCI demands intense focus of concentration on brain function and the intended motor task. Focus of attention on the intended motor task is one of the critical motor learning principles required for motor skill acquisition and motor learning.[6]

There is a dearth of information regarding whether BCI could be used for training the recovery of volitional motor control after stroke. Case studies and case series have raised questions regarding whether a usable brain signal was obtainable for this purpose[7] and whether a reasonable accuracy level of brain signal control could be obtained at an initial training session so that BCIs could be used immediately within a motor learning protocol[8] (rather than needing to waste multiple therapy sessions on learning to use the BCI itself, before it can be used in motor recovery training). Therefore, one purpose of this case study was to study the feasibility of BCI, specifically, whether a usable signal could be obtained from the lesioned hemisphere of a participant who had had a stroke and whether a good accuracy level could be obtained immediately so that a BCI could be used to engage the participant's own brain neural signal for the purpose of training motor recovery.

We recognized that it is important to correctly frame a rehabilitation intervention for optimum success.[9] Strong evidence indicates that the most credible existing framework for motor learning and skill acquisition is activity-dependent central nervous system plasticity[10] and the associated motor learning principles that are required to obtain motor skill acquisition or motor relearning after stroke. One of the critical motor learning principles is to practice the movement behavior in a manner that is as close to normal as possible.[11] For example, evidence indicates that when a more normal coordinated movement was demanded and practiced repetitively, there was recovery of that more normal coordinated movement versus no recovery of coordinated movement when the more normal coordinated movement was not demanded and not practiced.[11] Conversely, if abnormal movements are repeated, ingrained movements may become progressively more abnormal.

Unfortunately, many stroke survivors are not able to move in a way that approximates normal movement. In such cases, functional electrical stimulation (FES) can be used to assist movement. FES enables practice of the desired coordinated movement so that movement practice more closely approximates normal movement than would otherwise be possible for the stroke survivor with persistent dyscoordination.[4,12] FES can assist the individual with stroke to produce, practice, and learn a movement that is more normally coordinated. Some researchers have shown that it is efficacious to use movement-assist devices, such as robotics or FES, in this way.[4]

Within the framework of activity-dependent central nervous system plasticity, a second critical motor learning principle is to attend closely to the motor task.[6,13] Using one's brain signal in a BCI requires intense concentration on the brain signal control task, satisfying a second critical motor learning principle, focused attention. In our combined BCI + FES system, the brain signal activates the FES movement-assist device during practice of the coordinated movement. Accordingly, a second purpose of this study was to demonstrate the feasibility of combining BCI and FES across a series of motor learning training sessions. Therefore, this study, by combining BCI with FES-assisted movement, incorporates two motor learning principles: (1) close attention to the task and (2) practice of movement as close to normal as possible.

CASE DESCRIPTION

The participant was a 43-year-old woman who was 10 months post-stroke. This study was conducted under the oversight of the Louis Stokes Cleveland Veterans Affairs Medical Center Human Subjects Protection Board. The participant provided informed consent. Her stroke had occurred as a result of endocarditis and resulting cerebral emboli. The lesion area was in the left frontal and parietal lobes, cortical and subcortical regions, with insular area involvement. The lesion had a volume of 20.46 cc and was 3.3% of the volume of the hemisphere.

After the stroke, the participant had gait deficits and upper limb motor deficits at shoulder, elbow, wrist, and fingers. This participant was considered a good candidate for the study because at entry into the study she had volitional partial movement of mass finger and thumb extension (all digits extended simultaneously). There was sufficient muscle strength present to produce joint movement, but the participant was unable to produce isolated movement of the index finger or any of the fingers or the thumb. With persistent effort to perform isolated finger extension movements, there was abnormal simultaneous mass hyperextension of metacarpal phalangeal (MP) joints of all four fingers and thumb and simultaneous flexion of proximal interphalangeal and distal interphalangeal joints of all fingers.

Volitional isolated index finger extension at the MP joint was measured by an objective examiner, who was not associated with the study. Measures were made before initiation of the treatment at weeks −10, −9, −8, −1, just before treatment initiation (week 0), at mid treatment (week 1.5), and post-treatment (week 3). The study schedule is illustrated in Table 1.

At the baseline measurement sessions, there was no isolated movement of the index finger (or any single finger). At the mid- and posttreatment measurement sessions, a video document was made of three repetitions of index finger movement. In the video document, the presence of isolated index finger movement can be observed, and the absence of movement can be observed in digits 3, 4, and 5. Standard goniometry was used to measure the existing movement (three repetitions).

We tested the feasibility of combined use of BCI and FES to address stroke-related dyscoordination of isolated index finger joint extension of the MP joint. The BCI + FES intervention consisted of trials of either attempted finger movement and relax conditions or imagined finger movement and relax conditions. The tasks for the participant were to (1a) activate brain signal during attempted movement, (1b) deactivate brain signal during relaxation, (2a) activate brain signal during imagined movement, and (2b) deactivate brain signal during relaxation. The participant was provided feedback as to the accuracy of her brain signal control. We measured accuracy of the brain signal control during each of the training conditions, as well as pre- and posttreatment volitional isolated joint movement of the index finger. The method for calculation of brain signal accuracy is described in a subsequent section.

