Running Head

tDCS on MI BCI with robotic feedback for stroke

Full Title

Facilitating effects of transcranial direct current stimulation on motor imagery Brain-Computer Interface with robotic feedback for stroke rehabilitation

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Presentation

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Competing Interests

The authors have declared that no competing interests exist.

Clinical Trial Registration Number

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Abstract

Objective: To investigate the efficacy and effects of transcranial Direct Current Stimulation (tDCS) on Motor Imagery Brain-Computer Interface (MI-BCI) with robotic feedback for stroke rehabilitation.

Design: A sham-controlled, randomized control trial (RCT).

Setting: Patients recruited through a hospital stroke rehabilitation program.

Participants: 19 subjects who incurred a stroke 0.8 to 4.3 years prior, with moderate to severe upper extremity functional impairment, and passed BCI screening.

Interventions: 10 sessions of 20 minutes of tDCS or sham prior to 1-hour MI-BCI with robotic feedback upper limb stroke rehabilitation for 2 weeks. Each rehabilitation session comprised 8 minutes of evaluation and 1 hour of therapy.

Main Outcome Measures: Upper extremity Fugl-Meyer Motor Assessment (FMMA) scores measured end-intervention at week 2 and follow-up at week 4, online BCI accuracies from the evaluation part and laterality coefficients of the EEG from the therapy part of the 10 rehabilitation sessions.

Results: FMMA score improved in both groups at week 4, but no intergroup differences were found at any time points. Online accuracies of the evaluation part from the tDCS group were significantly higher than the sham group. The EEG laterality coefficients from the therapy part of the tDCS group were significantly higher than the sham group.

Conclusions: The results suggest a role for tDCS in facilitating motor imagery in stroke.

Keywords: Motor Imagery, transcranial direct current stimulation, brain-computer interface, stroke rehabilitation.

1 # List of Abbreviations

BCI	Brain-Computer Interface
EEG	Electroencephalogram
ERD	Event-related desynchronization
ERS	Event-related synchronization
FMMA	Fugl-Meyer Motor Assessment
MI	Motor Imagery
tDCS	transcranial Direct Current Stimulation

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INTRODUCTION

Stroke is a leading cause of serious disabilities in the United States.[1] Stroke survivors can partially recover their motor function control from rehabilitation that involved task-specific and repetitive motor exercises.[2] Since moving the stroke-impaired limb is often difficult or not possible, Motor Imagery (MI), the imagination of movements without physical execution, represents an alternate approach for rehabilitation.[3-5] However, while motor execution is observable, motor imagery is a concealed mental process. Nevertheless, advances in Brain-Computer Interface (BCI) technology have enabled stroke survivors to interact with the environment using their brain signals, and seem to be effective to restore impaired motor function.[6] Since neurophysiological phenomena called event-related desynchronization or synchronization (ERD/ERS) [7] are detectable from EEG during MI by healthy subjects[8] and majority of stroke patients,[9] EEG-based Motor Imagery Brain-Computer Interface (MI-BCI) [10] can be used to objectively assess the performance of MI.[6] In addition, a recent clinical study on chronic stroke patients who received BCI with hand and arm orthoses feedback showed greater motor improvements versus patients who received random feeback not linked to BCI.[11] Hence the use of MI-BCI presents a promising, alternative approach for stroke rehabilitation.

Another promising development in stroke rehabilitation is the use of transcranial Direct Current Stimulation (tDCS)[12,13] for neuromodulation and enhancement of motor recovery.[14] Facilitation of cortical excitability can be achieved with anodal stimulation, and inhibition with cathodal stimulation.[15] Both inhibition of excitability in the contra-lesional hemisphere by cathodal tDCS and facilitation of excitability in the ipsi-lesional

hemisphere by anodal tDCS had been shown to improve motor performance in stroke.[16] In a study, Matsumoto et al. studied the modulation of ERD with anodal, cathodal and sham tDCS on six healthy subjects in performing right hand MI.[17] They found that the ERD of the mu rhythm in the frequency range of 8-13 Hz (mu ERD) was significantly increased after anodal tDCS, and decreased after cathodal tDCS. Subsequently, Kasashima et al. investigated the modulation of ERD with anodal and sham tDCS on six hemiparetic stroke patients in performing MI of the stroke-affected finger.[18] They found significant increase in mu ERD and suggested that tDCS can be used as a conditioning tool for BCI in stroke. In a preliminary study, Ang et al. reported no differences between the online MI-BCI accuracies of three stoke patients who received anodal and cathodal tDCS versus two stroke patients who received sham tDCS,[19] but the result was inconclusive due to the small sample size. In a recent study, Wei et al. studied the modulation of ERD with anodal and sham tDCS on 32 healthy subjects in performing left and right hand MI.[20] They found that the anodal tDCS induced ERD pattern changes in the upper-mu (10–14 Hz) and beta (14–26 Hz) components.

While studies had demonstrated motor improvements in stroke patients,[16] and increase in mu ERD in healthy [17] and stroke patients using tDCS,[18] the use of tDCS to facilitate the stroke patients' ability to operate MI-BCI and subsequently the efficacy in post-stroke motor recovery has not been investigated. To the best of our knowledge, no randomized control study has previously investigated the effects tDCS on stroke patients ability to operate MI-BCI for stroke rehabilitation. In this study, we investigated the clinical efficacy of tDCS and sham-tDCS on MI-BCI with robotic feedback for stroke rehabilitation. We also investigated whether tDCS and sham-tDCS could facilitate the

stroke patients' performance of MI by studying the online MI-BCI accuracies of detecting MI of the stroke-affected upper limb versus the idle condition. We also studied the laterality coefficient of the mu ERD during MI-BCI with robotic feedback rehabilitation therapy of the stroke patients that received tDCS compared to sham.

