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Brain-Computer Interface-based Soft Robotic Glove Rehabilitation for Stroke

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Abstract— Objective: **This randomized controlled feasibility study investigates the ability for clinical application of the Brain-Computer Interface-based Soft Robotic Glove (BCI-SRG) incorporating activities of daily living (ADL)-oriented tasks for stroke rehabilitation.** ***Methods:*** **Eleven recruited chronic stroke patients were randomized into BCI-SRG or Soft Robotic Glove (SRG) group. Each group underwent 120-minute intervention per session comprising 30-minute standard arm therapy and 90-minute experimental therapy (BCI-SRG or SRG). To perform ADL tasks, BCI-SRG group used motor imagery-BCI and SRG, while SRG group used SRG without motor imagery-BCI. Both groups received 18 sessions of intervention over 6 weeks. Fugl-Meyer Motor Assessment (FMA) and Action Research Arm Test (ARAT) scores were measured at baseline (week 0), post-intervention (week 6), and follow-ups (week 12 and 24). In total, 10/11 patients completed the study with 5 in each group and 1 dropped out.** ***Results:*** **Though there were no significant intergroup differences for FMA and ARAT during 6-week intervention, the improvement of FMA and ARAT seemed to sustain beyond 6-week intervention for BCI-SRG group, as compared with SRG control. Incidentally, all BCI-SRG subjects reported a sense of vivid movement of the stroke-impaired upper limb and 3/5 had this phenomenon persisting beyond intervention while none of SRG did.** ***Conclusion*****: BCI-SRG suggested probable trends of sustained functional improvements with peculiar kinesthetic experience outlasting active intervention in chronic stroke despite the dire need for large-scale investigations to verify statistical significance.** ***Significance:*** **Addition of BCI to soft robotic training for ADL-oriented stroke rehabilitation holds promise for sustained improvements as well as elicited perception of motor movements.**

Index Terms**—Brain-Computer Interface, EEG, Glove, Motor Imagery, Soft Robotics, Stroke Rehabilitation.**

I. INTRODUCTION

STROKE is the leading cause of disability in many parts of the world. Upper limb impairment is common in stroke and can have a devastating impact on the daily lives of stroke survivors. Conventional rehabilitation strategies targeting motor impairments in stroke survivors include the multidisciplinary treatments of physical therapy and occupational therapy. Recently, the use of techniques such as constraint-induced movement therapy (CIMT) [1-7], mirror therapy (MT) [8-13], and robot-aided therapy utilizing end effector system, e.g., Amadeo [14, 15] and MIT-Manus [16, 17], exoskeleton, e.g., Armeo [18] or user intention detection, e.g., electromyographic signal [19, 20] has been explored to improve motor outcomes [21]. While such approaches have been reported to be efficacious in a number of studies, they largely require a minimum level of residual movement of the paretic limbs to carry out, and this excludes a large proportion of stroke patients, such as in the case of CIMT [22]. The use of brain-computer interface (BCI)-based motor imagery (MI) presents an alternative means of rehabilitation to address the issue faced by patients with negligible residual motor function. MI is the mental rehearsal of physical movement tasks, and during the performance of MI, distinct features known as event-related desynchronization (ERD) and synchronization (ERS) are detectable on the subject's electroencephalogram (EEG) [23]. These EEG features can be used as input to a BCI [24]. BCIs, broadly speaking, are processes that acquire, analyze, and translate brain signals into control commands of output devices [25]. Upon receiving this input signal arising from MI, the BCI can be typically made to trigger contingent sensory feedback for the subject. These feedback may be manifested in several forms, such as visual representations on a computer screen [26-28], or somatosensory and kinesthetic forms delivered through robotic [29-31], haptic [32, 33], or Neuromuscular Electrical Stimulation (NMES) systems [25, 34, 35].

BCI-based MI protocols, coupled with sensory feedback, are designed specifically to manipulate the cortical reorganization of the lesioned hemisphere [25, 36] for beneficial neuroplasticity, which forms the neural basis for motor recovery post-stroke [37-41]. In BCI-based MI rehabilitation, the sensorimotor rhythm power decrease in attempting to move

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the paretic limb is associated with an increase in motor cortex excitability [42, 43], GABAergic inhibitory interneurons disinhibition[44] and increased excitability of the corticospinal tract [45] and of the spinal motorneuron pool [46]. Coupling of a feedback system such as robotic actuators or virtual reality avatars closes the loop between cortical activity (motor intent) and movement [30, 47, 48], allowing subjects to purposefully control sensorimotor oscillations [49], and thereby producing afferent feedback activity that might restore corticospinal and corticomuscular connections [50].

Several authors have reported the results of clinical studies of BCI-based stroke rehabilitation approaches where robotic actuators and visual feedback were provided as sensory feedback [29, 30, 32, 33, 51-53]. Among the more recent examples, Frolov et al [29] reported a randomized control trial on 55 stroke patients in the BCI group, who received MI-BCI intervention with contingent hand exoskeleton-driven opening movements of the paretic hand, versus 19 stroke patients in the control group that utilized hand exoskeleton-driven opening movements of the paretic hand independent of brain EEG activity. Their results showed that a higher proportion of patients in the BCI group improved their Action Research Arm Test (ARAT) and Fugl-Meyer Motor Assessment (FMA) scores (21.8% and 36.4% respectively) as compared with the control group patients (5.1% and 15.8% respectively). In another recent study, Wang et al [53] reported a randomized control trial on 13 chronic stroke patients undergoing EEG-based, combined with action observation, BCI robot-hand training (BCI group) versus 11 chronic stroke patients undergoing robot-hand training without action observation and EEG-BCI (Control group). Their results showed that long-term significant improvement in upper-limb motor functions was only found for patients in the BCI group.

It is notable that in most of these BCI studies utilizing robotic feedback in the protocol, the robotic actuators used are typically driven by rigid linkages or joints, which subject the patient's hand into a single plane of motion that may feel unnatural and uncomfortable. As examples, three BCI studies [51, 52, 54] utilized the commercially-available MIT-Manus (Interactive Motion Technologies USA, Watertown, MA) as the robotic feedback component in the BCI protocol, which comprises a fixed robotic device with a planar workspace. To address these restrictions imposed by the use of contemporary rehabilitation robots, soft materials have been increasingly explored in the fabrication of robotic exoskeletons, giving rise to a class of exoskeletons termed as 'soft wearable robots', which are designed to be conform better to human limbs, and are lightweight and portable [55-57]. Several of the recent soft robotic devices developed for assistive and rehabilitative functions for the upper extremity include soft robotic gloves [58-61], elbow sleeves [62, 63], and a whole arm exoskeleton [64].

An aspect of neurorehabilitation that has been increasingly incorporated into modern approaches is that of task-specific and meaningful training. An element of skilled motor learning, in addition to repetition quantity, has been found to be important for cortical reorganization to occur and as such, rehabilitation should focus on tasks meaningful to the patient [65-67].

