INVITED PAPER

Brain–Computer Interface for Neurorehabilitation of Upper Limb After Stroke

This paper reviews strategies to use BCI technology for neurorehabilitation after stroke. It compares two strategies in three randomized control trials for upper limb rehabilitation.

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ABSTRACT | Current rehabilitation therapies for stroke rely on physical practice (PP) by the patients. Motor imagery (MI), the imagination of movements without physical action, presents an alternate neurorehabilitation for stroke patients without relying on residue movements. However, MI is an endogenous mental process that is not physically observable. Recently, advances in brain–computer interface (BCI) technology have enabled the objective detection of MI that spearheaded this alternate neurorehabilitation for stroke. In this review, we present two strategies of using BCI for neurorehabilitation after stroke: detecting MI to trigger a feedback, and detecting MI with a robot to provide concomitant MI and PP. We also present three randomized control trials that employed these two strategies for upper limb rehabilitation. A total of 125 chronic stroke patients were screened over six years. The BCI screening revealed that 103 (82%) patients can use electroencephalogram-based BCI, and 75 (60%) performed well with accuracies above 70%. A total of 67 patients were recruited to complete one of the three RCTs ranging from two to six weeks of which 26 patients, who underwent BCI neurorehabilitation that employed these two strategies, had significant motor improvement of 4.5 measured by Fugl-Meyer Motor Assessment of the upper extremity. Hence, the results demonstrate clinical efficacy of using BCI as an alternate neurorehabilitation for stroke.

KEYWORDS | Brain–computer interface (BCI); motor imagery; robotic; stroke rehabilitation

I. INTRODUCTION

Stroke is ranked as the third most common cause of disability worldwide, and the global burden of stroke is increasing [1]. Stroke survivors can partially recover their lost motor function from rehabilitation that involved repetitive and task-specific physical practice (PP) [2]. Since it is difficult or impossible for some stroke survivors to move the stroke-impaired limb during rehabilitation, motor imagery (MI), which is the mental process of imagination of movements without PP, represents an alternate rehabilitation approach [3], [4]. The rationale of performing MI arises from the neural correlation it shared with PP [5]. The main advantage of MI in rehabilitation is that stroke survivors who have difficulty in performing PP can still perform MI. However, while PP is observable, MI is an endogenous mental process. Hence, it is impossible to check the compliance of performing MI by stroke patients from simple observation during rehabilitation. As such, MI is delivered in rehabilitation by a large variety of manners, such as the use of audiotapes or one-to-one guidance by a therapist [6].

Recent advances in analysis of brain signals and improvements in computing capabilities have enabled people with motor disabilities to use their brain signals for communication and control without using their impaired neuromuscular system [7]. This technology, brain–computer interface (BCI), is useful in helping people who have suffered a nervous system injury by providing them with an alternative means of communication, mobility, and rehabilitation [8], [9]. It was found that neurophysiological

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phenomena called event-related desynchronization or synchronization (ERD/ERS) [10] are detectable from electroencephalogram (EEG) in a majority of stroke patients while performing MI [11]. Thus, EEG-based BCI can be used to objectively assess the performance of MI. In this way, stroke patients, who suffer from severe limb weakness, but are still able to imagine movements of the paretic hand can use BCI to trigger a contingent feedback upon the detection of MI-related brain signals [12]–[14]. By reestablishing contingency between cortical activity related to MI and feedback, the use of BCI might strengthen the sensorimotor loop and foster neuroplasticity that facilitates motor recovery [15], [16]. Hence, the use of BCI facilitates the alternate MI approach for neurorehabilitation in stroke.