METHODS

Ethics Statement

Ethics Committee approval was obtained from the National Healthcare Group Domain Specific Review Board.

Study Design

The randomized controlled trial is conducted from 1 January 2011 to 1 January 2014, involving subjects 21 to 70 years old who had their first ever subcortical stroke at least 9 months prior to recruitment, with moderate to severe impairment of upper extremity function (subscore of the Fugl-Meyer Motor Assessment (FMMA) 11-45). Since spontaneous recovery plateaus six-months after stroke onset,[21] motor improvements observed in subjects with 9 months post-stroke would most likely be due to the study intervention assigned and not from spontaneous recovery. In addition, subjects with moderate to severe impairments were recruited since they had greater difficulty with motor execution and hence had fewer therapeutic options.[22] Figure 1 shows a flow chart of the trial. Exclusion criteria included a history of seizures, major depression, and implants that may be triggered, moved, or heated by electrical current (eg. intracranial shunts, pacemakers, metal cranial implants). Depression was evaluated using the Beck

Depression Inventory[23], a 21-item questionnaire commonly used to assess post-stroke depression.[24]

EEG Data Acquisition

In this study, EEG data from 27 channels (Figure 2) were collected using the Nuamps EEG acquisition hardware[a] with unipolar Ag/AgCl electrodes channels, digitally sampled at 250 Hz with a resolution of 22 bits for voltage ranges of ±130 mV. The electrode impedance was kept below 5 kΩ. EEG recordings from all channels were bandpass filtered from 0.05 to 40 Hz by the acquisition hardware.

MI-BCI Screening

Since not all stroke patients could operate EEG-based MI-BCI,[9] the patients recruited in this study first underwent a MI-BCI screening session. In the screening session a total of 160 trials of EEG that randomly comprised 80 MI of the stroke-affected upper limb and 80 idle condition were collected. The stroke patients' abilities to operate MI-BCI were then evaluated based on the 10×10-fold cross-validations of the 160 trials of data collected using the Filter Bank Common Spatial Pattern (FBCSP) algorithm[25] without any removal of artifacts such as Electrooculogram. This analysis was performed similar to the screening session reported by Ang et al.[9] Subjects with MI-BCI classification accuracy >58% were then recruited for randomization.

Randomization and blinding

Subjects who passed BCI screening were checked to ensure that they were not enrolled in other clinical trials or receiving any other therapeutic activities aimed at improving stroke-affected upper limb function. Subsequently, subjects who passed and gave further consent were randomly assigned to receive either the tDCS or the sham-tDCS interventions. Figure 2 shows the setup for the tDCS and sham interventions. Subjects in both groups first underwent a calibration session where the stroke-affected upper limb of the subject was strapped to the MIT-Manus robot[b]. 160 trials of EEG data that comprised 80 MI of the stroke-affected upper limb and 80 idle condition were collected similar to the screening session. Subsequently, the subjects in both groups underwent 10 rehabilitation sessions for 2 weeks, 5 times a week. Each rehabilitation session comprised 20 minutes of stimulation with tDCS or sham-tDCS, followed by 8 minutes of evaluation and 1 hour of therapy using EEG-based MI-BCI with robotic feedback.

MIT-Manus robot

The MIT-Manus is a robot with 2 degrees of freedom that provides horizontal elbow and forearm reaching exercises using an 8-point clock face drawing interactive video game.[26] In this study, the stroke-affected upper limb of subjects from both groups was strapped to the MANUS robotic exoskeleton. The subjects were instructed to imagine moving their stroke-affected hand towards the target indicated on the 8-point clock face video game. They were also instructed to continue MI until successful or unsuccessful detection was indicated on the video screen. Voluntary movements during MI were restricted by locking the mobility of the MANUS robot. If MI was successfully detected, visual and

movement feedback was provided by the MANUS robot through passive movement of the stroke-affected arm from the center towards the target displayed on the screen and back to the target along a pre-determined robotic trajectory.[26] This robotic movement forms a proprioceptive afferent feedback that closes the loop in providing a reward for performing MI.[27,28]

Transcranial direct current stimulation (tDCS)

Direct current was applied for 20 minutes using a saline-soaked pair of surface sponge electrode from a battery-operated constant current stimulator[c] at an intensity of 1 mA with the anode placed over the M1 motor cortex of the ipsi-lesional hemisphere and the cathode placed over the contra-lesional M1. The M1 positions for the tDCS electrodes were located at channels C3 and C4 shown in Figure 2. The goal of this montage was to decrease cortical excitability in the unaffected motor cortex and to increase it in the affected motor cortex.[29,30] For the sham intervention, the current was only applied for the first 30 s out of the 20 minutes to give the sensation of the stimulation. This duration was established to be effective in blinding subjects to the assigned intervention[31] without altering cortical excitability in a number of studies.[29,30]

Quantification of motor improvements

The total FMMA score (range, 0-66) on the stroke-impaired upper extremity was used to measure the motor improvements in this study. The outcomes were measured at 3 time points: at baseline (week 0), at completion of intervention (week 2), and 2 weeks follow-up (week 4).