Building upon these insights provided by previous stroke rehabilitation work and in attempting to address some of the limitations of current BCI-based protocols, a stroke rehabilitation system was developed, which integrated EEG-based BCI-assisted motor imagery with an assistive soft robotic glove and task-specific visual feedback. Compared with conventional robotic systems, the soft robotic glove allows the free motion of the hand and fingers in unactuated directions and is also lighter in weight and more portable. With the help of a computer-based training system, we have also concurrently incorporated hand training in activities of daily living (ADL) for the subjects, thus achieving task-specific training. We therefore hypothesize that the combination of BCI-assisted MI, soft-robotic based, task-specific ADL training and the more vivid visual, kinesthetic and proprioceptive feedback provided by this system could potentially enhance the effects of beneficial neuroplasticity in a cumulative sense and provide a more pronounced improvement in upper limb motor function.

A preliminary version of this work has been reported in conference abstracts for 15th Congress of the European Forum for Research in Rehabilitation [68].

II. MATERIALS AND METHODS

A. *Ethics Statement*

This work was funded by the Biomedical Research Council (reference number: 1619077006), Agency for Science, Technology and Research, Singapore. Ethics approval was obtained from the Institution's Domain Specific Review Board, National Healthcare Group, Singapore (clinical trial registration number: NCT03277508 in ClinicalTrials.gov). All participants gave their informed consent prior to enrolment for this study.

B. *Study Design*

This was a single-blinded randomized controlled feasibility study. The total intervention period was 6 months (24 weeks), including 6 weeks of intervention (3 sessions per week, total 18 sessions) and 2 post-intervention reviews at the 12th and 24th week.

We recruited a total of 11 participants from the stroke outpatient clinic of a local hospital. Inclusion criteria were: age of 55-90 years regardless of lesion size; the occurrence of stroke was to be at least 6 months prior to the clinical trial; FMA scores of 10-45 out of 66; possessing ability to follow command and sit upright for 1.5 hours; cognitively intact; and should have scored sufficiently during BCI screening. We excluded participants with recurrent stroke, hemi-spatial neglect, severe spasticity, contracture, deformity, and poor skin conditions.

Participants were randomly assigned into two different intervention groups: BCI-assisted Soft Robotic Glove (BCI-SRG) group; or the Soft Robotic Glove (SRG) group. The BCI-SRG group's intervention involved the use of EEG-based MI integrated with the soft robotic glove. On the other hand, the SRG group underwent an exoskeleton intervention, which involves the manual activation of the soft robotic glove without EEG-based MI control. Each group received 18 sessions of

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intervention over 6 weeks and underwent 120-minute intervention per session which comprises 30-minute standard arm therapy and 90-minute experimental therapy (BCI-SRG or SRG). The details of these interventions and therapies are provided in the following sections.

The outcome measures assessed in this study were the Fugl-Meyer Assessment (FMA) for upper extremity [69-71], and the Action Research Arm Test (ARAT) [72]. All the participants' baseline outcome measures were assessed on the 0th week and post-intervention assessment was done on the 6th week. There were no further interventions after the completion of 18 sessions in the first 6 weeks. There were 2 post-intervention assessments of outcome measures on the 12th and 24th week to evaluate the post-interventional effects. In total, there were four outcome measure assessments conducted on the 0th, 6th, 12th, and 24th week. All assessments were conducted at the hospital by an occupational therapist who was blinded against the grouping of the subjects.

A flowchart of the subjects' progress through the phases of the clinical trial is provided in Fig. 1.

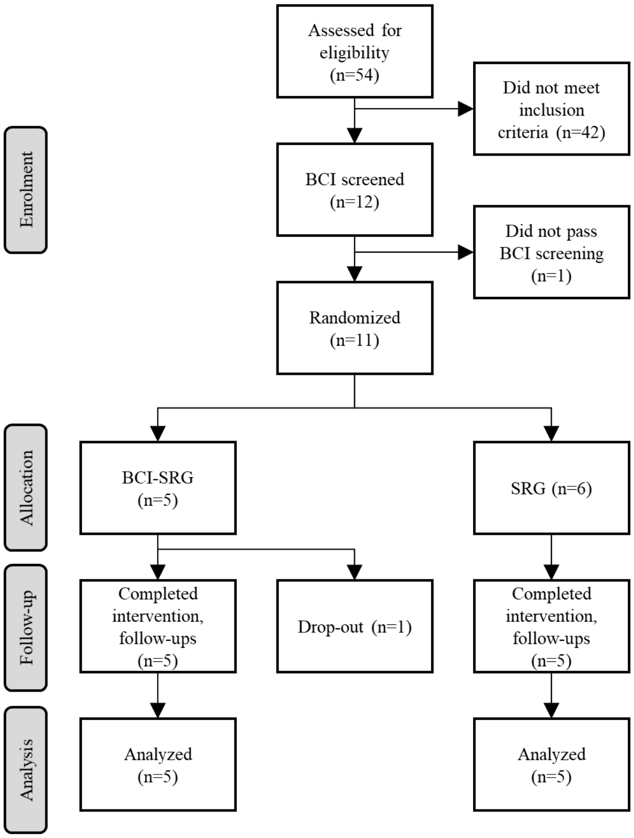

Fig. 1. CONSORT Diagram: a flow from recruitment through follow-up and analysis

C. *The BCI-assisted Soft Robotic Glove Technology*

1) *System Overview*

The BCI soft robotic glove system (Fig. 2) comprises several integrated modules to allow for the control of the soft robotic glove using subject-generated motor imagery: an EEG acquisition module; a BCI module; a robotic glove control module; a visual feedback module; and the soft robotic glove. In a typical BCI-SRG trial, a prompt for the subject's motor intent in carrying out a specified task is provided for the subject through the visual feedback module (computer screen). Upon seeing the prompt, the subject, whose EEG signals are collected via the donned EEG cap, then performs motor imagery. Successful motor imagery (manifested as ERD/ERS on the subject's EEG) is detected by the EEG acquisition module and immediately a signal is communicated simultaneously to both the robotic glove control module and the visual feedback system. The robotic glove control system responds by activating the soft finger actuators on the glove, thereby assisting the subject to achieve the desired hand posture for carrying out the task. In tandem, the visual feedback system presents a visual acknowledgement to the subject that the motor intent is detected and shows an animation of successful task execution. In essence, through this system, both visual and mechanical feedbacks are elicited from motor imagery input. A typical setup is shown in Fig. 2.