There were numerous clinical studies that reported the use of BCI for stroke rehabilitation [17], [18]. The following reviews studies that reported clinical efficacy:

- Buch *et al.* [12] first used a magnetoencephalography (MEG)-based BCI to detect mu rhythm (9–12 Hz) to provide visual feedback in which a screen cursor was raised or lowered toward the direction of a target displayed on the screen. Once MI was detected, an orthosis attached to the stroke-impaired hand was triggered to provide a sensorimotor feedback. The results showed that six out of eight patients could achieve BCI control, but no significant motor improvements were found.
- Mihara *et al.* [19] studied ten patients who received near-infrared spectroscopy (NIRS)-based BCI with visual feedback versus ten other patients who received NIRS-based BCI with irrelevant feedback. The results showed that the former group yielded averaged motor improvements of 5.0 measured by Fugl-Meyer motor assessment (FMMA) [20] compared to 2.3 in the latter group. Both groups yielded statistically significant motor improvements, but the former group yielded significantly greater improvements in the hand/finger subscale measured by FMMA compared to the latter group.
- Ramos-Murguialday *et al.* [13] performed a randomized control trial (RCT) on 16 patients who used EEG-based BCI to detect motor intention with hand and arm orthoses feedback versus 14 other patients who used EEG-based BCI with random orthoses feedback. Both groups received physiotherapy. The results showed that the former group yielded averaged motor improvements of 3.4 measured by combined hand and modified arm FMMA compared to 0.4 in the latter group. The results also showed that the former group yielded statistically significant motor improvements, but not the latter group.
- Rayegani *et al.* [21] studied ten patients who received occupational therapy (OT) with additional neurofeedback therapy (neurofeedback can be viewed as an operant conditioning concept of BCI operation [22]) for improving hand function versus ten patients who received OT with additional biofeedback therapy and ten patients who received only OT. In the study, neurofeedback involved the detection of motor imagery from sensorimotor rhythm (12–18 Hz), theta (4–8 Hz), and beta (13–30 Hz) bands of EEG to provide a visual feedback to the subject. The results showed that all three groups had similar motor improvements measured by Jebsen-Taylor Hand Function Test [23].
- Ono *et al.* [24] studied six patients who received EEG-based BCI with simple visual feedback of the open and grasp animated picture of the hand versus six patients who received EEG-based BCI with somatosensory feedback using motor-driven orthosis to extend the fingers of the stroke-impaired hand. The results showed that three out of six patients in the latter group had motor improvements measured by the Stroke Impairment Assessment Set [25], but none in the former group improved.

Although a systematic review had attested that adding to PP is an effective intervention for stroke [26], there is still scanty evidence in terms of clinical efficacy to indicate the benefits of MI compared to PP in stroke rehabilitation [27]. The studies of using BCI in [13], [21], and [24] had demonstrated clinical improvements. However, two of the studies have added PP in the BCI intervention (physiotherapy in [13] and OT in [21]). One of the studies showed significant motor improvements in using BCI and PP compared to random feedback and PP [13], but the random feedback may decrease the motor improvements of the latter group. Furthermore, the other study [21] showed no significant motor improvements of BCI and PP compared to PP alone [21], Hence, there is still scanty details on how to integrate BCI as neurorehabilitation intervention for stroke as well as scanty clinical evidence to indicate its effectiveness when compared to PP.

In this review, we present two strategies of applying BCI for neurorehabilitation after stroke. We then present the results of three RCTs we have conducted that utilized these strategies for upper limb stroke rehabilitation. Finally, we present motor improvements from all patients enrolled in these three RCTs to investigate the clinical efficacy of BCI as an alternate neurorehabilitation for stroke.

II. STRATEGIES FOR BCI NEUROREHABILITATION

Robotics has been used in stroke rehabilitation since the 1990s, and numerous robotic devices, such as the InMotion Arm Robot (Interactive Motion Technologies Inc., USA, also known as MIT-Manus) and the Armeo Power (Hocoma, Switzerland), are now commercially available. In a recent systematic review on robotics for stroke rehabilitation, there is clear evidence that robotic interventions improve upper limb motor functions in stroke rehabilitation [28]. Moreover, a recent study by Klamroth-Marganska *et al.* [29] performed an RCT on 38 patients who received robotic intervention versus conventional therapy. The results showed that the former group yielded averaged motor improvements of 3.4 measured by FMMA compared to 2.0 in the latter group. The results also showed that the former group yielded statistically significant motor improvements than the latter group, but it was noted that the absolute difference between the two groups was small and, hence, the clinical relevance was questionable.