Quantification of online MI-BCI performance

The calibration session consisted of 4 runs of 40 trials each for a total of 160 trials, and an inter-run break of at least 2 minutes was provided after each run (Figure 4(a)). Each run randomly comprised of 20 trials of MI of the stroke-affected upper limb and 20 trials of idle condition. Each trial lasted ~12 s and each run lasted ~8 minutes. The calibration session lasted ~1 hour inclusive of EEG setup time. A visual cue was used to prepare the subject, and subsequently another cue was used to randomly instruct the subject to perform either MI or idle. The EEG segment of 0.5 to 2.5 s from the instruction cue was then extracted to train a subject-specific MI detection model using the FBCSP algorithm.[25] No robotic feedback was provided in the calibration session.

The rehabilitation session comprised of an evaluation part and a therapy part. The evaluation part consisted of 40 trials that randomly comprised 20 MI of the stroke-affected upper limb and 20 idle condition (Figure 4(b)). Similar to the calibration session, a visual cue was used to prepare the subject, and subsequently an instruction cue was provided. The EEG segment of 0.5 to 4.5 s from the instruction cue was then extracted to classify the EEG segment to perform online detection of MI or idle using the FBCSP algorithm[25]. Once MI was detected, the robot was triggered to provide a feedback. The online accuracy of the evaluation part of the rehabilitation session was then recorded based on the detection of MI or idle condition compared to the instruction provided.

Quantification of ERD

The therapy part of each rehabilitation session consisted of 4 runs of 40 trials each for a total of 160 trials, and an inter-run break of 3-5 minutes was also given after each run (Figure 4(b)). Each trial lasted ~17-19 s and each run lasted ~13 minutes. Similar to the evaluation part of the rehabilitation session, prepare and instruction cues were provided to the subject. The EEG segment of 0.5 to 4.5 s from the instruction cue was then extracted to classify the EEG segment to perform online detection of MI. Once MI is detected, the robot was triggered to provide a feedback. The EEG segment of 0 to 8 s from the prepare cue was then extracted to perform offline ERD analysis.

ERD values in the offline EEG analysis were estimated from the change in the band power in the frequency band of the mu rhythm (8-13 Hz) from left (C3) and right (C4) channels in 2 to 6 s segment relative to a baseline of -1.5 to 0 s segment whereby the time are relative to the instruction cue. This time segment was selected to encompass the MI period performed by the subjects. The following method was used to compute the ERD strength value for each left and right channels:

1. Bandpass filtering of (8-13 Hz) on EEG time segment -2 to 6 s relative to prepare cue for all 160 trials in the therapy part of the rehabilitation session.
2. Squaring the bandpass filtered samples to obtain power samples.
3. Average power samples across all trials.
4. Compute power of baseline from average on time segment -1.5 to 0 s
5. Compute ERD/ERS strength values of channel *j* on time segment 2 to 6 s using[7]

$$S_j(t) = \frac{A_j(t) - R_j}{R_j} \times 100, \quad (1)$$

where $A_j(t)$ is the averaged power sample of time sample t of channel j from step 3, and R_j is the averaged power of baseline of channel j from step 4.

6. Compute the ERD strength value from the sum of the negative values for time samples t from 2 to 6 s of channel j using

$$E_j = \sum_{t \in [2,6]} \left(S_j(t) \mid S_j(t) < 0 \right) \quad (2)$$

The above method of computing the ERD strength followed closely the procedure provided by Pfurtcheller et al.[7] ERD values were defined as negative relative to the baseline, whereas ERS strength values were defined as positive.[7] As such, only negative values were included in the ERD analysis.

A laterality coefficient was then computed to assess the hemispheric asymmetries of the ERD pattern using

$$L = \frac{E_c - E_i}{E_c + E_i}, \quad (3)$$

where E_c and E_i denote the ERD strength value of the channel that is contra-lateral and ipsi-lateral to the stroke-affected hand respectively.

The laterality coefficient was used in Kaiser et al. to investigate hemispheric asymmetries of ERD and ERS in stroke.[32] A positive or negative *L* indicates higher or lower values respectively in the hemisphere contra-lateral to the stroke-affected hand.

Statistical Analysis

Analysis of Variance (ANOVA) was used to examine the demographic and baseline group differences. Two-sided t-tests were performed to analyze for significant motor improvements at weeks 2 and 4 from baseline at week 0 for tDCS and sham groups. Analysis of Covariance (ANCOVA) was used to examine the group differences at each time point between the two groups after adjusting for baseline differences. To compare the performance of MI-BCI and the ERD laterality coefficient between the two groups, the p-value of two samples t-test were computed between the subjects from the evaluation and therapy part of the 10 rehabilitation sessions respectively. In this case, we assumed that the data collected in one session from a subject is independent from the data from another session collected on a different day. The justifications for this assumption are:

1. The stimulation of a session on a subject is independent from other sessions for the same subject, since it had shown that that motor cortical excitability increased for up to 90 minutes after the end of stimulation.[33]
2. The performance of MI-BCI and the ERD laterality coefficient of one session from a subject is independent from other sessions for the same subject, since there is inherent non-stationarity in EEG across sessions record on different days from the same subject.[34]

RESULTS

Patients

Twenty-six out of 37 patients recruited passed the screening sessions, and 19 gave further consent and were recruited for randomization with 10 and 9 allocated to tDCS and sham group respectively. Details on the demographic of the patients are shown in Table 1. There were no significant baseline differences in the two groups in terms of age ($p = .40$), gender ($p = .17$), stroke type ($p = .43$), stroke nature ($p = .36$), affected limb ($p = .49$), Cerebrovascular Accident (CVA) to intervention ($p = .91$), BCI screening ($p = .13$), and FMMA at week 0 ($p = .46$).