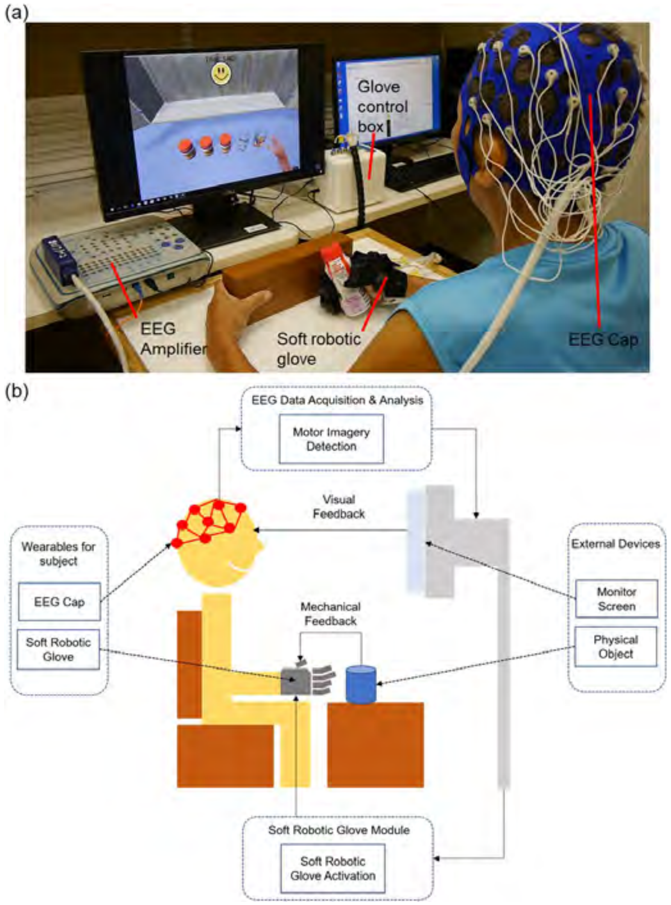

Fig. 2. Setup of BCI-assisted soft robotic glove (BCI-SRG) intervention for stroke rehabilitation at a local hospital (a), with (b) depicting an illustrated overview. The setup comprises a EEG cap, EEG amplifier, and soft robotic glove. The system will sense the subject intent and translate it into direct control of the soft robotic glove to achieve a desired hand configuration

2) *EEG Acquisition and Processing*

In this study, the EEG feature used in the BCI was the event-related desynchronization/synchronization (ERD/ERS) arising from the performance of MI. Scalp EEG data were collected using the medical-grade Neurostyle NS-EEG-D1

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(Manufacturer: Neurostyle Pte Ltd, Singapore) device with 24 unipolar Ag/AgCl channels placed in the international 10-20 system positioning with the reference at mastoid (Fig. 3). The EEG was digitally sampled at 256Hz with a resolution of 24 bits for voltage ranges of ±300mV.

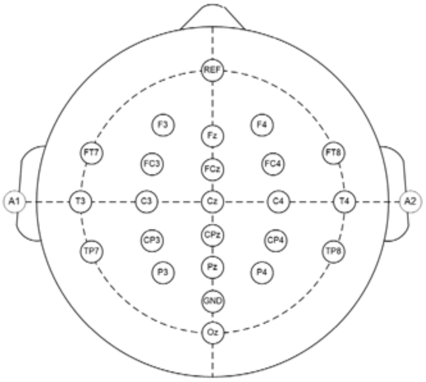


Fig. 3. Location of EEG channel according to the international 10-20 system position

The Filter Bank Common Spatial Pattern (FBCSP) algorithm was used to process and detect the ERD/ERS arising from MI [73]. The algorithm consisted of four key stages of EEG processing to construct a subject-specific MI detection model. First, a filter bank decomposed the EEG signal into multiple frequency pass bands using a total of 9 band-pass filters, namely, 4 to 8 Hz, 8 to 12 Hz, 12 to 16 Hz, 16 to 20 Hz, 20 to 24 Hz, 24 to 28 Hz, 28 to 32 Hz, 32 to 36 Hz, and 36 to 40 Hz. Second, the common spatial pattern (CSP) algorithm was applied to detect the ERD/ERS from the filtered EEG signal in the event of MI whereby each pair of band-pass and spatial filters computed the CSP features that were specific to the bandpass frequency range. The third stage generates m pairs of computed CSP features for each frequency band, from which k discriminative CSP features were selected to build a subject-specific model. Lastly, a Fisher's linear discriminant classifier was used to obtain the accuracy of the model, which was also the overall BCI accuracy in detecting MI.

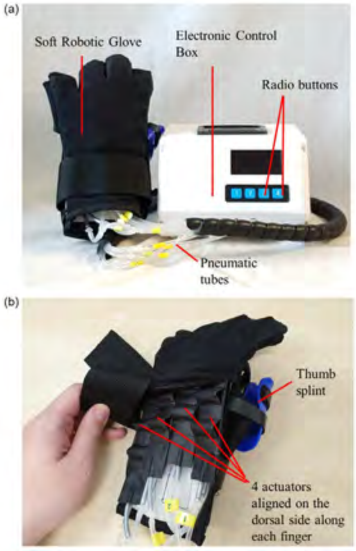


Fig. 4. Soft Robotic Module components: (a) entire setup; (b) close-up of glove embedded bidirectional actuators of the soft robotic glove and thermoset thumb splint.

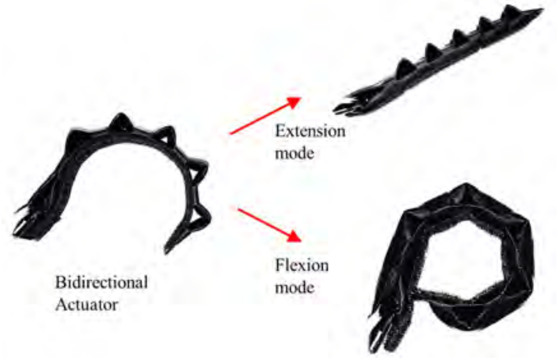


Fig. 5. Two different modes of the bidirectional actuator, the basic element of movement in the soft robotic glove.

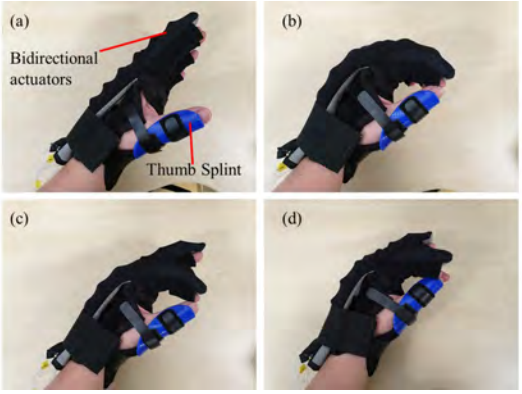


Fig. 6. Coordination of actuator activations allow for: (a) full extension; (b) full flexion grasping; (c) 2-finger pinching; (d) 3-finger tripod pinching.

Notably, the EEG data could not distinguish the motor intent to move individual fingers. As such, the individual finger movement for each ADL task was predefined by the computer program. In short, the EEG processing system detected only the motor intent in a binary fashion to initiate the preprogrammed movement.