INTERVENTION

EEG, FES, and Magnetic Resonance Imaging (MRI) Equipment and Data Acquisition

EEG was performed using a SynAmps[2] (Compumedics, El Paso, TX) amplifier system and an Electro-Cap (ECI, Eaton, OH) that had 58 monopolar channels referenced with linked earlobe electrodes. The signal was sampled at 250 Hz and bandpass filtered from 0.1 to 60 Hz. The BCI2000 software package[14] (Wadsworth Center, Albany, NY) was used to process the EEG signal during the online use of the BCI system. We modified the graphical user interface and added an external trigger signal output capability using a digital output card added to the computer.

A Universal External Control Unit (UECU; DVA FES Center, Cleveland, OH) was custom configured to serve as a surface functional electrical stimulator. The brain signal and UECU were automatically synchronized by a trigger output so that the brain signal could trigger the UECU to deliver the FES stimulus to the stimulating electrode. FES was triggered when the integrated brain signal exceeded a specified threshold.[15] The FES parameters were frequency (83.3 Hz), pulse width (255 μsec), and amplitude adjusted within a comfortable range. The surface electrodes (PALS; Alex Gard, San Diego, CA) were 1.2 × 0.3 cm and were placed over the indicis proprius muscle and the portion of the extensor digitorum communis muscle serving the index finger.

TABLE 1. Testing and Treatment Schedule

Week	Volitional Index Finger Testing	Treatment	
		BCI Sessions	Functional Task Practice
−10	√		
−9	√		
−8	√		
−1	√		
0	√		
1		3	1.6 H (including 30 min FES)
2	√	3	1.6 H (including 30 min FES)
3		3	1.6 H
4	√		

MRI was used to determine lesion location and volume and electrode location. T1-weighted anatomical MRI was performed using a Siemens Symphony 1.5-T system (voxel size of 1 × 1 × 1 mm, repetition time = 2160 msec, echo time = 3.45 msec, flip angle = 15 degrees, and data matrix = 192 × 256). Lesion region and volume were determined using the MRICron tool (C. Rorden, University of South Carolina). We superimposed a three-dimensional reconstruction of electrode locations on the subject's magnetic resonance image, using the CURRY software package (Compumedics: Charlotte, NC), to determine the relationship of the 10 to 20 EEG cap electrode locations with the magnetic resonance image structures.

EEG Signal Screening and Analysis

During the screening process, brain signal was acquired while the participant volitionally attempted each of two types of tasks: (1) attempted actual index finger extension on demand, randomly alternated with attempted relaxation of index finger extensor muscles on demand, and (2) imagined index finger extension on demand, randomly alternated with attempted relaxation of index finger extensor muscles on demand. Our team generated computer graphics whereby cues were presented in a six-second sequence (three seconds visible rectangle cue and three seconds blank screen waiting time).

Before work with the BCI system, we worked with our subject to ensure that she did not physically overexert herself during the attempted motor task trials. We were aware of the potential for electromyography contamination of the EEG signal, and we followed the standard practice for inspecting for electromyographical signal contamination. The EEG spectrum is known to be concentrated in the α band, with the β-band peak being flatter and lower. Measured in decibel, the EEG spectrum decreases almost linearly after 12 Hz (except for the β peak). Conversely, the electromyography spectrum increases at ~20 Hz and remains high even at higher frequencies.[16] We inspected the EEG signal and determined that the spectrum was consistent with EEG signal and not contaminated with electromyographical signal.[16] A frequency power analysis was conducted using the maximum entropy method for spectral estimation across epochs of three-hertz bins from 0 to 30 Hz. The optimal signal feature was selected according to the electrode or frequency combination yielding the highest explained variance (R^2)[17] between a given pair of conditions (eg, attempted movement and attempted relaxation). The brain signal accuracy was calculated as follows: number of correct target hits ÷ number of completed attempts, where completed attempts = attempts for which one or the other target state was achieved in the allocated time; trials resulting in no outcome were recorded separately as errors.[18–20]

The training approach focused on modulation of the brain signal power in the selected frequency band and selected electrode region. The steps for selection of the electrode sites for BCI training were (1) acquire EEG data during performance of the motor task by the uninvolved limb, (2) identify the electrode locations and frequency ranges that exhibited the most highly activated brain signal during uninvolved limb motor performance, (3) acquire EEG data during the performance of the motor task by the involved limb, (4)

constrain the available "training" electrode sites to C, P, and CP electrodes on the lesioned hemisphere, (5) select from the constrained set, the four electrode sites that were most highly active and most comparable to the brain signal for uninvolved limb movement. The signal level from the screening data was calculated for all electrode and frequency band combinations (58 electrodes and 3-Hz epochs from 5 to 30 Hz) to extract information regarding which electrode and frequency epoch combinations would be potentially usable and suitable for BCI motor recovery training.

We used the standard methods for EEG signal analysis that are provided with the BCI2000 software (Wadsworth Laboratory, Albany, NY). Specifically, the EEG signal was analyzed by measuring signal power for each electrode location. It is known that the brain produces increased narrow band power at certain frequencies when at rest because of mass synchronization of neural circuits. During motor actions, this synchronized activity and the corresponding power peaks disappear, resulting in event-related desynchronization. The BCI control signal was interpreted from the signal deviation of the narrow band power in the selected frequency bands and electrode regions from the time-averaged power in those frequency band and electrode combinations. The time average was updated at the end of every trial based on data from the last three trials in order to compensate for slow drifts in the average power over time. In this way, the power in the selected frequency bands for the current trial was compared with the mean power for a series of trials. If the power in the selected bands was higher than the time average, the BCI system interpreted the signal as representing a "rest" state of the brain, and conversely, if the power in the selected bands and electrodes was lower than the time average, the BCI system interpreted the signal as representing a "move" state of the brain. The chosen frequency bands and electrodes were determined from the screening data based on those bands and electrodes that had the highest capability to discriminate the conditions of move versus rest. These methods are the standard methods provided in the BCI2000 software.