There are several modes of human–robot interaction in robotic stroke rehabilitation, such as active, passive, assistive, active-assistive, passive-mirrored, corrective, path guidance, and resistive. (The reader is referred to [28] for details.) For example, in assistive mode, the robot provides assistance to the subjects in completing a voluntary movement task. In passive mode, the robot performs the movement without any voluntary movement by the subject. Thus, the basic strategy of robotic stroke rehabilitation is to provide PP on the stroke-impaired limb of the stroke patient, with or without voluntary movement, in the form of a sensorimotor feedback shown in Fig. 1.

An example of a robot that provides PP for stroke rehabilitation is the MIT-Manus, which is a robot with two degrees of freedom that provides horizontal elbow and forearm reaching exercises using an 8-point clock face-drawing interactive video game [30]. A small yellow circle on the screen indicates the current position of the robotic arm that holds the patient's stroke-impaired arm, and a big red circle indicates a target position. During rehabilitation, the stroke-impaired upper limb of a subject is strapped to the MANUS robotic exoskeleton. The subject is required to move the stroke-impaired upper limb from the center toward the target on the screen and back along a predetermined trajectory. If the subject cannot perform the movement task, the MIT-Manus robot will provide assistance to move the subject's upper limb toward the target. The MIT-Manus robot, which delivers intense PP training with sensorimotor feedback, has been shown to yield motor improvements in stroke patients that matched the motor improvements of patients who received intense PP training delivered by therapists [31].

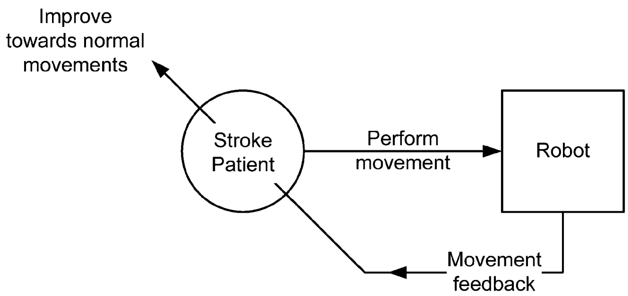

Fig. 1. ***Strategy of using a robot to provide intensive PP for stroke rehabilitation.***

A. BCI Triggered Feedback

Fig. 2 shows a strategy of using BCI to detect MI to provide feedback for neurorehabilitation after stroke. This strategy was first employed by Buch *et al.* [12] using an MEG-based BCI. Once MI was detected, an orthosis attached to the stroke-impaired hand was triggered to provide sensorimotor feedback. This was also employed by Mihara *et al.* [19] using a NIRS-based BCI to provide visual feedback, and by Ramos-Murguialday *et al.* [13] using an EEG-based BCI to provide sensorimotor feedback with a hand and arm orthoses. Ono *et al.* [24] also employed this strategy to study the efficacy of EEG-based BCI to provide

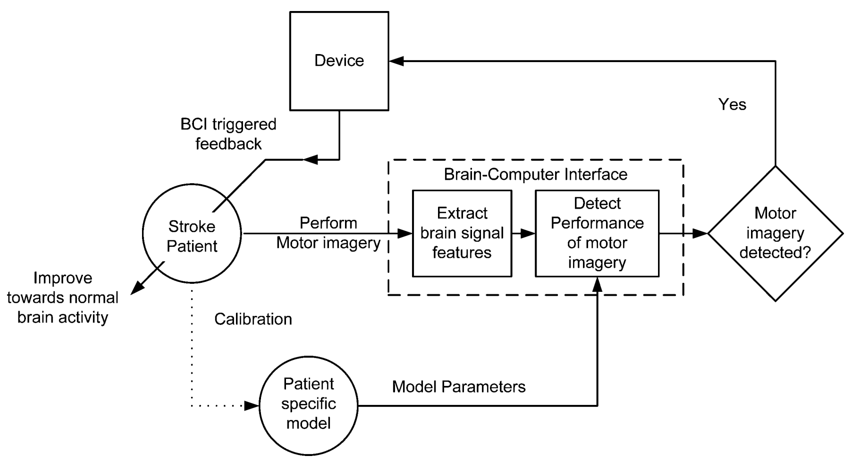

Fig. 2. ***Strategy of using the brain–computer interface (BCI) to detect motor imagery (MI) to trigger a feedback for neurorehabilitation in stroke.***

