

Combined action observation- and motor imagerybased brain computer interface (BCI) for stroke rehabilitation: a case report

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Research

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- 1 Combined action observation- and motor imagery-based brain computer
- 2 interface (BCI) for stroke rehabilitation: a case report
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6 Abstract

- 7 **Introduction:** Upper extremity impairment is a problem usually found in poststroke patients, and
- 8 it is seldom completely improved even following conventional physical therapy. Motor imagery
- 9 (MI) and action observation (AO) therapy are mental practices that may regain motor function in
- 10 poststroke patients, especially when integrating them with brain-computer interface (BCI)
- technology. However, previous studies have always investigated the effects of an MI- or AO-based
- BCI for stroke rehabilitation separately. Therefore, in this study, we aimed to propose the
- effectiveness of a combined AO and MI (AOMI)-based BCI with functional electrical stimulation
- 14 (FES) feedback to improve upper limb functions and alter brain activity patterns in chronic stroke
- patients.
- 16 Case presentation: A 53-year-old male who was 12 years post stroke was left hemiparesis and
- unable to produce any wrist and finger extension.
- 18 **Intervention:** The participant was given an AOMI-based BCI with FES feedback 3 sessions per
- week for 4 consecutive weeks, and he did not receive any conventional physical therapy during
- the intervention. The Fugl-Meyer Assessment of Upper Extremity (FMA-UE) and active range of
- 21 motion (AROM) of wrist extension were used as clinical assessments, and the laterality coefficient
- 22 (LC) value was applied to explore the altered brain activity patterns affected by the intervention.

- Outcomes: The FMA-UE score improved from 34 to 46 points, and the AROM of wrist extension
- 24 was increased from 0 degrees to 20 degrees. LC values in the alpha band tended to be positive
- 25 whereas LC values in the beta band seemed to be slightly negative after the intervention.
- 26 **Conclusion:** An AOMI-based BCI with FES feedback training may be a promising strategy that
- 27 could improve motor function in poststroke patients; however, its efficacy should be studied in a
- larger population and compared to that of other therapeutic methods.
- 29 **Trial registration:** Thai Clinical Trial Registry: TCTR20200821002. Registered 17 August 2020,
- 30 http://www.thaiclinicaltrials.org

31 Key words

32 Stroke, motor imagery, action observation, brain-computer interface, case report

Introduction

- Stroke is a major cause of global deaths, and most stroke survivors usually have hemiparesis on one side of the body that greatly affects their activities of daily living (ADLs) (1). In particular, weakness of the wrist or hand muscle is a common problem in poststroke patients that vastly impacts their ADLs, such as eating, dressing, and opening a door; moreover, it is rarely
- 38 completely improved. Therefore, it is important to create an effective therapeutic method to
- improve upper limb function in poststroke patients (2).
- 40 Currently, constraint-induced movement therapy (CIMT) is an effective therapy that can
- 41 help poststroke patients restore their upper limb function. However, this method may be suitable
- 42 for poststroke patients who have mild motor impairment, and it is not proper for moderately to
- 43 severely symptomatic patients due to the limited capability to produce upper limb movement.

Hence, there should be some solutions to solve this problem and help these patients regain function in their upper extremities (2, 3).

Motor imagery (MI) is a mental simulation of a movement without an actual action (4). It is one of the therapeutic techniques that may be appropriate for poststroke patients who are unable to move their limbs because MI can activate brain areas involved in movement execution; thus, MI may be a promising therapeutic method for poststroke patients to improve their motor function, especially upper extremity function (5, 6). Nevertheless, it is difficult for a therapist to determine whether a patient is performing MI effectively. Thus, brain-computer interface (BCI) technology also plays a key role in fixing this problem (7).

A BCI is a system that can monitor brain activity and translate an ongoing signal to be a control signal that is used to command external devices to achieve a user's purpose or desired task. Currently, noninvasive electroencephalogram (EEG)-based BCI is a popular method usually used to decode a brain signal during MI and provide neurofeedback such as images, robots, tactiles and functional electrical stimulations (FESs) backward to a user to inform MI performance and enhance the learning process (3, 7). From EEG studies, it has been well known that executing MI produces a phenomenon called event-related desynchronization (ERD). ERD is power attenuation of the ongoing EEG signal in a specific frequency band, especially in the alpha or mu band (8 – 13 Hz) and beta band (20 – 24 Hz). ERD usually occurs prominently over sensorimotor areas and is associated with motor cortex activation (8, 9). In BCI systems, ERD occurrence is always used as a spectral feature to indicate MI and provides meaningful feedback backward to a user to encourage the learning process, which is a key factor of neural plasticity (3, 7); moreover, previous studies have shown that an MI-based BCI with neurofeedback training could improve upper extremity function (10-14).