BCI Training Paradigm

A computer monitor display was used to provide the participant with commands to move or to relax. The first training paradigm included the tasks of attempting to extend the index finger or attempting to relax the index finger (Fig. 1, commands 1 or 2). A red rectangle at the top of the screen cued the participant to actively attempt to perform isolated index finger extension. In doing so, if the participant achieved and maintained heightened brain activity beyond the identified threshold, the rectangle color changed from red to green signaling success. A red rectangle at the bottom of the screen

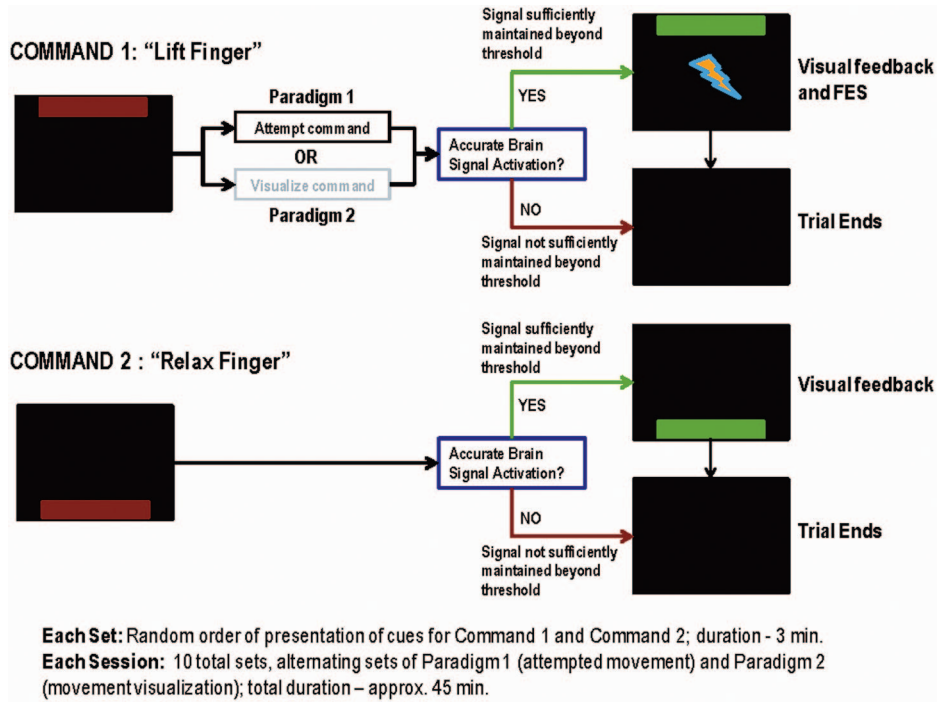

FIGURE 1. Schematic of the BCI + FES training protocol. For the training protocol, Command 1 (top row of protocol) was to either "attempt" or "imagine" the movement. If the brain signal was sufficiently activated and maintained beyond threshold, then the red bar at the top of the screen turned green (top right example). In addition, if the brain signal was sufficiently activated, then the brain signal triggered FES-assisted movement practice (lightning bolt in center of top upper right screen). If the brain signal was not sufficiently activated, then the trial ended with a blank screen (second row, right blank screen). The "relax" trials were randomly presented with either the attempted or the imagined movement trials. For the "relax" trials, if the brain signal was sufficiently deactivated, then the red command bar at the bottom of the screen (lower left) turned green (third row of right screens). If the brain signal was not sufficiently deactivated, then the trial ended with a blank screen (bottom row of right screens).

cued the participant to relax. During the attempt to relax, if the participant achieved and maintained a brain signal beyond the identified threshold for relaxation, the bottom rectangle changed from red to green signaling success at relaxation. The top and bottom cuing rectangles were presented in a random order, and a maximum of 15 seconds was allowed for each rectangle presentation.

The combination of the BCI system and the participant can be viewed as two adaptive controllers coupled together. The "threshold" discussed above is adapted by the BCI software in response to the statistical mean and variance of the user's brain signal over the previous three trials; this compensates for changes in the baseline brain activity that occurs over the course of the training. The effect of this normalization process is to compensate for changes in any bias in the brain signal [toward either "move" (top target) or "rest" (bottom target)] and to scale the signal such that the average cursor speed (and thus the required time to hold the signal for a success) remains consistent over the course of the trial.

The second training paradigm was identical to the first, except that instead of responding to the top rectangle cue with an attempt to perform the movement, the participant was instructed to simply imagine the movement. We incorporated practice of the imagined movement task to provide the subject with a task for which there would be no overt motor indication of failure. That is, she did not visually observe failure to perform a motor task because the task was imagined. For both the attempted and imagined movement paradigms, if the participant achieved and maintained brain signal beyond the identified threshold, not only did the rectangle turn green but also the brain signal activated the FES device (Fig. 1, top upper right box), delivering an electrical stimulus to the index finger extensor muscles. The FES-induced motor response was index finger extension (no movement at any other digits). The visual rectangle cues on the monitor were presented in 10 sets with an attempted movement set alternated with an imagined movement set.