3) *Soft Robotic Module*

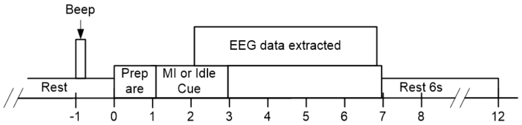
The soft robotic glove module [74], comprising the robotic glove control box and the soft robotic glove, was responsible for providing mechanical feedback to the subject. The soft robotic glove was constructed entirely using fabrics, with four actuators on the dorsal side of the glove, aligned with the four digits (excluding the thumb), and a thermoset plastic was used like a splint to hold the thumb in opposition with the four digits (Fig. 4b). Due to the misalignment and immobility of most stroke survivors' thumbs, this was necessary to allow the subjects to grasp and manipulate objects. Each of the actuators of the four digits was bidirectional, having two separate components to allow for either straightening or bending [74, 75](Fig. 5). The actuators were pneumatically driven, and the supply of air pressure to either of the two components (straightening or bending) allowed the actuator to be configured correspondingly. By acquiring a straightened or bent configuration, the actuator provided the necessary forces to extend or flex digits, respectively. Coordination of the straightening and bending of all four actuators enabled a variety of hand postures, such as grasping, 2-finger pinching or tripod pinching, which were used in different activities (Fig. 6). This task of coordinating which actuator to straighten and which to bend was the purpose of the soft robotic control box (Fig. 4a), which is an electronic control box that uses a microcontroller to control an air compressor and valves leading to each actuator component. The air compressor was the power source of the actuator, while the valves acted as gates for actuator activation. Upon receiving input, the microcontroller relayed the information to switch on and off the air compressor and valves, which resulted in the desired configuration of the soft robotic glove.

D. BCI Screening Session

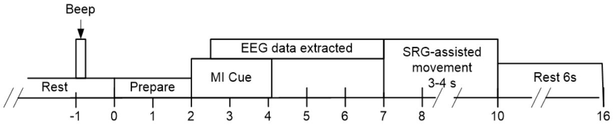
Prior to starting the interventions, all participants underwent a BCI screening session, and only successful participants were randomized into the BCI-SRG or SRG group. The purpose of the screening session was to ensure that the system was able to detect the kinesthetic MI performed by the subject. The subject's BCI accuracy rate (computed by the system) must exceed 57.5% to pass the screening. Our previous clinical trial [76] indicated that most subjects can pass the screening if they are not cognitively impaired and do not fall asleep during the session. During each of these sessions, 4 runs of EEG data corresponding to the performing of two types of tasks, MI and idling, were collected. Each run comprises 20 trials of MI and 20 trials of resting (idle) task (order was randomized), making a total of 40 trials and a break of 2 minutes was given after each run. Visual cues were provided on the computer screen for prompting subjects to carry out the MI task or resting (idle) task (Fig. 7). For the MI task, the subjects were instructed to perform upper-arm kinesthetic MI by imagining moving their stroke-affected hand repeatedly while minimizing any bodily movement. For the resting (idle) task, the subjects were instructed to keep still and look straight at the blank computer screen. The timing for events during the screening session is shown in Fig. 8a.

(a) MI task cue (b) Idling cue

Fig. 7. Visual cue for screening / calibration session.



(a) Screening and calibration sessions



(b) Therapy session

Fig. 8. (a) Timing of the kinesthetic motor imagery of the stroke-affected hand or background rest (idle) tasks for the calibration session before commencement of the therapy; (b) Timing of the kinesthetic motor imagery of the stroke-affected hand with on-line soft robotic glove feedback for the therapy session.

E. BCI-SRG Intervention Procedures

The intervention progression for BCI-SRG participants is mapped out in Fig. 9. BCI-SRG participants had to first undergo a preintervention screening and calibration session on Week 0. The purpose of the calibration session was to collect EEG data from the subject for training a subject-specific model for subsequent therapy sessions, which allowed the system to identify the brain signal of the subject when they were performing MI (Fig. 8).

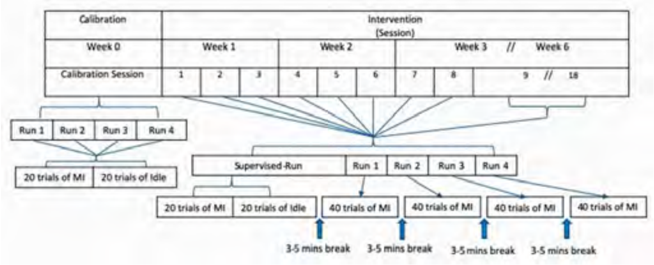
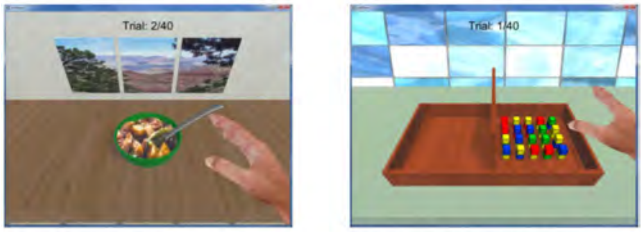


Fig. 9. BCI-SRG Intervention progression

The therapy sessions were conducted after the calibration session. There were a total of 18 sessions over the span of 6 weeks, at a frequency of 3 sessions per week. Each therapy session comprised single supervised run, and 4 ADL-oriented task runs. An inter-run break of 3-5 minutes was given after each run. The purpose of the supervised run was to collect more EEG data from the subject to further train the subject-specific model for subsequent therapy sessions. This was necessary because an individual's EEG waveforms varied at different times and collating more EEG data helped to improve the

(a) Week 1: Scanning goods (b) Week 2: Shelving items

(c) Week 3: Moving towel (d) Week 4: Pouring drinks



(e) Week 5: Lifting spoon (f) Week 6: Picking blocks

Fig. 10. Six different set of Activities of daily living (ADLs) task are performed by the subject for 18 sessions over 6 weeks (3 sessions per week)

subject-specific model. The supervised run was identical to single run performed during the calibration session (and pre-intervention session), as described in the preceding section.

During the ADL-oriented task runs, participants were instructed to perform MI of activity-specific tasks. There were 6 different ADL-oriented tasks enacted through a virtual arm and virtual objects (Fig. 10), which formed the visual feedback for the participants. Each week, different tasks were given, which included: scanning goods (week 1), moving an object upward to a cabinet (week 2), using two hands to move a towel (week 3), pouring of water into a cup (week 4); eating action (week 5) and fine motor movement of picking up a small block using two fingers (week 6).

The display of the virtual arm on the screen did not mirror the actual position of the subject's arm. The visual display of the movement of the virtual arm upon successful detection of MI was preprogrammed and standardized for the six ADL tasks (Fig. 10). The MI task was involved in imagining arm movements and was matched to the performance of the particular ADL for the session. During the MI task, subjects were instructed to imagine moving their stroke-affected arm and fingers to carry out the task. No assistance was provided for the participants with regards to arm movement, specifically referring to movement of the elbow or shoulder. The only assistance came from the soft robotic glove in moving the fingers. This was because the design and intent of the ADL tasks were to emphasize the use of fine motor skills involving the fingers. Though movements of the arm in vertical or horizontal plane were inevitable in some tasks, they were minimized so as not to require large movements by participants.

Each ADL-oriented task run comprised 40 trials. During each trial, the subjects were tasked to perform upper-arm kinesthetic MI of their stroke-affected hand with on-line visual and SRG feedback. The cue for performing MI is shown visually on-screen, and the participants had to imagine moving their stroke-affected hand to carry out the ADL-oriented task while minimizing voluntary head and body movements. The subjects were given two attempts to perform the respective MI task, if MI was still not detected, the system activated the SRG. Fig. 8b shows the timings of events for single trial. Each trial lasted ~16 seconds and each run lasted ~11 minutes. Each therapy session lasted ~1.5 hours inclusive of EEG setup time.