In addition to MI, action observation (AO) is another therapeutic method that can be used for rehabilitation in poststroke patients who have a severe motor disability. AO is implemented to carefully observe a movement or an action performed by others. It can activate the neural structures involved with the observed movement. Generally, AO is easier than MI to practice and requires less cognitive ability than MI, particularly in poststroke patients who always have mental impairment (15). Furthermore, AO can provoke ERD as well as MI (16), and a previous EEG study in poststroke patients showed that performing AO could generate ERD power greater than MI (17). Therefore, an AO-based BCI with neurofeedback is another option that may be appropriate for poststroke patients who have cognitive impairment and could also improve upper limb function (18, 19).

Normally, the effectiveness of MI and AO for improving motor function in poststroke patients has been studied separately; however, recent evidence from EEG, functional magnetic resonance imaging (fMRI), and transcranial magnetic stimulation (TMS) studies has revealed that combined AO and MI (AOMI) can provoke the activation of brain areas related to motor function to a greater extent than pure MI or AO alone. AOMI imagines an action in terms of a movement sensation concurrently with observing the same action displayed on the screen (20, 21). However, evidence of using AOMI in the poststroke patient to enhance upper extremity function is still lacking, and from our literature reviews, there are only two studies from Sun et al. (22) and Wang et al. (23) that have studied the effectiveness of AOMI-based BCI to restore upper limb function in the poststroke patient. In Sun's study, they investigated the effect of MI practice guided by synchronous AO on improving upper limb function in subacute stroke patients with an onset of less than 2 months. They found that the upper limb function in the participants who received MI practice guided by synchronous AO was improved more than that in the participants who received

MI practice guided by asynchronous AO; however, they did not give any neurofeedback to the participant while executing the cognitive task. The same result was found in Wang's, although their intervention was different. In Wang's study, the participants had chronic stroke, and they also provided robotic hand feedback to the participant while they were performing the cognitive task.

The purpose of this case report was to support the concept of using AOMI to recover upper extremity function in poststroke patients. We propose an AOMI-based BCI with FES feedback training to improve upper limb function in a chronic stroke patient who experienced a stroke 12 years prior and had moderate impairment in upper limb function.

Participant and methods

Case description

The participant was a 53-year-old male who experienced a stroke 12 years prior. He had muscle weakness on the left side of the body, particularly in the wrist and hand muscle caused by right cerebral hemorrhage. After stroke onset, he received physical therapy only in the first three years and stopped it because his financial problems and symptoms seemed to improve. Currently, he is unable to voluntarily extend his wrist and all fingers. The participant's conditions before the intervention were as follows: Fugl-Meyer Assessment of Upper Extremity (FMA-UE) score was 34 points from a maximum of 66 points, active range of motion (AROM) of left wrist extension was 0 degrees, Modified Ashworth scale (MAS) of the left wrist flexor was 0, and the Mini-Mental State Exam (MMSE) score was 30 points. The participant provided written informed consent to participate in this study, which was approved by the Mahidol University Central Institutional Review Board (COA No. MU-CIRB 2020/097.3107), and the Thai Clinical Trial Registry identification number was TCTR20200821002.

AOMI-based BCI with FES feedback training

In each training session, the participant was seated in a comfortable chair and placed his left forearm in the prone position on a desk. A 14-inch laptop computer was placed in front of him, and its display distance was appropriate for his eyesight. A g. tec biosignal amplifier (g. USBamp, Graz, Austria) with 16 grids of Ag/AgCl electrodes was used to record the EEG data, and their details are further described in the data acquisition section. For the FES, we attached electrodes over the left extensor digitorum muscle to generate wrist and finger extension, and the whole system is presented in Figure 1.



Figure 1. The components of AOMI-based BCI with the FES system that the participant was given on each training day. The system was composed of a g. tec biosignal amplifier, computer, and the FES.

The participant received the AOMI-based BCI with FES feedback training for 3 days per week for 4 consecutive weeks. On each training day, he had to execute the cognitive task for 6 sets with resting time between sets for 3 minutes, and each set comprised 20 trials. The EEG data from the first 2 sets were used to create the classification model, and FES feedback was not activated in these sets. The classification model was applied in the next 4 sets to control the FES device, so there were a total of 80 trials of FES feedback on each training day.