The duration of a single daily session was ~45 minutes (average of 75 total attempted/imagined trials and 75 total relax trials per session). Training was provided three times per week for three weeks (nine sessions total). A BCI + FES system training session with the participant is shown in the supplementary video (see Video, Supplemental Digital Content 1, http://links.lww.com/JNPT/A3).

During the three weeks of the BCI + FES training for index finger extension, the participant had three additional therapy visits (mean time, 1.6 hours each) during which she practiced volitional functional task movements such as attempting to pick up objects and manipulate a fork. During these visits, she also received surface FES (two 30-minute bouts, for practice of mass whole-hand opening and thumb abduction, respectively).

OUTCOMES

BCI Screening Results

A brain map of BCI screening results is given in Figure 2. The R^2 value is a measure commonly used in previous BCI device-control applications[17,21] for which the vertical color bar shows the range.

For the uninvolved limb, the CP4 electrode location in the nonlesioned hemisphere provided the most prominent signal (in terms of the highest R^2 value) for the index finger extension task; there was no activity in the hemisphere ipsilateral to the uninvolved finger. For the impaired right finger attempted movement, two of the most highly activated brain signal electrode locations, CP3 and CP6, are shown in Figure 2A. For the involved finger task, the CP3 electrode location in the lesioned hemisphere was most comparable with the CP4 electrode in the unlesioned hemisphere during the uninvolved finger task. Because we were attempting to retrain brain control, we selected the signal from the CP3 electrode (left, lesioned hemisphere; $R^2 = 0.10$); we selected this electrode location even though R^2 for CP6 in the nonle-

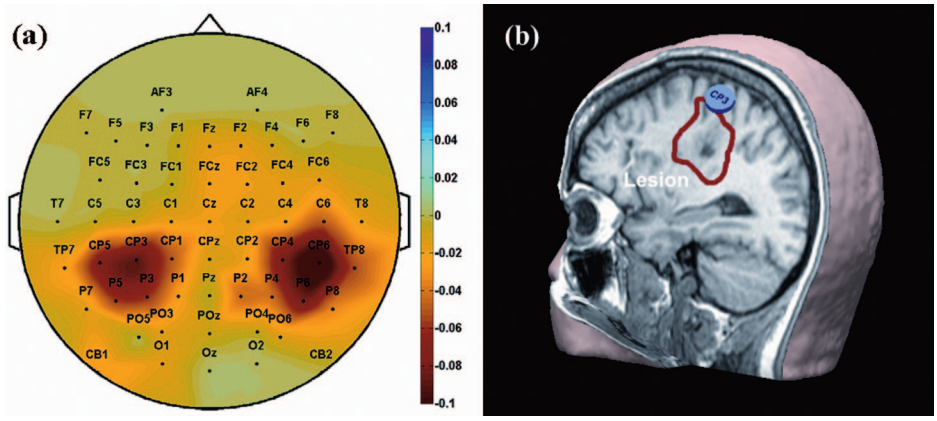

FIGURE 2. A, Brain signal at CP3 and CP6 electrodes at 21 to 24 Hz produced a usable signal for motor training. The level of brain activity is illustrated according to R^2, which is a measure without units, and the vertical color bar shows the range of R^2. The brain map shows signed $R^2 = -0.10$ (at 21–24 Hz) for the CP3 electrode region during attempted right finger extension (left, lesioned hemisphere, more dense color region). In the right hemisphere, the signed R^2 value was -0.12 (at 21–24 Hz) for the CP6 electrode (right, nonlesioned hemisphere). B, Relationship of the CP3 electrode to the left hemisphere lesion. The figure shows the CP3 electrode location with respect to the lesion area (outlined region).

sioned hemisphere was slightly greater (right side; R^2 = 0.12). A reason for not selecting the CP6 for training is that it was abnormally activated based on our screening data for the uninvolved index finger movement. For these reasons, we considered the signal location at CP3 to be more promising for use in a brain-directed motor training intervention for involved finger movement. Furthermore, the signal at CP3 proved usable for discriminating between the imagined finger movement and the relaxed finger condition.

The CP3 electrode and its location in relationship with the MRI are shown in Figure 2B, illustrating the infarct region in the left hemisphere (bolded outline on MRI). We superimposed a three-dimensional reconstruction of electrode locations on the subject's magnetic resonance image by using the CURRY software package (Compumedics, Charlotte, NC). We found that the CP3 surface electrode location projected to the postcentral sulcus and the intraparietal sulcus indicating that signals that were recorded from the CP3 site originated, at least in part, from the somatosensory cortex (Brodmann areas 1 and 2[22] serving integration of motor and sensory information for hand and finger[22,23]) and from somatosensory association cortex (Brodmann area 5[22]). The lesion represented 3.3% of left cerebral hemisphere volume (20,460 voxels in the lesion/621,923 total left hemisphere voxels).