F. The Manual Soft Robotic Glove Technology

The manually operated soft robotic glove replaced the EEG-acquisition and BCI module with radio buttons (as shown in Fig. 4a), allowing for the manual operation of the soft robotic glove through selecting a set of predefined options via button-control. This system was utilized in the SRG intervention. The radio buttons were located on the control box of the soft robotic glove system and presented options for activating full grasp, pinch, tripod pinch, and full extension of the soft robotic glove. These different options represented the actuation profiles for the soft robotic glove relevant for assisting in carrying out the ADLs. The user selected the desired glove actuation mode from the menu displayed on the control box's built-in screen, and this was relayed to the pneumatic-valve control system to activate the specific actuators on the soft robotic glove.

G. SRG Intervention Procedures

The SRG group followed the same exercise tasks as BCI-SRG group (Week 1: scanning goods; Week 2: shelving items; Week 3: moving towel; Week 4: pouring drinks; Week 5: lifting spoon; Week 6: picking blocks). However, the SRG group used the soft robotic glove to perform the exercise tasks without motor-imagery.

The manual SRG intervention's dosage for the rehabilitation exercises were matched to the BCI-SRG intervention. The therapy session consisted of 1 run of 20 trials (matching the supervised run of the BCI intervention) followed by 4 runs of 40 trials each for a total of 180 trials, and an inter-run break of 3-5 minutes was also given after each run.

H. Standard Arm Therapy

Both groups received a standard hand therapy which was provided by an occupational therapist. It was based on the Graded Repetitive Arm Supplementary Program (GRASP) [77], which included stretching, arm strengthening, hand strengthening, coordination, and hand skill exercises. The GRASP was developed in Canada and it is widely used in many rehabilitation facilities worldwide. There are 3 levels for GRASP program depending on residual hand function post-stroke.

The therapist assessed each participant's hand function individually and allocated the participant to a suitable level of GRASP program based on evaluation on the first session. The appropriate GRASP program was administered to the participant during every session of the intervention and was conducted after the experimental intervention for 30 minutes. The therapist reviewed the participant every 2 weeks for exercise progression. The therapist was also blinded to the grouping.

I. Data Analysis

Due to a relatively small sample size in our study, non-parametric statistical methods were used in the analyses. Mann-Whitney *U* test was used to examine the demographic and baseline group differences, as well as intergroup differences in FMA and ARAT scores at different time points post-intervention. Wilcoxon signed-rank test was used to examine paired outcomes at different time points within the same group. In all analyses, statistical significance is set at <0.05. All statistical analyses were carried out using R [78]. The minimal detectable change (MDC) and the minimally clinically important difference (MCID) were also utilized to estimate the clinical improvements [79].

J. Post-Trial Questionnaire

A post-trial survey was conducted during the 24th week follow-up session to gather general feedback from the subjects on the clinical trials, their self-perceived performance in activities of daily living, as well as any experiences they might have encountered in the course of the clinical trials.

In particular, throughout the course of the trials, subjects of the BCI-SRG group reported that they were sporadically experiencing sensations in which they felt that their paretic hands were moving, though, when in fact there were no visible movements occurring. There were no such incidents reported by the SRG group. Though not being included in the original study plan, a questionnaire was newly designed and applied in the post-trial survey, referring to relevant questionnaires regarding dream and hallucination [80], [81], to characterize and quantify this phenomenon.

The questionnaire consists of 10 multiple-choice questions which required all subjects to respond if they experienced sensations of moving hands (before, during and after the trials), the time of the day at which it had occurred, a general description of the type of sensation, the duration of each episode of sensation, the frequency of such episodes, the intensity of the sensation, and if there had been any noticeable physical movements in their hands. The entire questionnaire can be retrieved via the following link: https://github.com/chengzyn/bci-srg-manuscript/blob/master/BCI-SRG_questionnaire.pdf.

III. RESULTS

A. Subject Enrolment

Twelve subjects were found to be eligible and subsequently screened for their ability to use EEG-based MI BCI. During screening, the EEG data showed 1 subject achieving accuracies that were lower than chance level (57.5%) and was excluded. The remaining 11 subjects gave their consent and were randomized into 2 intervention groups as follows: BCI-SRG (5 subjects), and SRG (6 subjects). Ten subjects completed the study and follow-up with 1 drop-out from the SRG group. The study was terminated in April 2019.

Table I shows the demographic of the 10 subjects who completed the study. Altogether, there were 5 men and 5 women [mean age 61.9 years (56 – 69)], mean stroke duration, 683.5 days (197 – 1279). There were no statistically significant differences between groups for baseline characteristics at week 0 as determined by Mann-Whitney *U* test.

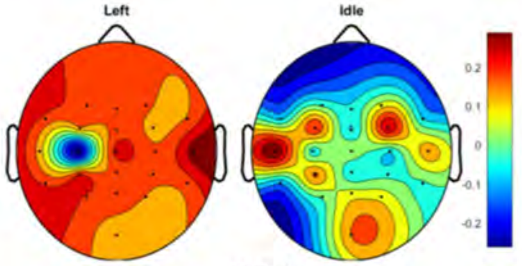
TABLE I
DEMOGRAPHICS AND BASELINE CHARACTERISTICS OF SUBJECTS BY INTERVENTION

	BCI-SRG (n=5)	SRG (n=5)
Age	62.4±4.7	61.4±4.5
Gender (male/female)	3/2	2/3
Stroke type: (infarct/hemorrhage)	3/2	5/0
Duration since stroke (days)	476.8 ±302.0	890.2 ±257.23
Baseline FMA-UE	24.2±7.01	30±7.84
Baseline ARAT	5. ±3.42	8.8±7.56

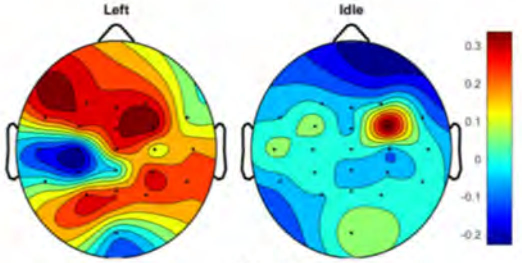
* denotes statistically significant difference between two groups

B. EEG Spatial Patterns and Features

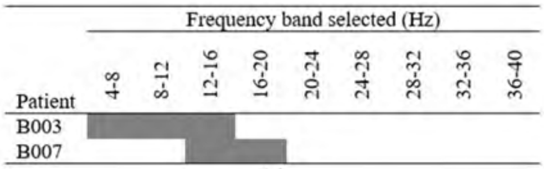
The EEG from the calibration sessions of patients in the BCI group were used to compute a subject-specific calibration model using the FBCSP algorithm [73]. This EEG analysis was performed similar to that reported in [32]. Fig. 11(a) shows the EEG spatial patterns from patient B003 who performed MI of left stroke-impaired hand versus the idle condition. The pattern for detecting MI-related brain signals of left hand showed an ipsilateral negative region on the left hemisphere around the motor cortex area. The pattern from this region corresponded to ERD respectively for performing left hand motor imagery [82].