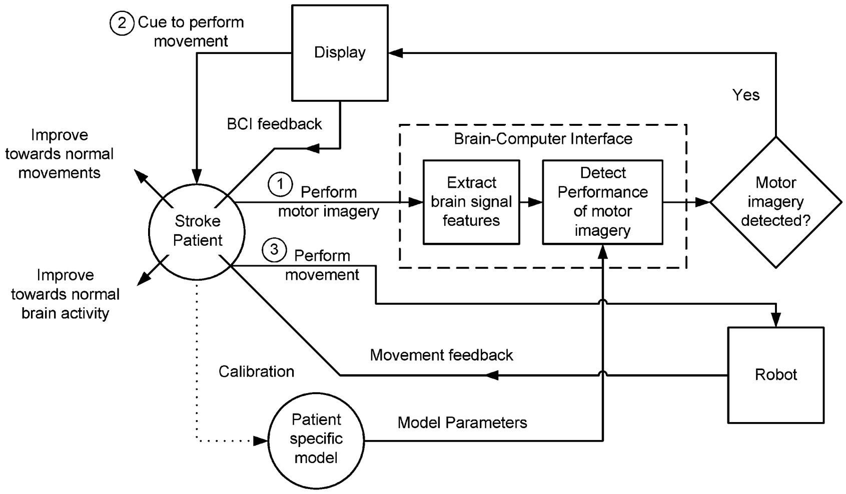

Fig. 3. *Strategy of using the BCI to detect MI with a robot to provide concomitant MI and PP for neurorehabilitation in stroke.*

simple visual feedback versus somatosensory feedback using a motor-driven orthosis.

An advantage in the strategy of using BCI to provide feedback shown in Fig. 2 is that any form of feedback can be deployed. However, the result from a large RCT of 121 stroke patients had demonstrated that there was no significant difference between patients who performed MI, without using BCI, compared to patients who received standard arm therapy in early poststroke. This raised an important issue on the clinical benefit of MI in stroke rehabilitation [27]. In addition, it was further pointed out that integrating MI in rehabilitation had yielded an inconclusive clinical outcome [6], [27], [32].

B. Concomitant BCI and PP

Practically, stroke survivors who have residue movements, or recovered some motor abilities from stroke rehabilitation will have little difficulty in performing PP. Furthermore, a systematic review of 15 studies in the literature from 1985 to 2009 had shown that MI is effective for upper-limb rehabilitation after stroke only when added to PP [26]. Hence, another strategy of using BCI for neurorehabilitation after stroke is by integrating BCI with a robot to provide concomitant MI and PP shown in Fig. 3. In this strategy, once MI is detected using the BCI, feedback is provided to cue the stroke patient to perform voluntary movement while the stroke-impaired limb is strapped to a robotic end-effector. In this way, if the subject has difficulty in performing the voluntary movement task, the robot can provide assistance in the form of a sensorimotor feedback as shown in Fig. 1.

The main advantage of using the BCI-triggered feedback strategy in Fig. 2 compared to PP in Fig. 1 is that it facilitates the rehabilitation of stroke patients without a residual motor function. Nevertheless, the best way to improve motor function is to have more physical practice [33]. This underlying principle of more practice is better, which can be readily observed from the years it takes for a child to reach and grasp like an adult [34]. Thus, once a stroke patient recovered some motor function, PP is still required to recover further. In contrast, the Concomitant BCI and PP strategy in Fig. 3 combines MI with PP to facilitate the rehabilitation of a larger population of stroke, with or without a residue function. Hence, a plegic stroke patient who recovered some motor function using this strategy can perform PP to improve further.

III. RANDOMIZED CONTROL TRIALS

We had conducted three RCTs that employed two strategies of using BCI for stroke rehabilitation shown in Figs. 2 and 3 over six years from April 1, 2007 to June 31, 2013. This section provides a description of the three RCTs.

A. EEG Signal Recording

In all the three RCTs, EEG measurements from 27 channels were collected using the NuAmps EEG acquisition hardware (http://www.neuroscan.com) with unipolar Ag/AgCl electrodes channels, digitally sampled at 250 Hz with a resolution of 22 b for voltage ranges of $\pm$130 mV. EEG recordings from all channels were bandpass filtered from 0.05 to 40 Hz by the acquisition hardware.