Motor Improvements

Table 2 shows the FMMA score measured at weeks 0, 2 and 4 for the tDCS and sham groups. No significant FMMA score gains at week 2 compared to baseline at week 0 were observed: tDCS group (0.9 ± 3.0, $p = .36$), sham group (2.8 ± 4.0, $p = .07$). At week 4, significant FMMA score gains compared to baseline at week 0 were observed: tDCS group (5.0 ± 4.4, $p = .006$), sham group (5.4 ± 5.7, $p = .02$).

No significant intergroup differences were observed at any time point during the study after adjusting for baseline FMMA score at week 0: week 2 ($p = .243$) and week 4 ($p = .874$).

Online MI-BCI performance

Figure 5 shows a plot of the averaged online accuracies of detecting MI versus the idle condition for the tDCS and sham groups across the evaluation part of the 10 rehabilitation sessions. The results showed deviation of online accuracies across subjects and sessions, and the averaged accuracies of the subjects from the tDCS group across most of the 10 rehabilitation sessions are higher than the sham group. The averaged accuracy of classifying the MI of the stroke-affected upper limb versus the idle condition across the evaluation part of the 10 rehabilitation sessions from the tDCS group (62.9%) is significantly higher than the sham group (57.0%, $p = 0.002$).

ERD laterality coefficient

Figure 6 shows a plot of the averaged ERD laterality coefficient of the therapy part of the rehabilitation sessions for the tDCS and the sham groups. The results again showed deviation of the ERD laterality coefficient across subjects and sessions, and the averaged ERD laterality coefficient of the subjects from the tDCS group across most of the 10 rehabilitation sessions are higher than the sham group. The averaged ERD laterality coefficient of the therapy part of the 10 rehabilitation sessions from the tDCS group (0.050) is significantly higher than the sham group (-0.063, $p = 0.016$).

DISCUSSION

This study presents the results from a clinical study that investigated the effects of tDCS on EEG-based MI-BCI with robotic feedback compared to sham for upper limb stroke rehabilitation. Since it had been shown that motor cortical excitability increased for up to

90 minutes in subjects who received tDCS [33], this study investigated whether tDCS will facilitate motor improvements and MI performance in stroke patients that underwent MI-BCI with robotic feedback rehabilitation.

There were no significant motor improvements observed upon completion of 2 weeks of intervention in both the tDCS and sham groups. The results from a recent RCT yielded similar average FMMA score improvement of 1.1 from 11 stroke patients after 2 weeks, but increased to 4.5 after completing 4 weeks of MI-BCI with MIT-Manus robotic feedback intervention.[4] The results from another recent RCT yielded significant higher FMMA score improvement of 7.2 from 6 stroke patients after completing 6 weeks of MI-BCI with Haptic Knob robot for arm rehabilitation compared to an improvement of 4.9 from 7 patients who received 6 weeks of standard arm therapy.[35] The results from these studies indicate that 2 weeks intervention in this study may be too short to observe significant motor improvements. As a whole, no intergroup differences were found, which suggests there may be no additional benefit in adding tDCS to the MI-BCI training. However, this warrants further investigation due to the short intervention in this study.

The results on the therapy part of each rehabilitation session showed that the ERD laterality coefficient from subjects in the tDCS group was significantly higher than the subjects in the sham group. Since the standard deviations were large, the significant differences observed were most like from the first 3 sessions. A higher positive ERD laterality coefficient indicated higher ERD strength values in the ipsi-lesional hemisphere that is contra-lateral to the stroke-affected hand. The result is also consistent with studies that show significant increase in mu ERD after tDCS compared to sham. [17,18,20] The

mechanism of ERD is thought to be due to a decrease in synchrony of the underlying neuronal population.[7] Since anodal tDCS increases cortical excitability of the ipsilesional M1,[15] tDCS may result in more activated desynchronized neurons when MI is performed.[18]

The results on the evaluation part of each rehabilitation sessions showed that the averaged online accuracy of MI-BCI from subjects in the tDCS group was also significantly better than the subjects in the sham group. Although the results showed large deviations across subjects and across sessions, the results indicated that there is a significant effect of tDCS in improving the online accuracy of MI-BCI performance compared to sham. This significant improvement in online accuracies correlates with the higher positive ERD laterality coefficient observed because the FBCSP algorithm[25] used in this study performed spatial filtering to discriminate mental states that are characterized by ERD and ERS.[36] In the study by Wei et al., only a slight increase in averaged online accuracy of MI-BCI between pre- and post-anodal tDCS on healthy subjects was reported, but no significant difference was found despite a significant increase in ERD observed.[20] In contrast, significant improvement in online accuracy is observed in this study, which may be due to the relatively lower baseline ERD of stroke patients compared to healthy subjects.[18] The ERD may also be underestimated in this study because it was quantified on a trial-wise basis by comparing post-cue segments to pre-cue segments. This is because the subjects may be anticipating the cue, thereby causing some ERD in the pre-cue segment and diluting the effect in the post-cue segment.