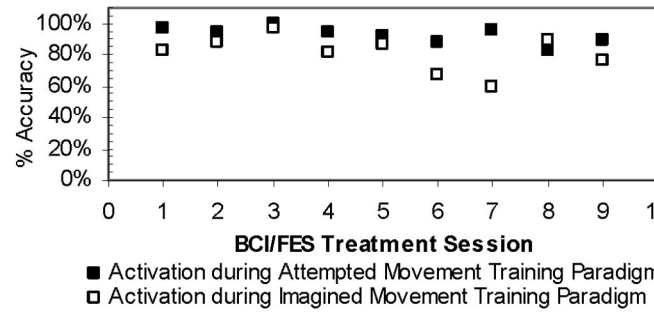

FIGURE 3. Accuracy of brain signal control during either attempted or imagined index finger extension. The percentage of accuracy of brain signal activation control is shown on the vertical axis, and the session number is shown on the horizontal axis for nine training sessions. Accuracy of brain signal control is shown for each session for conditions of attempted movement (solid squares) and imagined movement (open squares). Accuracy of brain signal control during attempted movement began relatively high (97%) and remained high throughout. Accuracy of brain signal control during imagined movement began somewhat lower (83%) than that for attempted movement and was maintained across the sessions, with the exception of two sessions of lower performance. See text for description of accuracy calculation.

Control of Brain Signals for Muscle Activation

After identifying the electrode location and frequency band that were most likely to be optimal for training, we assessed whether the participant could gain sufficient control of the brain signal to permit the use of the signal in a motor training intervention. The first training paradigm that we tested required that the participant generate, on demand, a brain signal beyond a specified threshold in the lesioned hemisphere at the CP3 electrode. The participant was instructed to generate this brain signal by attempting to produce an index finger extension movement, despite the fact that she was unable to produce active isolated finger movement at the beginning of the study. When the brain signal was generated beyond the specified threshold, the participant was given visual feedback indicating success. Concurrently, the brain signal triggered FES to the muscles serving the index finger, and index finger extension movement was achieved with the assistance of the FES system. The second training paradigm was identical, except that the participant was instructed to generate the brain signal by only imagining index finger movement (no attempt to produce actual movement).

To effectively use the brain signal for this type of motor retraining, it is preferable that the brain signal is useful at the beginning or early in the training. For attempted movement, Figure 3 shows that at the initial training session, the accuracy of brain signal control was 97% (session 1, solid square), and across the first five sessions, accuracy was greater than 90% (range, 92%–100%). For the subsequent four sessions, brain signal control accuracy ranged between 82%–95%. For imagined movement, Figure 3 shows that at the initial training session, accuracy of brain signal control was 83% (session 1, open square) and for the first five sessions ranged from 82% to 97%. For the subsequent four sessions, accuracy ranged from 59% to 89% (chance = 50%).

Control of Brain Signals for Muscle Relaxation

After stroke, impairment of brain control for muscle relaxation is a significant obstacle to recovery of normal coordination. In training for both attempted and imagined movement, practice of brain signal control for relaxation was randomly alternated with either attempted movement or imagined movement, respectively. When the relaxation task was alternated with attempted movement, brain signal control for the relaxation task had an initial accuracy of 65% (Fig. 4, session 1, solid diamond) and improved during the subsequent sessions through session 6, ranging from 69% to 83% (with one session of low performance at 66%).

When the relaxation task was alternated with imagined movement, brain signal control of relaxation had an initial accuracy that was not different than chance (52%; session 1, open diamond, Fig. 4). Brain signal control for the relaxation task made steady improvement through session 6, ranging from 58% to 93%.

Motor Function Change During Combined BCI + FES Training

The participant had no volitional isolated index finger extension for the 10 weeks before BCI + FES training, as illustrated in Figure 5.

After three weeks of BCI + FES training, the participant regained volitional control of 26 degrees of isolated index finger MC joint extension. The performance of the index finger test before and after the end of treatment is illustrated in Figure 6. Prebaseline performance (Fig. 6A) and baseline performance (Fig. 6B) indicated that no isolated

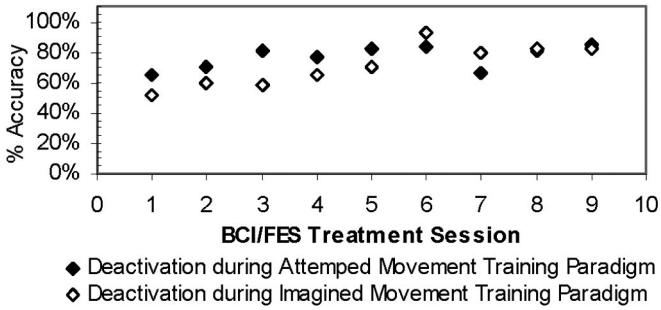

FIGURE 4. Accuracy of brain signal control during attempted relaxation of index finger muscles. The percentage of accuracy of brain signal deactivation control is shown on the vertical axis, and the session number is shown on the horizontal axis for nine training sessions. This brain signal deactivation task (relaxation of muscles) was performed in alternation with either attempted movement or imagined movement. The accuracy of brain signal deactivation is shown (black diamonds) when it was alternated with attempted movement, with a range of 69% to 83% accuracy across the nine sessions. The accuracy of brain signal deactivation is shown (open diamonds) when that task was alternated with imagined movement, with a range of 52% to 93%. See text for description of accuracy calculation.

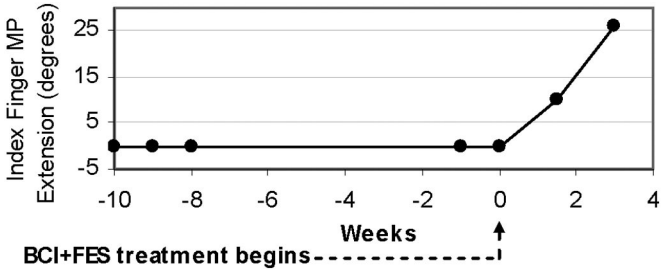

FIGURE 5. Gain in volitional isolated index finger extension after BCI and FES intervention. Volitional isolated index finger MP extension is shown across 14 weeks (black circles). For the 10 weeks before the study, there was no capability to volitionally perform isolated index finger MP extension (0 degrees). After three weeks of BCI and FES intervention for motor training, the patient recovered 26 degrees of volitional isolated index finger MP extension.

joint movement occurred beyond the initial test position. At the end of the intervention period, the participants was able to execute 26 degrees of isolated index finger MC joint extension; Figure 6C shows the end position of the movement that began in the same initial test position as shown in Figure 6A and B. There was no FES and no BCI during testing.