(a) B003



(b) B007



	Frequency band selected (Hz)								
Patient	4-8	8-12	12-16	16-20	20-24	24-28	28-32	32-36	36-40
B003	■	■	■						
B007			■	■					

(c)

Fig. 11. EEG Spatial patterns and frequency bands used to classify motor imagery of stroke-impaired hand versus idle condition. (a) Spatial patterns of B003 (b) Spatial patterns of B007, (c) frequency bands used for patients B003 and B007. Blue and red colors in the spatial patterns correspond to negative (ERD) and positive (ERS) values respectively.

Fig. 11(b) shows the EEG spatial patterns from patient B007 who also performed MI of left stroke-impaired hand versus the idle condition. Similarly, the patterns for detecting MI-related brain signals of left hand showed an ipsilateral negative region on the left hemisphere around the motor cortex area. The pattern from these two regions again corresponded to ERD for performing left hand MI. For both patients, the EEG spatial patterns for the idle condition were not coherent since this condition was not controlled. Fig. 11(c) show the frequency bands selected by the FBCSP algorithm for both patients. The results in Fig. 11 showed subject-specific spatial patterns and frequencies that are consistent with the results presented in our previous study [32].

C. Clinical Efficacy – FMA

The FMA scores for individual subjects for the BCI-SRG group and SRG groups are separately presented in Figures 12 and 13, respectively, as well as Table II. There were no significant intergroup differences at each time point during the study for both groups. The p-values for intergroup comparisons for weeks 6, 12 and 24 were 0.528, 0.462, and 0.300

respectively.

Intragroup comparisons were also carried out by comparing the FMA scores of each of the post-intervention outcome assessments (Week 6, 12, and 24) with the baseline values (Week 0). After the interventions, the BCI-SRG group demonstrated significant FMA score gains compared to baseline FMA score at week 12 (p=0.0431), but not at week 6 (p=0.176) and 24 (p=0.0679). The SRG group demonstrated significant FMA score gains compared to baseline FMA score at week 6 (p=0.0422), but not at week 12 (p=0.138) and 24 (p=0.343).

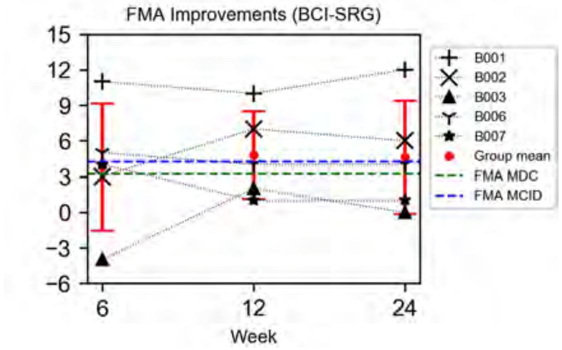


Fig. 12. FMA Improvements for BCI-SRG intervention relative to week 0.

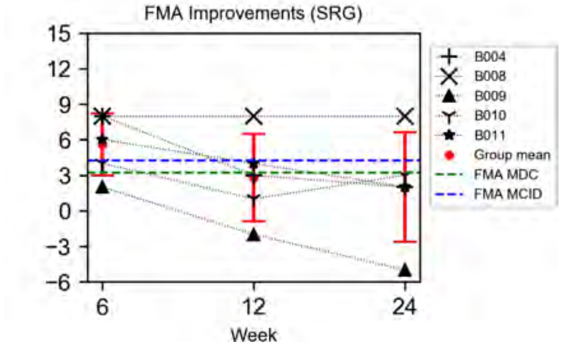


Fig. 13. FMA Improvements for SRG intervention relative to week 0.

TABLE II
EFFICACY MEASURES FOR FMA AND ARAT SCORES

		6th week	12th week	24th week
FMA	BCI-SRG	3.80±5.36*	4.80±3.70*§	4.60±4.77*§
	SRG	5.60±2.61*	2.80±3.70	2.00±4.64
ARAT	BCI-SRG	0.40±2.07	2.20±2.59	3.40±2.88#
	SRG	0.20±2.17	1.20±1.30	0.20±1.48

Results expressed as mean ± standard deviation

*denotes value of improvement more than the reported minimal detectable change (MDC) of FMA-UE (3.2) reported in literature.

§denotes value of improvement more than the reported minimally clinically important difference (MCID) of FMA-UE (4.25) reported in literature.

#denotes values of improvement more than the reported minimal detectable change (MDC) of ARAT (3.0) reported in literature.

The increase in terms of FMA raw scores relative to baseline values for the BCI-SRG group for week 6, 12, and 24 was 3.8, 4.8 and 4.6 respectively. All of these values exceeded the minimal detectable change (MDC) value for FMA of 3.2 [83] throughout the intervention and the post-intervention period. The results for week 12 and 24 were greater than the minimal clinically important difference (MCID) value of 4.25 [84]. On the other hand, the increase in terms of FMA raw scores relative to baseline values for the SRG group for week 6, 12, and 24 was 5.6, 2.8 and 2 respectively, which shows that only the sixth week's score exceeded the MDC value for FMA with subsequent phase-out.

D. Clinical Efficacy – ARAT

The ARAT scores for individual subjects for the BCI-SRG group and SRG groups are separately presented in Figures 14 and 15, respectively, as well as Table II. There were no significant intergroup differences at any time point during the study for both groups. The p-values for intergroup comparisons for weeks 6, 12 and 24 were 0.749, 0.664, and 0.09 respectively.

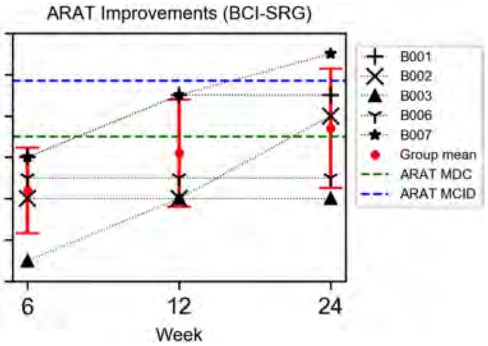


Fig. 14. ARAT Improvements for BCI-SRG intervention relative to week 0.

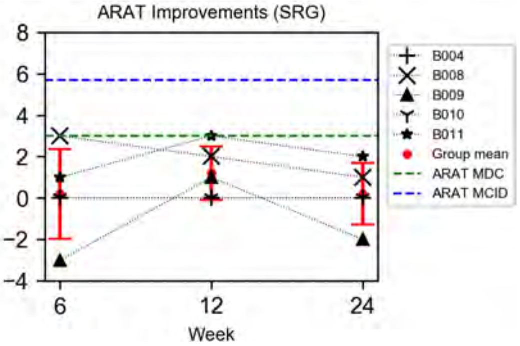


Fig. 15. ARAT Improvements for SRG intervention relative to week 0.