The results on online accuracy of MI-BCI from subjects in both groups showed a trend of deterioration over time. Since only an initial calibration session was used to train the subject-specific MI detection model in this study, the deterioration may be due to the increasing session-to-session transfer non-stationarity [37] when the FBCSP algorithm[25] was used to detect MI in sessions that were days apart from the training session. Therefore, adaptation methods[37,38] are recommended to address this issue in future studies.

The limitations in our study are its small sample size, heterogeneity within subjects and the assumption of independence in the statistical test of the data collected from same subject for the 10 rehabilitation sessions. If the data collected from the same subject across the 10 rehabilitation sessions were assumed to be dependent, a repeated measure ANOVA will have to be performed. Performing this analysis would yield *p*-values of 0.19 and 0.15 for the online MI-BCI performance and ERD laterality coefficient respectively between the tDCS and sham group. These results are then not statistically significant due to the reduction of the sample size for analysis.

Finally, the clinical study had also collected secondary outcome measures such as resting motor threshold using Transcranial Magnetic Stimulation[39], grip strength[40], box and block test[41] and neuroimaging pre and post therapy for the tDCS and MI-BCI with robotic feedback stroke rehabilitation compared to sham. Detailed results on the secondary outcome measures and the analysis on the neuroimages will be reported in separate papers.

CONCLUSIONS

Although there are studies that have shown significant increase in mu ERD from the EEG in healthy subjects [17] and stroke patients,[18] we investigated whether 20 minutes of tDCS or sham stimulation prior will have a significant effect on 1-hour rehabilitation sessions of MI-BCI with robotic feedback rehabilitation. We performed a randomized clinical trial and collected data from 19 chronic stroke patients with moderate to severe upper extremity functional impairment that underwent 10 sessions of intervention, each comprised 8 minutes of evaluation and 1 hour of therapy. We found that the addition of tDCS did not result in additional motor improvements compared to sham. Nevertheless, we found that the averaged online accuracy of the evaluation part and averaged ERD laterality coefficient of the therapy part for subjects that underwent tDCS was significantly higher than sham. Hence the results suggest a role for tDCS in facilitating MI in stroke. The facilitation of MI may translate to enhanced sensorimotor integration and the efficacy of MI-BCI as a tool for motor recovery following stroke. It may also avail MI-BCI to stroke patients who initially fail the screening test for ability to operate MI-BCI. However, further investigations are necessary on a larger sample with a longer intervention period.

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SUPPLIERS

[a] Neuroscan Nuamps EEG Amplifier. Compumedics USA, Compumedics Neuroscan and Compumedics DWL, 6605 West W.T. Harris Blvd, Suite F, Charlotte, NC 28269, USA.

[b] MIT Manus Robot. Interactive Motion Technologies, 80 Coolidge Hill Road, Watertown, MA 02472 USA.

[c] neuroConn DC Stimulator. neuroConn GmbH, Grenzhammer 10, 98693 Ilmenau, Germany.

Figure 1 CONSORT Flow Diagram

Figure 2 Positions of EEG channel locations. The reference electrode is located on the Naison. Channels on the left and right hemisphere for offline ERD analysis are labelled blue and green respectively.

Figure 3 Setup of (a) transcranial Direct Current Stimulation (tDCS) and (b) EEG-based Motor Imagery Brain-Computer Interface (MI-BCI) with robotic feedback rehabilitation for stroke in a local hospital. The same setup is employed for sham.

Figure 4 Acquisition of EEG for online and offline analysis. (a) Timing of the motor imagery of the stroke-affected hand or background rest tasks for the calibration session before commencement of the therapy; (b) Timing of the motor imagery of the stroke-affected hand using on-line MI-BCI with robotic feedback for the rehabilitation session.

Figure 5 Plot on the online accuracies of detecting motor imagery (MI) of the stroke-affected hand versus the idle condition for the tDCS and the sham groups during online evaluation part of the rehabilitation sessions. The accuracies are computed online by performing session-to-session transfer using the FBCSP algorithm trained on data from the calibration session to the evaluation part of each of the 10 rehabilitation sessions. The horizontal axis represents the 10 rehabilitation sessions that the patients underwent. The vertical bar plots the standard deviations across subjects in each group.

Figure 6 Plot on the averaged ERD laterality coefficient of the therapy part of the rehabilitation sessions for the tDCS and the sham groups. The vertical axis represents the ERD laterality coefficient computed by averaging the ERD computed from 0 to 8 s of EEG of all the 160 trials of the MI-BCI with robotic feedback rehabilitation. The horizontal axis represents the 10 rehabilitation sessions that the patients underwent. The vertical bar plots the standard deviations across subjects in each group.

Table 1 Demographics and baseline characteristics by intervention

Table 2 Efficacy measures by FMMA scores for each intervention group (N=10 for tDCS, N=9 for sham)

Figure 1:

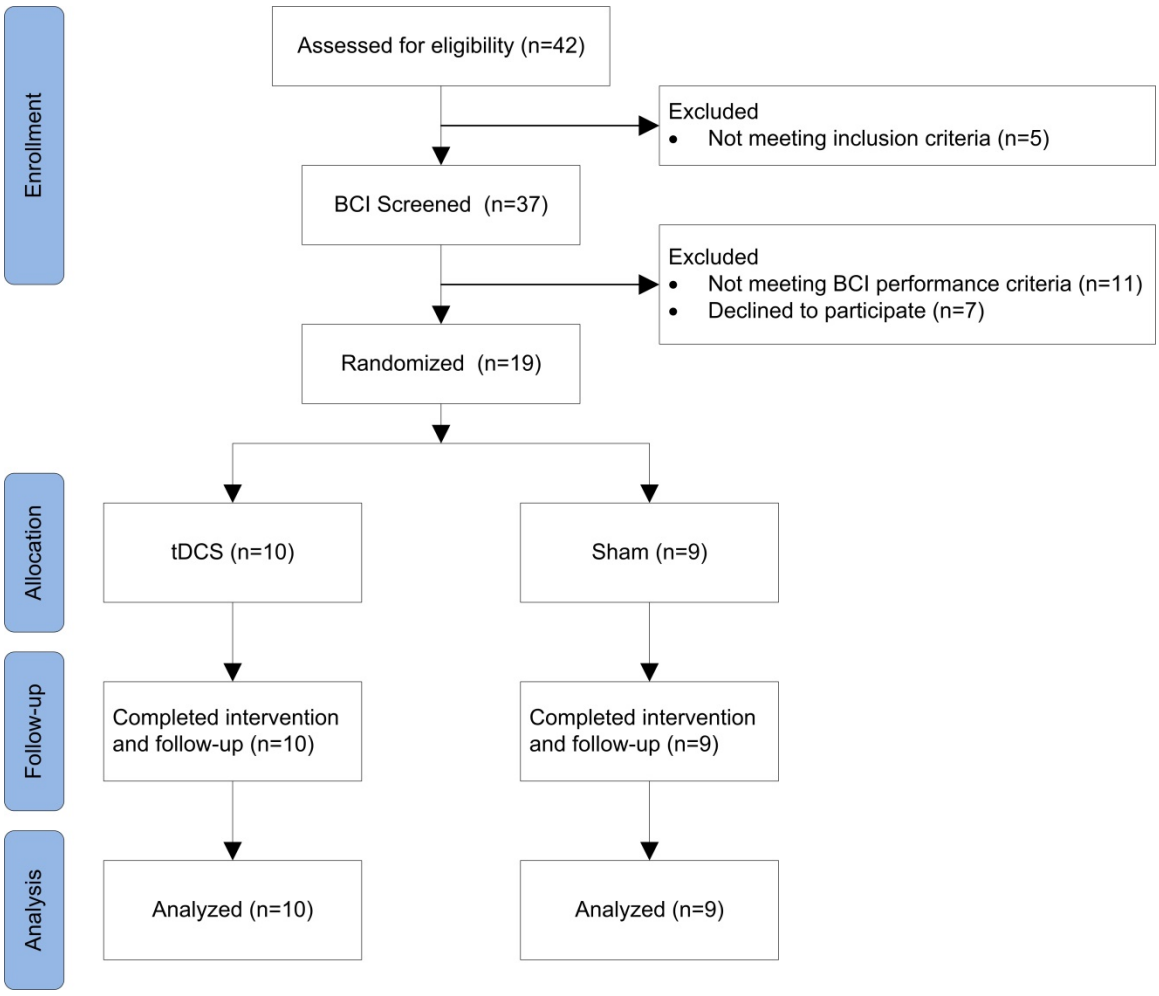

Enrollment
Assessed for eligibility (n=42)
Excluded
Not meeting inclusion criteria (n=5)
BCI Screened (n=37)
Excluded
Not meeting BCI performance criteria (n=11)
Declined to participate (n=7)
Randomized (n=19)
Allocation
tDCS (n=10)
Sham (n=9)
Follow-up
Completed intervention and follow-up (n=10)
Completed intervention and follow-up (n=9)
Analysis
Analyzed (n=10)
Analyzed (n=9)

Figure 2:

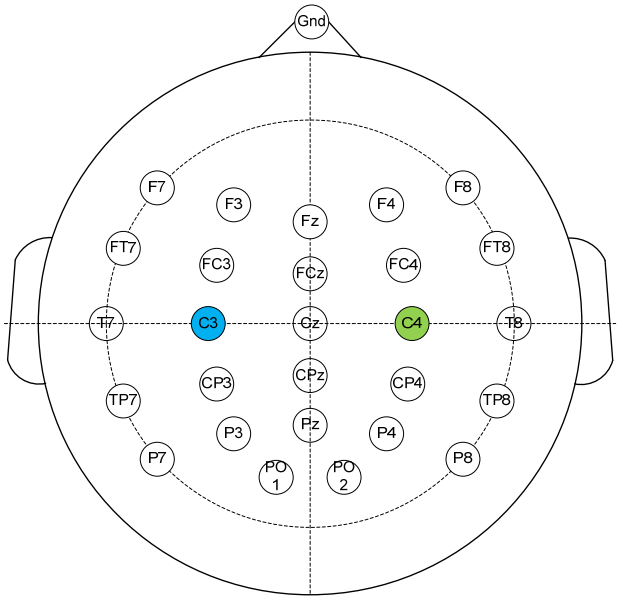
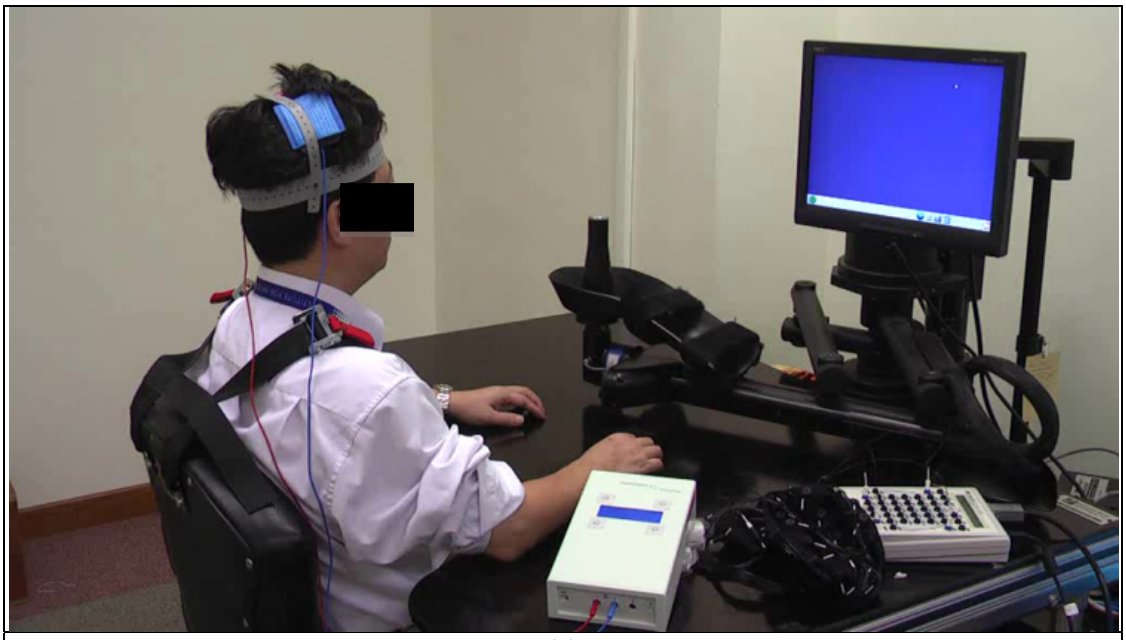