DISCUSSION

Our results indicate that an individual with stroke was able to exhibit control over the brain signal for attempted and imagined isolated finger extension tasks, even though volitional isolated index finger movement was not possible at the initiation of the intervention. The training task was specific and highly relevant to the motor learning goal of isolated index finger extension. In previous BCI work,[5,8,24] the brain signal has been used to control communication devices and environmental devices. However, in the previous applications of noninvasive BCIs for device control, a motor task was neither required nor imposed, and therefore, the required location of the brain signal was less specific than for the current motor relearning application.

Furthermore, in the previous BCI applications, the cognitive task that generated the brain signal was less relevant to the task to be executed than was the case for the current motor control relearning application. In some previous BCI applications, an array of imagined movements (eg, feet, hands) or other thoughts were screened for potentially useful brain signals that might control a light switch or a computer cursor; subsequently, the electrode location and cognitive tasks were selected according to that which generated the signal that best discriminated control of device on/off switches. In this case study, the procedure used for identification of the most relevant electrode location used the reverse process. That is, the attempted and imagined tasks were imposed on the participant as was the task of relaxation of the muscles (deactivation of the brain signal). These tasks were imposed because they were the specific focus of the intervention for motor recovery. Our results are encouraging because they indicate that it is feasible to identify and extract brain signal features from the lesioned hemisphere and that the participant could use and learn to control these signals during the

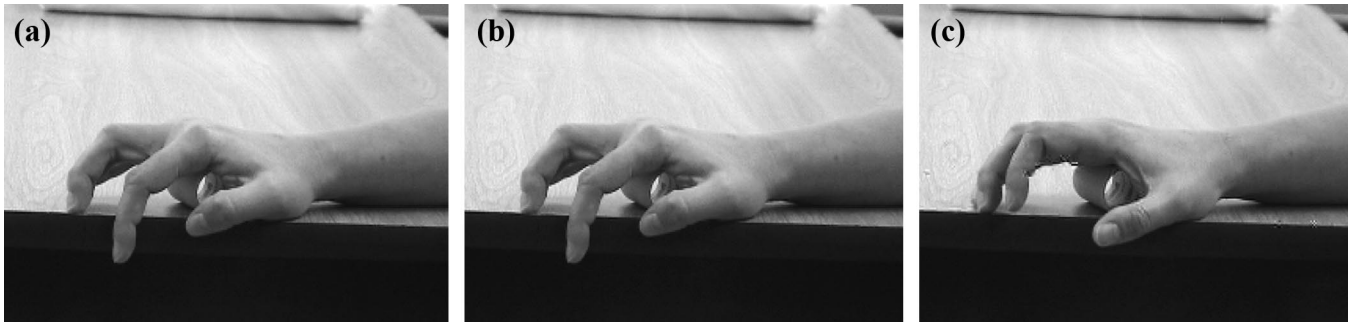

FIGURE 6. Participant's rest test position and volitional movement endpoint position for isolated finger extension end position. (A), At prebaseline, the participant was unable to move the index finger from the rest position; at baseline, the participant was unable to move the index finger from the rest position (B); and the end position of the isolated index finger MP extension test performed after the nine sessions of BCI and FES (during testing, no BCI and no FES were used) (C); post-treatment: Index finger MP active extension, end-point position shown (begining position was at the MP flexed position shown at Baseline).

attempted task, the imagined task, and the relaxation task. These signals likely represented integrated sensory and motor information for finger control.

A second promising result concerns brain signal accuracy using the BCI. Our study demonstrates that an individual with stroke can produce a high initial accuracy of brain signal control for both the task of attempted movement (97%) and of imagined movement (83%). The accuracy exhibited in the initial session is positive in comparison with another study using magnetoencephalography-based BCI.[25] In that study of six participants with chronic stroke, initial accuracy was 52.84% (±20.59%). Another important point concerning brain signal control accuracy is that in the current study, brain signal accuracy was maintained above 88% for the attempted movement task for eight of the nine sessions. These accuracy levels are higher than those previously reported for case series of stroke survivors,[7,8,25] although it should be noted that the participants in the previously reported studies may have been more severely impaired than the participant in the current case study and accuracy my have been calculated differently. This raises an important unanswered question regarding the severity level of stroke in individuals who will be able to use BCI as a motor training paradigm.[26]

A third positive finding was that brain signal control of the motor imagery task was good at the first session and improved further over the intervention period. We used the motor imagery task for the practical reason of providing a task in which the subject would not fail in the motor aspect of the task. Others have reported that motor imagery training for finger movement related to pinch force recovery is comparable with a repetitive finger exercise and superior to conventional physical therapy.[27] That work supports the possibility that motor imagery contributed to the motor recovery observed in this study. For those who have had a stroke, the specific neural activation patterns of motor imagery are not well studied, and understanding of the mechanism is incomplete.[28] In healthy adults, brain function studies indicate that motor imagery activates nonprimary motor structures. However, for the highly summated signal of scalp BCI, others have reported that in healthy adults, motor imagery induces activation of the primary sensorimotor area.[29] Our findings for imagined movement (and attempted movement) were consistent with those of others[28,29] in that the most highly active electrodes were those over the somatosensory and sensory motor association regions serving finger motor function.