B. Detecting MI Using EEG-Based BCI

The main challenge in detecting MI using EEG-based BCI is the huge intersubject variability in the EEG with respect to the brain signal characteristics [35]. Hence, in all three RCTs, we employed the Filter Bank Common Spatial Pattern (FBCSP) algorithm [36] to construct a patient-specific model from a calibration session in order to detect MI as shown in Figs. 2 and 3.

The FBCSP algorithm had been shown to be an effective algorithm in detecting MI from EEG in BCI Competition IV held in 2008 [37]. (The reader is referred to [36] for details on the FBCSP algorithm.) The algorithm comprises four progressive stages of EEG processing to compute the patient-specific model. The first stage employs a filter bank that decomposes the EEG into multiple frequency passbands. The second stage performs spatial filtering using the common spatial pattern (CSP) [38]. Each pair of bandpass and spatial filters in the first and second stages computes the CSP features that are specific to the bandpass frequency. The third stage selects discriminative CSP features based on the subject's task using the mutual information-based best individual feature (MIBIF) algorithm [39]. The fourth stage employs a classifier to model and classify the selected CSP features.

C. First RCT on BCI With Robotic Feedback

We conducted the 1st RCT of using EEG-based BCI for neurorehabilitation after stroke over 2.5 years from April 1, 2007 to October 30, 2009 [11], [40]. Since stroke patients suffer neurological damage to their brains, the portion of their brain that is responsible for generating ERD/ERS can be compromised. Thus, we first sought to investigate the extent of detectable brain signals on a population of stroke patients.

We collected EEG data from 54 stroke patients of which 46 performed MI and eight performed finger tapping. We analyzed the EEG collected using the FBCSP algorithm described in Section III-B. The results showed that only six patients yielded accuracies of detecting MI at chance level. Hence, the results showed that a majority of stroke patients (87%) can use EEG-based BCI for stroke rehabilitation [11]. Despite the high percentage of usability, the results showed that a BCI screening session is still necessary to identify subjects who can use the EEG-based BCI system. Hence, in the subsequent RCTs that we had conducted, we performed a BCI screening session to recruit patients who can use BCI.

In the BCI screening session, a total of 160 trials of EEG that randomly comprised 80 MIs of the stroke-affected upper limb and 80 idle conditions were collected from each patient. The patients' abilities to perform MI were then evaluated based on 10×10-fold cross-validations of these 160 trials of EEG data using the FBCSP algorithm described in Section III-B. Patients with classification accuracy $>$ 58% (95% confidence estimate of the accuracy at chance level) were deemed to have passed BCI screening.

In addition, we sought to compare the efficacy of the EEG-based BCI with robotic feedback using the strategy illustrated in Fig. 2 versus intense robotic training using the commercially available MIT-Manus robot using the strategy illustrated in Fig. 1. The MIT Manus robot was chosen for its positive results in hemiplegic stroke [41]. In this RCT, we analyzed the motor improvements of 12 sessions of 1-h BCI with robotic feedback compared to robotic upper limb stroke rehabilitation for four weeks. Clinical efficacy, in terms of motor improvements, was measured using upper extremity FMMA scores preintervention at week 0, mid-intervention at week 2, end-intervention at week 4, and follow-up at week 12.

D. Second RCT on BCI With Robotic Feedback

We conducted the second RCT over three years from January 1, 2011 to January 1, 2014 [42]. While other existing studies had demonstrated motor improvements in stroke patients using transcranial direct current stimulation (tDCS) [43], [44], we sought to investigate whether tDCS could facilitate the stroke patients' ability to operate BCI with robotic feedback and subsequently the efficacy in poststroke motor recovery. The setup of BCI with robotic feedback in this trial employed the strategy in Fig. 2 that was similar to the first RCT.

In this RCT, we analyzed the motor improvements of ten sessions of 20 min of tDCS compared to sham-tDCS prior to 1-h BCI with robotic feedback using the MIT-Manus robot for upper limb stroke rehabilitation for two weeks. Clinical efficacy, in terms of motor improvements, was measured using upper extremity FMMA scores preintervention at week 0, end-intervention at week 2, and follow-up at week 4.