Gnd
F7
F3
Fz
F4
F8
FT7
FC3
FCz
FC4
FT8
T7
C3
Cz
C4
T8
CP3
CPz
CP4
TP7
TP8
P3
Pz
P4
P7
P8
PO 1
PO 2

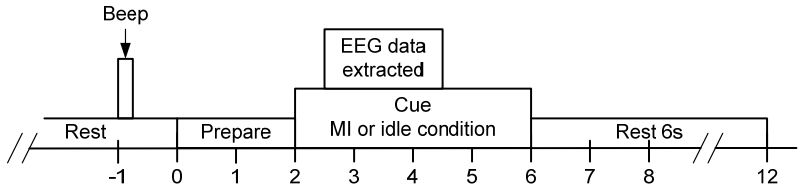
Figure 3:



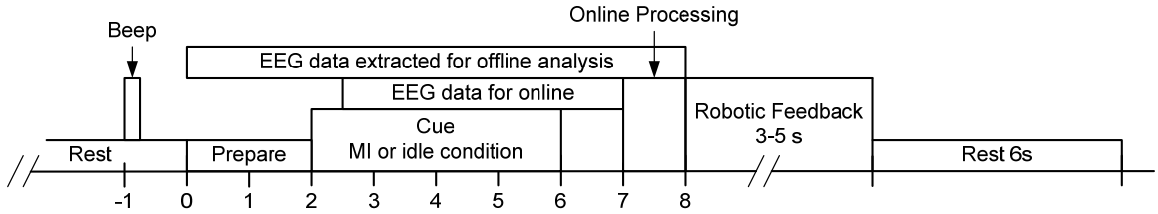
(a)

(b)

Figure 4:



(a) Calibration session before commencement of the therapy



(b) Evaluation and therapy parts of MI-BCI with robotic feedback rehabilitation session

Figure 5:

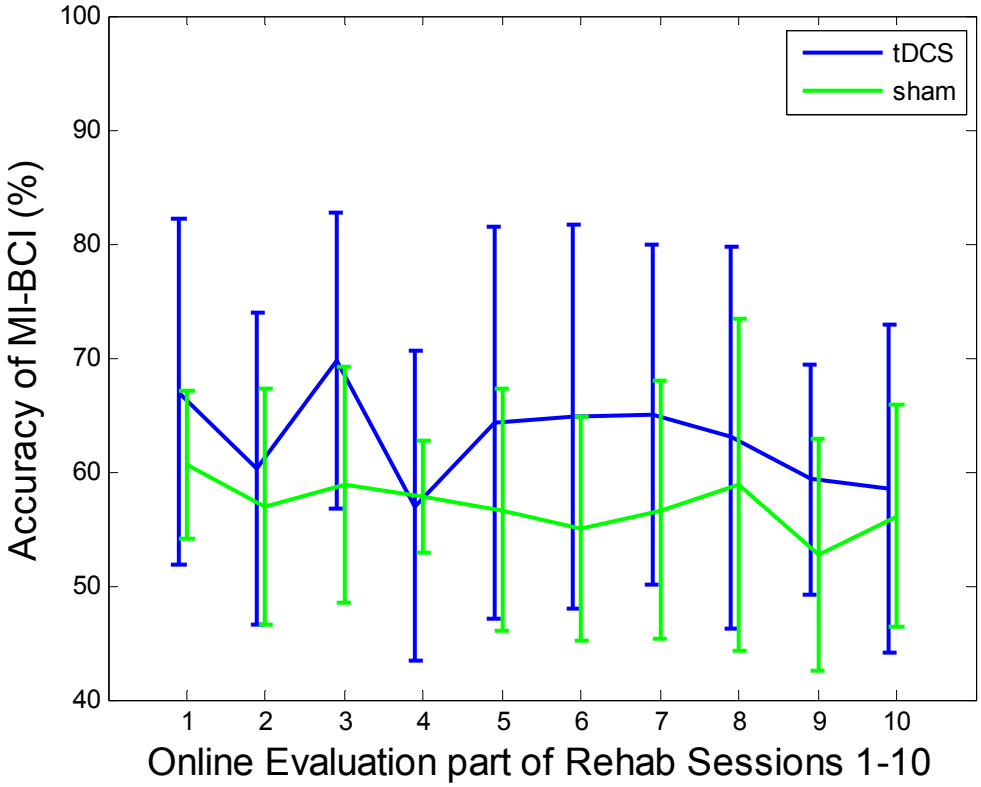

tDCS
sham
Accuracy of MI-BCI (%)
100
90
80
70
60
50
40
1
2
3
4
5
6
7
8
9
10
Online Evaluation part of Rehab Sessions 1-10

Figure 6:

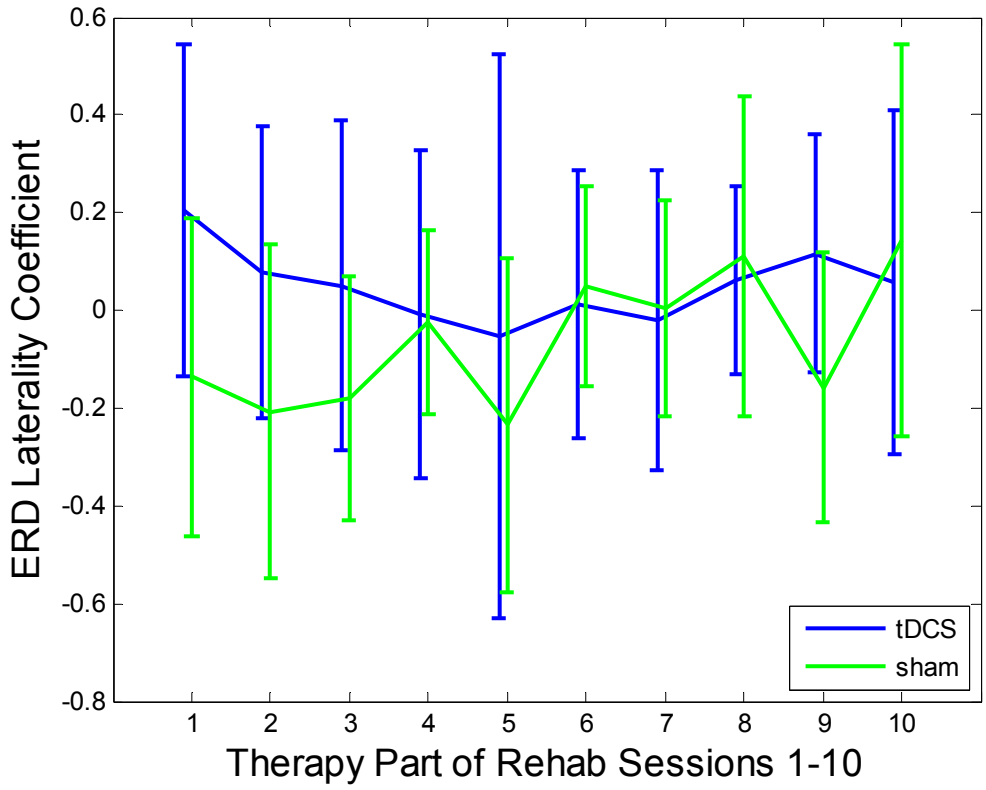

ERD Laterality Coefficient
0.6
0.4
0.2
0
-0.2
-0.4
-0.6
-0.8
1
2
3
4
5
6
7
8
9
10
Therapy Part of Rehab Sessions 1-10
tDCS
sham

Table 1:

		Intervention	
Variable	**Total**	**tDCS**	**sham**
N	19	10	9
Age (years)	54.1±10.6	52.1±11.7	56.3±9.5
Gender N(%)			
Male	14 (73.7%)	6 (60.0%)	8 (88.7%)
Female	5 (26.3%)	4 (40.0%)	1 (11.1%)
Stroke type N(%)			
Infarction	13 (68.4%)	6 (60.0%)	7 (77.8%)
Haemorrhage	6 (31.6%)	4 (40.0%)	2 (22.2%)
Stroke nature N(%)			
Cortical	1 (5.3%)	1 (10%)	0 (0%)
Subcortical	18 (94.7%)	9 (90%)	9 (100%)
Affected limb N(%)			
Right	11 (57.9%)	5 (50.0%)	6 (66.7%)
Left	8 (42.1%)	5 (50.0%)	3 (33.3%)
CVA to intervention (days)	1037±598	1052±722	1021±465
BCI screening	75.6±10.4	79.1±9.4	71.7±10.7
FMMA at week 0	34.0±7.9	35.3±7.8	32.6±8.1

CVA indicates Cerebrovascular accident; FMMA, Fugl-Meyer Motor Assessment

Table 2:

Outcome	Group	Baseline Week 0	Improvements relative to week 0 Week 2	Week 4
Upper Extremity (0~66)	tDCS	35.3±7.8	0.9±3.0	5.0±4.4
	Sham	32.6±8.1	2.8±4.0	5.4±5.7