Intragroup comparisons were also carried out by comparing the ARAT scores of each of the post-intervention outcome assessments (Week 6, 12, and 24) with the baseline values (Week 0). After the interventions, there were no demonstrable significant ARAT score gains compared to baseline ARAT score at any time points for both groups: BCI-SRG p-values for week 6, 12 and 24 were 0.713, 0.103, and 0.0679 respectively, and SRG p-values for week 6, 12 and 24 were 0.786, 0.109, and 0.786 respectively.

The increase in terms of ARAT raw scores relative to baseline values for the BCI-SRG group for week 6, 12, and 24 was 0.4, 2.2 and 3.4 respectively. Only the ARAT score for the 24th week exceeded the MDC value for ARAT of 3.0. On the other hand, the increase of ARAT raw scores relative to baseline values for the SRG group for weeks 6, 12, and 24 was 0.2, 1.2 and 0.2 respectively. None of these values exceeded either the MDC value or the MCID value.

E. Post-trial Questionnaire on Imagined Hand Movement

The results of the post-trial questionnaire are tabulated in

Table III. All 5 subjects from the BCI-SRG group reported experiencing vivid kinesthetic sensations during the course of their intervention, while none from the SRG group reported such incidents. All 5 BCI-SRG subjects reported that the sensations were localized in the paretic hand and fingers, describing the sensations as physical movements, as opposed to sensations such as pain, numbness, tingling or spasm, among others. Accompanying this, 4 did not observe any physical movements in the hand associated with the sensations, while 1 was uncertain if there were any physical movements. All 5 BCI-SRG subjects also affirmed that they were conscious about the sensations and would not classify them as dreams or hallucinations.

Out of the 5 BCI-SRG subjects reporting the intensity of the sensations, on a scale of 5 being very intense and 1 being not at all intense, 4 subjects reported the sensations as being somewhat intense (score of 3), while 1 subject reported the sensation as not that intense (score of 1). All 5 BCI-SRG subjects reported that they had not experienced the phenomenon prior to the clinical trials. While 3 of the BCI-SRG subjects continued to experience the sensations after the interventions, 2 subjects reported that the sensations ceased after the end of the intervention.

TABLE III

QUESTIONNAIRE REGARDING VIVID SENSATION OF HAND MOVEMENTS DURING AND AFTER INTERVENTION

	BCI-SRG (n=5)	SRG (n=5)
Unexpected event during the clinical trial	Yes (5)	No (5)
Before the clinical trial	No (5)	No (5)
Keep presenting after the clinical trial	Yes (3) No (2)	No (5)
Description:		
Time of onset	Early Morning (1) Evening (1) Midnight (3)	N.A.
Type	Hand/fingers movement (5)	N.A.
Duration	Less than 10mins (4) 30-60mins (1)	N.A.
Frequency	Almost every day (2) About once a week (1) 2-3 times a month (2)	N.A.
Intensity	Somewhat intense (4) Not that intense (1)	Nothing (5)
Physical Movement (Affected Hand)	No (4) Not sure (1)	No (5)
Dream or hallucination	No (5)	No (5)
Record	Never (5)	Never (5)
Caregiver notification	No (5)	No (5)
Perceived impact on ADL	Yes, Positive (5)	No impact (5)

N.A. = Not Applicable

For the time of onset for the kinesthetic sensation episodes, 3 of the BCI-SRG subjects reported that the kinesthetic sensations occurred near midnight, 1 reported that it occurred in the early morning, and 1 reported occurrence in the evening. Four BCI-SRG subjects reported that the sensations lasted for less than 10 minutes, while 1 subject reported that the sensations lasted about 30-60 minutes. In terms of the frequency of occurrences, 2 BCI-SRG subjects reported that it occurred almost every day, 1 reported that it occurred once a week, and 2 reported that it occurred 2 to 3 times a month.

All 5 BCI-SRG subjects did not record down the occurrence of the episodes, nor did they inform their family members about the phenomena, but all of them opined that these sensations had an overall positive impact on performance of activities of daily living.

IV. DISCUSSION

This two-arm clinical study is a preliminary study investigating the clinical efficacy of utilizing EEG-based brain computer interface assisted motor imagery in combination with a soft robotic hand exoskeleton for upper limb recovery in chronic stroke patients. In relation to preceding clinical studies[32, 51], part of the novelty of this work includes the incorporation of the soft robotic hand exoskeleton into EEG-based brain computer interface assisted motor imagery therapy. The exoskeleton is capable of actuating the fingers of the paretic hand to perform certain grasps and pinches on everyday objects. Another novel aspect is the gamification of the practice of motor imagery orientated towards the performance of activities of daily living. Together, the hand exoskeleton and the rehabilitation game introduce kinesthetic and visual feedback to the patient undergoing motor imagery therapy, to enhance the benefits of therapy. The groups in this study differed in the inclusion of EEG-based brain computer interface assisted motor imagery in the intervention and was designed as such to bring out the effects of motor imagery in rehabilitation. Previous works on motor imagery suggested that sensory feedback could refresh memory of the motor task [85], and the combination of mental and physical practice might improve motor performance, and counteract the negative effect of mental fatigue which is commonly seen in prolonged MI. Therefore, the main research question investigated was whether combining EEG-based MI with the SRG system can enhance the overall effects of stroke rehabilitation than using the SRG system alone.

After intervention, our statistical tests did not reveal any significant differences between both groups at all time points. Given that the sample size of this feasibility study is too small to provide sufficient power or to adequately estimate population variability, inferential statistics would be inconclusive. As such, descriptive statistics such as MDC or MCID, the indicators of significance of clinical improvements, should be more suitable to report participant responses. It is notable that all the follow-up FMA scores for the BCI-SRG group exceeded the MDC value, with results for the week 12 and week 24 exceeding the

MCID value. In comparison, for the SRG group, only the score for the week 6 exceeded the MDC without any sustaining effect during the post-intervention period. In observing the trends in FMA scores post-intervention, it can be seen that the FMA scores increase for the BCI-SRG group from the week 6 to week 12, before decreasing slightly for the week 24. On the other hand, the SRG group's FMA score showed decreases from the week 6 to the week 24. This deterioration is also retrospectively observed in the standard arm therapy group (SAT) in our previous study [32]. It seems that the BCI-SRG therapy resulted in FMA improvements that persisted as compared to the SRG therapy. Since the FMA measures movement, speed and coordination, it is possible that practicing motor imagery is an important aspect in retaining of these qualities of movement as opposed to simply carrying out the movement with an exoskeleton, as was the case for the SRG group.

For ARAT, the score for BCI-SRG group gradually improved over time even after intervention period and exceeded the MDC value at week 24, whereas the SRG group never exceeded the MDC value throughout the study. Given that ARAT measures performance on task-specific activities, higher ARAT scores could imply that the BCI-SRG group was able to translate practiced movements during rehabilitation to actual practice. Observation of the trends of ARAT scores also showed persistent increase in the BCI-SRG group from the week 6 to week 24, while those of the SRG group did not. The results from the current study corroborates the findings on a similar recent clinical study which showed that sustainable motor function improvement could be achieved through proper neural guidance, and that neuroplasticity could be promoted more profoundly by an intervention with proper neurofeedback [53].