In each trial, the computer provided the sequences of cognitive tasks for the participant to perform, which are shown in Figure 2. First, the participant started by looking at the blank screen for 5 seconds. Then, a black cross appeared in the center of the screen for 3 seconds to warn the participant to prepare himself for executing the coming task, and this stage was called the "Preparation stage". Next, the video-guided movement that demonstrated extension of the left wrist and fingers in first-person view was played on the screen for 5 seconds. At this moment, the participant was asked to attentively look at the screen and simultaneously imagined as if he was extending his left wrist and fingers, and this stage was called the "AOMI stage". After that, the screen was blank to inform the participant to relax, and the relaxation time was random between 10 and 13 seconds.

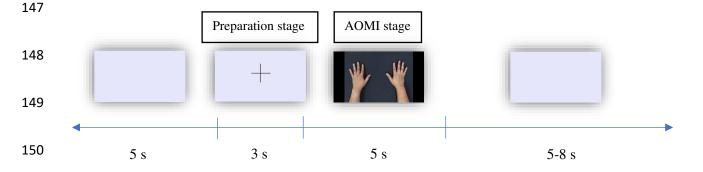


Figure 2. The sequences of cognitive task that the participant had to perform in each trial. The participant was started watching the blank screen for 5 s. Next, the black cross appeared for 3 s to

warn the participant for the coming task. Then, the video-guided movement was played and the participant had to execute the cognitive task. Last, the blank screen was showed again for relaxation period.

For this study, the FES device was custom-made, and the parameters for muscle stimulation were composed of biphasic square waves, pulse width 200 µs, frequency 50 Hz, and voltage intensities of approximately 30-40 volts, which were sufficient to produce extensor digitorum contractions and were painless. The FES was activated if EEG data in the imagination stage were classified as "AOMI class", and it was not activated if EEG data were classified as "Preparation class". These details are described more in the feature extraction and classification model section.

AOMI-based BCI system

Data acquisition

We used a g. tec biosignal amplifier (g. USBamp, Graz, Austria) with 16 electrodes placed in the FP1, FP2, FC3, FC4, C5, C6, C3, C4, C1, C2, CP3, CP4, P3, P4, O1 and O2 positions according to the international 10-20 system to record the EEG data at a sampling rate of 512 Hz. The ground electrode and reference electrode were placed in the AFz position and right earlobe, respectively. The electrode impedances used to record EEG data were below 5 K Ω , and OpenVibe software (v2.2.0) was used for EEG data processing (data preprocessing, feature extraction, and the classification model) (24).

Data pre-processing

We used a notch 50 Hz filter to remove the power-line noise and common average reference (CAR) for re-reference EEG data. A bandpass filter at frequencies of 8 – 30 Hz was used to filter the EEG data because ERD occurred prominently in this frequency range (12).

Feature extraction and classification model

For the feature extraction method, we chose EEG data of the second at 1 to 3 from the preparation stage and AOMI stage as the two-class condition. Then, a common spatial pattern (CSP) filter that simultaneously maximizes the variance for one class and minimizes the variance of another class (25) was implemented on EEG data from two conditions. Next, fast Fourier transform (FFT) was used to transform EEG data filtered by CSP; then, we selected the power spectrum of the alpha band (8 - 15 Hz) and beta band (16 - 24 Hz) from the C3 and C4 channels as the feature vectors because these electrodes were placed over the sensorimotor areas of the hand. Later, the feature vectors in each condition were subjected to linear discriminant analysis (LDA) to establish the classification model, in which all processes were performed with OpenVibe software (v2.2.0).

Outcome measurement

In this study, FMA-UE and AROM of left wrist extension were used as motor function assessments, and the participant was evaluated within 7 days before and after intervention. We also analyzed the laterality coefficient (LC) (26) of the alpha band (8 – 13 Hz) and beta band (14 – 30 Hz) in each training session as neurophysiological signal assessments, and explored LC trending by using linear regression. Furthermore, we also analyzed an online classification

accuracy to evaluate AOMI performance in each training session. The more accuracy reflected the higher number of FES feedback given to the participant in each training day.

First, to compute the LC, we had to calculate the ERD/ERS values according to the following equation (9):