E. Third RCT on BCI With Concomitant MI and PP

We conducted the third RCT recently over 2.5 years from January 1, 2011 to June 30, 2013 [45]. We sought to investigate the clinical benefits of concomitant MI and PP using the strategy shown in Fig. 3 by using an EEG-based BCI coupled with a haptic knob (HK) robot [46], [47]. We investigated the hypothesis of whether that this strategy could facilitate the beneficial effects of therapist-assisted arm mobilization for stroke patients compared to robot-assisted PP shown in Fig. 1 and to standard arm therapy (SAT).

In this RCT, we analyzed the motor improvements of 18 sessions of intervention over six weeks, three sessions per week, 90 min/session. The primary outcome measure was upper extremity FMMA scores measured preintervention at week 0, mid-intervention at week 3, end-intervention at week 6, and follow-up at weeks 12 and 24.

IV. RESULTS FROM CLINICAL TRIALS

A. First RCT on BCI With Robotic Feedback

The first RCT screened 54 chronic stroke patients, of whom 48 passed the BCI screening. Among those who passed the BCI screening, 38 had performed well with accuracies above 70%. Subsequently, 26 of those who passed BCI screening were recruited for randomization [40], and the remaining 22 declined further participation. A total of 11 patients were randomized to the BCI-Manus group that underwent EEG-based BCI with robotic feedback intervention. The remaining 15 patients were randomized to the Manus group that underwent MIT-Manus robotic intervention. The group size was not balanced because simple randomization was performed. Twenty-five patients completed the study and follow-up with one dropping out from the Manus group.

The results showed that the BCI-Manus and Manus groups improved with an average FMMA score of 4.5 and 6.3 end-intervention at week 4, respectively, measured relative to the baseline FMMA before intervention. Clinically important changes in the upper extremity FMMA were estimated in the range from 4.25 to 7.25 to have an effect on important functional tasks [48]. Hence, there were statistically and clinically significant motor improvements in both groups, but no significant intergroup differences were found. (The reader is referred to [40] for details on the results of the RCT.)

The result of 11 stroke patients from the BCI-Manus group using the BCI-triggered feedback strategy illustrated in Fig. 2 is further analyzed in Section IV-D.

B. Second RCT on BCI With Robotic Feedback

The 2nd RCT screened 37 chronic stroke patients, of whom 26 passed the BCI screening. Among those who passed the BCI screening, 18 patients had performed well with accuracies above 70%. Subsequently, 19 of those who passed BCI screening were recruited for randomization [49], and the remaining seven declined further participation. A total of ten patients were randomized to the tDCS group that underwent tDCS and EEG-based BCI with robotic feedback intervention. The remaining nine patients were randomized to the sham-tDCS group that underwent EEG-based BCI with robotic feedback intervention. All 19 patients completed the study and follow-up.

The results showed that the tDCS group and sham-tDCS groups improved with an average FMMA score of 0.9 and 2.8 end-intervention at week 2 respectively, measured relative to the baseline FMMA before intervention. There were statistically significant motor improvements in both groups, but these improvements were not clinically significant and no significant inter-group differences were found. The results also showed that the online BCI accuracies and laterality coefficients from the tDCS group were significantly higher than the sham group. (The reader is referred to [49] for details on the results of the RCT.)

The result of nine stroke patients from the sham-tDCS group using the BCI-triggered feedback strategy illustrated in Fig. 2 is further analyzed in Section IV-D. The result from ten patients in the tDCS group is not included in further analysis since the use of tDCS was a confounding factor that improved the online BCI accuracies of the patients in this group.

C. Third RCT on BCI With Concomitant MI and PP

The third RCT screened 34 chronic stroke patients, of whom 29 passed the BCI screening. Among those who passed the BCI screening, 19 had performed well with accuracies above 70%. Subsequently, 22 of those who passed BCI screening were recruited for randomization [45], and the remaining seven who passed BCI screening declined further participation. A block randomization was performed with a block size of three to balance the group size. A total of seven patients were randomized to the BCI-HK group that underwent the EEG-based BCI and HK robot to perform concomitant MI and PP intervention using the strategy illustrated in Fig. 3. Another eight patients were randomized to the HK group that underwent robot-assisted hand grasping, and knob manipulation PP intervention shown in Fig. 1. The remaining seven patients were randomized to the SAT group that underwent repetitive task training [50], focusing on forearm pronation-supination movements incorporating wrist control and grasp-release of various objects. All three groups received 30 min of therapist-assisted arm mobilization following the principles of the professionally recognized Neurodevelopmental Treatment Approach for stroke rehabilitation [51] for each session of intervention. Twenty-one subjects completed the study and follow-up with one dropout from the BCI-HK group.