A fourth outcome of interest is the differences in the control of the attempted and imagined movement trials compared with the relax trials. For the relax trials, the initial session accuracy was approximately the same as chance with either the attempted or imagined movement condition trials (64% and 52%, respectively; Fig. 4). Others have identified the lack of information related to the relax condition during the use of BCI and have called for further development of the relax task for BCI and for study of the accurate control of the brain relax task.[26] In healthy adults, it is sometimes more difficult to volitionally relax a muscle than to activate it. For many individuals with stroke, this difficulty is greatly magnified, as was the case for our participant. During training, the improvement of brain signal control during the relax task to 83% and 93% accuracy (during imagined and attempted trial bouts, respectively) may have occurred because of improved understanding of the task or learning to control the brain signal during the relax task. There may have been other causes of variation in brain signal accuracy. In session 7, the low relax accuracy of 66% (attempted move or relax condition) and low motor imagery accuracy of 59% may have indicated that the subject had a difficult day in some regard, relative to other sessions for which she had >80% accuracy. Open questions remain about the differential control of muscle activation versus relaxation and about the range of variation for brain signal accuracy within which motor recovery can still be facilitated by using BCI.

A fifth finding of importance was that it was feasible to use BCI in combination with a surface FES system for the purpose of motor learning. The technology and software interface was reliable, and the tasks were understood by the participant. It was encouraging that the participant regained 26 degrees of volitional isolated index finger extension within the three weeks of combined BCI + FES training. Because of the nature of this feasibility case study design, it was not possible to determine an exact single source of influence causing the volitional coordination recovery. The FES alone could have produced the recovery. Others have reported recovery of volitional mass hand opening and closing[3,4,30] in response to FES and motor learning, but little has been reported regarding recovery of isolated finger control, especially within three weeks of treatment for individuals 10 months or more after stroke. Alternatively, the BCI alone could have been the basis for recovery. The BCI imagined trials, the BCI attempted movement trials, or both could have contributed. To our knowledge, there are no previous reports regarding recovery of volitional motor control in response to BCI training. The combination of BCI + FES could have been the cause of volitional motor recovery of index finger coordination or other unidentified influences could have been at work. One unique aspect of BCI is that focused concentration is required. From the brain signal accuracy data, it was obvious that the participant exerted the concentration required to control the brain signal. Concentration and attention to task are critical components of motor learning and skill acquisition.[6] The high degree of concentration required for BCI accuracy is not demanded for users of FES alone. Further study is required to learn the answers to these questions.

Although the recovery of isolated index finger joint movement could have been the result of any one or a combination of several influences, the fact is that there was volitional recovery of isolated finger movement at the end of the ninth BCI session. The one available publication on BCI for exercise after stroke showed that subjects could use a magnetoencephalography-based brain signal for BCI to activate an exercise device that passively opened or closed the hand. In that study, no subject exhibited any motor recovery.[25] Isolated movement of the fingers is required to manipulate objects in the hand and execute the fine, individuated finger movements required to manipulate objects and tools. These movement components of the fingers underlie functional activities such as picking up a pen, positioning it, and using it to write; picking up a utensil and moving it into

position for eating; typing on a computer keyboard; using a cell phone; and playing an instrument such as a guitar or piano. Recovery of isolated index finger movement for the participant in the current study was a first step in her goal to recover isolated finger movement in all her fingers. Before recovery of isolated index finger control, she was forced to pick up an object using her thumb and the medial border of the first phalanx of her index finger, and an inordinate amount of time was required, even for that uncoordinated movement. With the recovery of isolated index finger extension control, she was able to more normally position the index finger so that she could then use the normal thumb or index finger opposition movements for grasping an object.

Clinical Implications

BCI as a motor learning intervention was feasible for an individual with stroke, as was the combination of BCI + FES. It was not necessary to choose the best brain signal across multiple electrodes and across multiple irrelevant motor and cognitive tasks; rather, the stroke participant was able to control brain signal for the imposed training tasks of attempted index finger movement, imagined index finger movement, and relaxation of index finger muscles. The brain signal control was established at the first session for the attempted and imagined movement tasks. Within five sessions, brain signal control was established for the relaxation task. After three weeks of combined BCI and surface FES for index finger extension, the participant regained volitional control of isolated index finger MP extension coordination. More studies will be required to determine the characteristics of stroke survivors who can successfully use BCI as a motor learning paradigm. Also, a randomized controlled trial will be necessary to determine whether BCI actually can have an additive effect beyond FES alone or beyond other less staff-intensive or time-intensive motor learning methods.