The sensation of physical movement in the paretic hand was an unexpected finding that was casually reported by the patients during the course of the clinical trials. It was then decided by the study team to characterize these findings in the form of a questionnaire administered at follow-up session in the week 24. From the results, it was interesting that the experiences of movement sensations were exclusive to the BCI-SRG group. None of the SRG group reported such phenomena, despite being asked specific questions to probe if they had similar experiences.

The sensations felt in the paretic hand were not accompanied by observable physical movements, as reported by almost all of the BCI-SRG subjects (4 out of 5) with one subject being uncertain if their hand exhibited movements.

Such a phenomenon, which involves the perception of a moving limb without overt physical movement e, was reported in the literature and termed kinesthetic illusion [86, 87]. There are a few possible ways whereby this kinesthetic illusion can be induced.

Naito *et al.* [86]showed that both the practice of motor imagery, as well as afferent inputs to the muscle spindles induces kinesthetic illusion in the hand. These afferent inputs come in the form of physical vibrations at a frequency of 83Hz at the wrist. This group also conducted Positron Emission Tomography (PET) scans of the subjects' brains and found that kinesthetic illusion of a certain movement activates the same motor areas (the contralateral cingulate motor areas, supplementary motor area, dorsal premotor cortex, and ipsilateral cerebellum) as when the actual movement is executed. Another method to trigger kinesthetic illusion is by visual stimulus. In a series of experiments by Kaneko *et al.* [88-91], they introduced a video display set over the forearm of the subject such that the position of the display would give the illusion that the subject's forearm was the same as that depicted in a movie. They showed that such a visual stimulus was able to trigger kinesthetic illusions in the hand. Again, functional magnetic resonance imaging (fMRI) showed that the brain regions activated by visually induced kinesthetic illusion were the same as those activated during actual movement execution.

In two other studies[92, 93], it has been reported that in the event of visually induced kinesthetic illusions, corticospinal tract excitability was also increased, as shown by transcranial magnetic stimulation (TMS). Most notably, in their clinical study on a small number of stroke patients, they applied visually induced kinesthetic illusion for the hand as a means of stroke rehabilitation[88]. They showed that a positive effect on motor function was detected immediately after the intervention, and the appearance of reciprocal muscular control was observed in surface electromyography, although there were no significant changes in the FMA scores. In another study using visual stimulus, Ishihara *et al.* [94]was able to show that mirror visual feedback was also able to effect in kinesthetic illusions.

In all these studies reporting kinesthetic illusions, they were only present when triggered by the visual or vibratory stimulus and would cease once the intervention stopped. However, in our study, this phenomenon occurred spontaneously at the time when there was no intervention and persisted weeks after the intervention. We were unable to find any studies which also showed this persistence of kinesthetic illusions.

Since this phenomenon was an unexpected finding, we were not able to have further investigations like functional imaging to depict the reasons of its occurrence. We reviewed all our previous clinical trials which have used similar MI-BCI systems but found that there were no incidences of such experiences. Of note, one of the studies [32] was quite close to the current study in terms of the inclusion criteria and total training time. The only major difference was that this study used soft robotic glove which can mobilize individual finger joints to generate proprioceptive stimuli instead of haptic knob robot [32] and more immersive virtual reality displaying six ADLs tasks. Barsotti et al [95] showed that rich and natural multi-sensory feedback (combination of visual and kinesthetic feedback) resulted in better MI-BCI performance with more stable EEG event-related desynchronization. Therefore, we suppose that the more intense and realistic feedback provided by the system in this study compared with the previous haptic-knob study could have facilitated the occurrence of the spontaneous kinesthetic illusion.

We further postulate that the persistence in kinesthetic illusion is an indication of increasing motor activity and possibly recovery in motor functionality. The possible neural mechanism linking kinesthetic illusion to the increase in motor

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activity and subsequent functional recovery would be neuroplasticity. Various stimulation from the environment is known to induce remodeling of neurosynaptic organization. Relevant to kinesthetic phenomenon in this study, quite a few studies provide clues for sensory stimulation-associated motor activation; BCI-based MI protocols coupled with sensory feedback [25, 36], sensorimotor rhythms to increase in motor cortex excitability [42, 43], proprioception-induced motor cortex activation [96]. In two kinesthetic illusion studies [93, 94], it has been reported that in the event of visually induced kinesthetic illusions, corticospinal tract excitability was increased, as shown by transcranial magnetic stimulation.

Regarding the potential mechanism ensuing kinesthetic illusion from combined use of MI and SRG movement, we suppose that the repetitive multimodal sensorimotor stimuli comprising the drive from motor cortex via MI, proprioceptive input produced by SRG assisted individual finger movement, visual input coupled with the graphical display on the screen might have contributed to formulate memory engrams [97]. The engrams, highly interacting circuits of neurons, could link between neuronal activity, persistent synaptic changes and memory-associated behavior, which is proved by the presence of dendritic spines that are formed or modified during learning. These changes might have perpetuated the kinesthetic illusion [98].

The novel features of this device, combined multimodal sensorimotor stimulation, comprising optimized user intent detecting algorithms to evoke finger movement, visual input through interactive gamified video, proprioceptive input by actuating paretic joints with robotic glove should be contributing to the enhanced effects of neuroplasticity in stroke rehabilitation.

The major limitations of our study were the small sample size and lack of a third arm to act as a control group for the soft robotic glove. The small sample size is due to strict criteria required (only 11 out of 54 were found to pass the inclusion criteria as well as the BCI screening). Due to a small sample size, differences in characteristics such as stroke type and duration since stroke may have an impact on the therapy results. This can be addressed in an extension of this study with a bigger sample size. As a further limitation, in this study, we were able to compare the effects of using the BCI-assisted motor imagery in a robotic rehabilitation setup but lacked a baseline comparison for decoupling the effects of the robotic rehabilitation. In addition, the current soft robotic glove primarily focused on moving the fingers of the hand without offering any assistance to the elbow and the shoulder. Given that performing ADLs relies on the entire upper limb motion for proper execution, the soft robotic glove design should be extended to an upper limb exoskeleton to provide assistance for the elbow and the shoulder.

Due to the interesting finding of vivid experience in the BCI group, in future research, functional neuroimaging like fMRI could be used to better characterize and monitor this type of experiences. Mental fatigue, a feature of mental imagery practice, and the effects on rehabilitation, should also be monitored.

V. CONCLUSIONS

The BCI-controlled soft robotic glove (BCI-SRG) group that underwent a 6-week intervention showed probable trends of prolonged improvements in FMA and ARAT scores over the span of 24 weeks although no significant intergroup differences were observed during the study. All of them experienced an interesting phenomenon of kinesthetic illusion lasting beyond the active intervention period. This may suggest that BCI-SRG which features concomitant virtual, mental and physical feedback on activities of daily living might be able to illicit sustained functional improvements. However, these findings warrant further large scale investigations regarding neuroplasticity facilitated by multimodal sensorimotor interactions within the practice of BCI-assisted motor imagery.

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