The results showed that the BCI-HK, HK, and SAT groups improved with an average FMMA score of 7.2, 7.3, and 4.9 end-intervention at week 6, respectively, measured relative to the baseline FMMA before intervention. There were statistically and clinically significant motor improvements in all groups, but no significant intergroup differences were found. Significantly greater FMMA improvements were observed in the BCI-HK group compared to the SAT group mid-intervention at weeks 3 and post-intervention at weeks 6 and 12. However, no significant greater FMMA improvements were observed in the HK group compared to the SAT group. (The reader is referred to [45] for details on the results of the RCT.)

The result of six stroke patients from the BCI-HK group using the Concomitant BCI and PP strategy shown in Fig. 3 are further analyzed in Section IV-D.

D. Results From All RCTs

The three RCTs that we had conducted performed EEG-based BCI screening for 54, 37, and 34 chronic stroke patients, respectively. A total of 48, 26, and 29 patients passed the screening in the RCTs, and a total of 38, 18, and 19 had good performance with accuracies above 70%, respectively. Hence, a total of 125 stroke patients were screened, of whom 103 passed the BCI screening and 75 had good performance. The results thus show that 82% of the chronic stroke patients can use the EEG-based BCI system for neurorehabilitation, of which 60% of them had performed well with accuracies above 70%.

Fig. 4 shows the clinical outcome measured by the FMMA score of the upper extremity on stroke patients recruited to receive EEG-based BCI stroke rehabilitation. The clinical outcomes were analyzed from all 11 patients

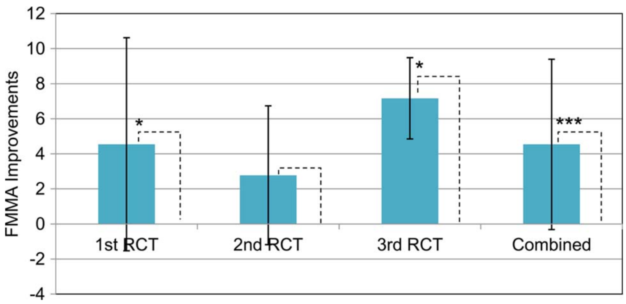

Fig. 4. ***Clinical outcome in FMMA improvements of stroke patients who received EEG-based BCI intervention in three clinical trials (n = 11, 9, 6), and all patients combined (n = 26). The vertical bar plots the standard deviations across subjects in each group.*** $^{*}P < 0.05$, $^{***}P < 0.001$.

who completed the BCI-Manus intervention in the 1st RCT, all nine patients who completed the sham-tDCS intervention in the 2nd RCT, and all six patients who completed the BCI-HK in the 3rd RCT. The clinical outcomes of all the 26 patients from these three RCTs were then combined to perform an overall analysis. Paired *t*-tests were performed on the FMMA scores' improvements after the intervention that were relative to the baseline FMMA before intervention.

The results showed motor improvements of 4.55 ± 6.07, 2.78 ± 3.96, and 7.17 ± 2.32 from the three clinical trials, respectively. The results from 2 of the 3 clinical trials were both statistically and clinically significant. The combined results from all three clinical trials showed a statistically significant improvement of 4.54 ± 4.86 from 26 stroke patients.

V. CONCLUSION

In this paper, we presented a strategy to use BCI to detect MI to trigger a feedback, and another strategy to use BCI to detect MI with a robot to provide concomitant MI and PP for neurorehabilitation after stroke. We described the three RCTs that we had conducted that employed these two strategies.