REFERENCES

1. Butler AJ, Wolf SL. Putting the brain on the map: Use of transcranial magnetic stimulation to assess and induce cortical plasticity of upper-extremity movement. *Phys Ther.* 2007;87:719–736.
2. Wolf SL, Winstein CJ, Miller JP, et al. Effect of constraint-induced movement therapy on upper extremity function 3 to 9 months after stroke: The EXCITE randomized clinical trial. *JAMA.* 2006;296:2095–2104.
3. Alon G, Sunnerhagen KS, Geurts AC, et al. A home-based, self-administered stimulation program to improve selected hand functions of chronic stroke. *NeuroRehabilitation.* 2003;18:215–225.
4. Daly JJ, Hogan N, Perepezko E, et al. Response to upper-limb robotics and functional neuromuscular stimulation following stroke. *J Rehabil Res Dev.* 2005;42:723–736.
5. Daly JJ, Wolpaw JR. Brain-computer interfaces in neurological rehabilitation. *Lancet Neurol.* 2008;7:1032–1043.
6. Singer R, Lidor R, Cauraugh JH. To be aware or not aware? What to think about while learning and performing a motor skill. *Sport Psychologist.* 1993;7:19–30.
7. Hill NJ, Lal TN, Schröder M, et al. Classifying EEG and ECoG signals without participant training for fast BCI implementation: Comparison of nonparalyzed and completely paralyzed participants. *IEEE Trans Neural Syst Rehabil Eng.* 2006;14:183–186.
8. Birbaumer N, Cohen LG. Communication and restoration of movement in paralysis. *J Physiol.* 2007;579:621–636.
9. Daly JJ, Ruff RL. Evidence-based construction and measurement of efficacious gait and upper limb functional interventions after stroke. *ScientificWorldJournal.* 2007;7:2031–2045.
10. Nudo RJ. Mechanisms for recovery of motor function following cortical damage. *Curr Opin Neurobiol.* 2006;16:638–644.
11. Nudo RJ, Milliken GW, Jenkins WM, et al. Use-dependent alterations of movement representations in primary motor cortex of adult squirrel monkeys. *J Neurosci.* 1996;16:785–807.
12. Daly JJ, Roenigk K, Holcomb J, et al. A randomized controlled trial of functional neuromuscular stimulation in chronic stroke subjects. *Stroke.* 2006;37:172–178.
13. Bütefisch C, Hummelsheim H, Denzler P, et al. Repetitive training of isolated movements improves the outcome of motor rehabilitation of the centrally paretic hand. *J Neurol Sci.* 1995;130:59–68.
14. Schalk G, McFarland DJ, Hinterberger T, et al. BCI2000: A general-purpose brain-computer interface (BCI) system. *IEEE Trans Biomed Eng.* 2004;51:1034–1043.
15. Dohring ME, Daly JJ. *Development of Hardware and Software to Integrate BCI2000 with the Universal External Controller, Serving as a Surface Functional Electrical Stimulator. Research Records*. Cleveland, OH: Cognitive and Motor Learning Laboratory, Research Service, Louis Stokes Cleveland VA Medical Center; 2008.
16. Schalk G. Mu Rhythm analysis. Presented at: 1st BCI2000 Workshop, June 13–14, Albany, NY, 2000:107.
17. Montgomery DC. *Design and Analysis of Experiments.* 6th ed. Hoboken, NJ: Wiley; 2005:389.
18. Wolpaw JR, Flotzinger D, Pfurtscheller G, et al. Timing of EEG-based cursor control. *J Clin Neurophysiol.* 1997;14:529–538.
19. Kelly SP, Lalor EC, Finucane C, et al. Visual spatial attention control in an independent brain-computer interface. *IEEE Trans Biomed Eng.* 2005;52:1588–1596.
20. Schalk G, Miller KJ, Anderson NR, et al. Two-dimensional movement control using electrocorticographic signals in humans. *J Neural Eng.* 2008;5:75–84.
21. Wolpaw JR, McFarland DJ. Multichannel EEG-based brain-computer communication. *Electroencephalogr Clin Neurophysiol.* 1994;90:444–449.
22. Thompson M, Thompson J, Wenqing W. Brodmann Areas (BA), 10–20 Sites, Primary Functions, ADD Centre, Biofeedback Institute of Toronto, American Applied NeuroScience Institute. Available at: http://www.addcentre.com/Pages/professionaltraining.html. Accessed June 30, 2009.
23. Kandel ER, Schwartz JH, Jessell TM. *Principles of Neural Science.* 4th ed. New York, NY: McGraw-Hill; 2000:chap 19.
24. Sellers EW, Krusienski DJ, McFarland DJ, et al. A P300 event-related potential brain-computer interface (BCI): The effects of matrix size and inter-stimulus interval on performance. *Biol Psychol.* 2006;73:242–252.
25. Buch E, Weber C, Cohen L, et al. Think to move: A neuromagnetic brain-computer interface (BCI) system for chronic stroke. *Stroke.* 2008;39:910–917.
26. Popescu F, Blankerz B, Muller KR. Computational challenges for noninvasive brain computer interfaces. In: Nijholt A, Tan D, eds. *Brain-Computer Interfacing for Intelligent Systems* (*IEEE Intelligent Systems).* 2008:72–79.
27. Muller K, Butefisch CM, Seitz RJ, et al. Mental practice improves hand function after hemiparetic stroke. *Restor Neurol Neurosci.* 2007;25:501–511.
28. Sharma N, Pomeroy VM, Baron JC. Motor imagery: A backdoor to the motor system? (review). *Stroke.* 2006;37:1941–1952.
29. Pfurtscheller G, Neuper C. Motor imagery activates primary sensorimotor area in humans. *Neurosci Lett.* 1997;239:65–68.
30. Ring H, Rosenthal N. Controlled study of neuroprosthetic functional electrical stimulation subacute post stroke rehabilitation. *J Rehabil Med.* 2005;37:32–36.