In the three RCTs, we performed a BCI screening of a total of 125 chronic stroke patients over six years. In our studies, a patient passed the BCI screening if the accuracy of detecting MI using the FBCSP algorithm [37] was above the chance level. This process is more simple and objective compared to the use of subjective tools, such as the Kinesthetic and Visual Imagery Questionnaire [52], to assess whether the patient is able to imagine vivid images of movement [6]. The results showed that a majority 82% of stroke patients could use EEG-based BCI for neurorehabilitation, and 60% had performed well with accuracies above 70%. The 18% BCI illiteracy in stroke patients who had BCI accuracy of less than 58% at the chance level is close to our initial finding in [11], and falls within the estimated range of 15%–30% commonly found in the BCI Laboratory [53]. As shown in the study by Ramos-Murguialday *et al.* [13], stroke patients who received BCI with hand and arm orthoses feedback had significant improvements, but not those who received random feedback. Since a BCI with random feedback is functionally similar to a BCI with an accuracy of about 50% at chance level, the results from the study showed that BCI accuracy had an effect on the improvements of the patients. Therefore, it is important to select patients who passed the BCI screening for stroke rehabilitation. However, it is noted that the passing accuracy at the chance level may be too low for optimal detection of MI compared to the recommended accuracy of 70% for BCI in communication and control [54]. Nevertheless, in another study by Mihara *et al.* [19], patients who received BCI with random feedback also had significant improvements. The significant improvements obtained, despite the low BCI accuracy, may be due to a higher level of engagement by the patient to perform motor imagery of the stroke-impaired upper limb for rehabilitation. Therefore, high accuracy may not be a crucial factor in neurorehabilitation since the BCI is used to provide feedback and not as a communication and control system that requires a high degree of accuracy [55].

We also presented the motor improvements measured using FMMA scores of the upper extremity from the three RCTs. The first and second RCTs employed the strategy of using an EEG-based BCI to drive a robot to provide a sensorimotor feedback for neurorehabilitation in stroke. The patients in the first RCT had significant motor improvements measured by FMMA scores, but not the patients in second RCT. This is due to the shorter intervention of two weeks in the second RCT compared to four weeks in the first RCT. Hence, the results showed that the length of intervention may affect the outcome of the studies. However, the results of the first RCT showed motor improvements that were similar to the strategy of using a robot to provide PP without using EEG-based BCI to detect MI [40]. This result is consistent with the study in [27] that showed no significant difference between patients who performed MI without using BCI compared to patients who performed PP. Hence, the results from the first and second RCTs on using BCI with robotic feedback were not entirely promising.

The third RCT employed the other strategy of using EEG-based BCI and a robot to provide concomitant MI and PP for neurorehabilitation in stroke. The patients in the third RCT had significant motor improvements, and the averaged improvement across the patients was greater than the first RCT. This may be due to the longer six weeks of intervention compared to the first and second RCTs. Nevertheless, these patients had motor improvements that were significantly better than patients who received PP from SAT, and patients who received PP using a robot were not significantly better than those who received PP from

SAT [45]. Hence, the results from the third RCT on using BCI with a robot to provide concomitant MI and PP were more promising than using BCI with a robot to provide a sensorimotor feedback in the first and second RCTs.

Overall, 26 patients who received EEG-based BCI neurorehabilitation in the three RCTs had significant motor improvements. This overall result demonstrates the clinical effectiveness of the two strategies in using EEG-based BCI for neurorehabilitation in stroke.

From the results, the length of intervention appeared to be a confounding factor. Hence, we recommend adopting an intervention of at least six weeks, three sessions per week, to observe significant improvements in the use of BCI for neurorehabilitation after stroke. Furthermore, the patients in the three RCTs who received EEG-based BCI neurorehabilitation either performed MI of the left or right upper limb. On the other hand, four actions of MI can be detected using BCI, namely, left hand, right hand, foot, and tongue [56]. Since MI of the foot and tongue are detectable, BCI for neurorehabilitation can also be extended to lower limbs [57] and dysphagia [58], respectively. Moreover, dry EEG electrodes have now been successfully used for visual-evoked potential BCI [59]. Although the use of dry EEG electrodes for MI BCI was found to be inferior to gel-based EEG electrodes [60], future development of dry EEG for MI BCI may help to reduce the setup time for neurorehabilitation. Last but not least, research to address the BCI inefficiencies of current algorithms [61] is crucial so that more patients will be able to use BCI for stroke rehabilitation. ■

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