$$ERD/ERS \% = \frac{(A-R)}{R} \times 100$$

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A is the power spectrum value during AOMI, and R is the power spectrum value of the baseline period, which is the period before the AOMI period. In this study, we used EEG data from the first 2 sets, in which FES feedback was not triggered on each training day to calculate ERD/ERS values. EEG data of seconds at 1 to 3 in the preparation stage and seconds at 1 to 5 in the AOMI stage are represented R and A in the equation above, respectively. Consequently, we derived 40 epochs of both the baseline period and cognitive task period to compute the ERD/ERS values on each training day. The data processing of ERD/ERS analysis was started by using independent component analysis (ICA) (27) to remove eyeblink, electrocardiograms (ECG), and muscle-related artifacts, and then the data were re-referenced to CAR. After that, Welch's periodogram with a Hamming window with 50% overlap was used to estimate the power spectral density (PSD) and averaged across all epochs. Next, we obtained the power spectra of the alpha band (8-13 Hz) and beta band (14-30 Hz) by summing the PSD values and dividing by the number of frequencies. Afterward, we computed ERD/ERS % in each channel, and ERD/ERS values from FC3, C5, C3, C1, and CP3 were summed and averaged to represent the brain activity of the left hemisphere; in contrast, the ERD/ERS values from FC4, C6, C4, C2 and CP4 were summed and averaged to represent the brain activity of the right hemisphere. All processes were performed by EEGLAB, which is a MATLAB (R2020a) toolbox.

After receiving ERD/ERS values of both hemispheres, we could also analyze LC continuously, and its formula was as follows (26):

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$$LC = (C - I)/(C + I)$$

C is ERD/ERS values of the hemisphere on an opposite side of an imagined hand, and I denotes ERD/ERS values of the hemisphere on the same side of an imagined hand. The value of LC is between -1 and 1, which indicates a higher or lower value in the hemisphere on the opposite side of an imagined hand. This implies how lateralization of the brain functions during the cognitive task (26, 28).

Results

After 12 training sessions, FMA-UE was increased from 34 to 46 points, the AROM of left wrist extension was increased from 0 to 20 degrees, The LC values in the alpha and beta bands were changed from -0.03 to 0.47 and from -0.08 to -0.18, respectively, which showed in Table 1. The alteration trend of LC values throughout 12 training sessions in the alpha band seemed to be positive (regression coefficient = 0.016) while that in the beta band seemed to be slightly negative (regression coefficient = -0.006) over time, which showed in Figure 3 and 4, respectively. For analysis of the online classification accuracy, the averaged accuracy from total 12 training sessions was 83.85 percentage, and the percentage of classification accuracy in each training session showed in Figure 5.

Assessments	Pre	Post
FMA-UE	34	46
AROM of wrist extension	0	20
LC values in alpha band	-0.03	0.47
LC values in beta band	-0.08	-0.18

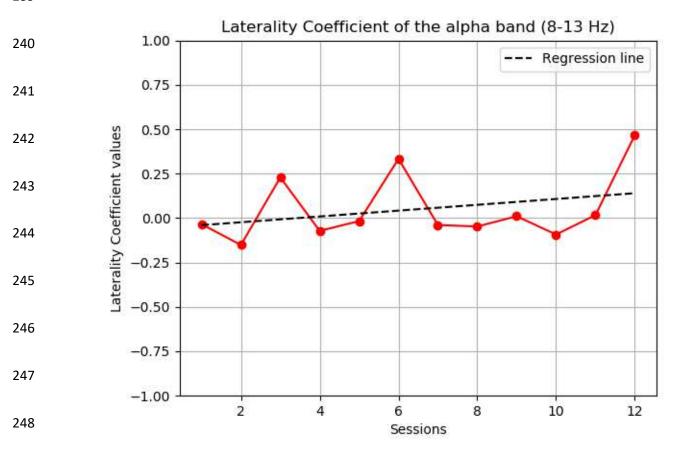


Figure 3. The LC values in the alpha band (8-13 Hz) in each training session seemed to be positive over time.



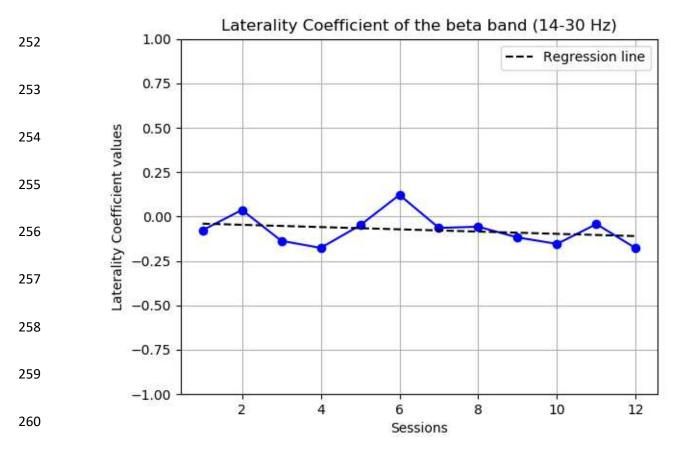


Figure 4. The LC values in the beta band (14-30 Hz) in each training session seemed to be slightly negative over time.

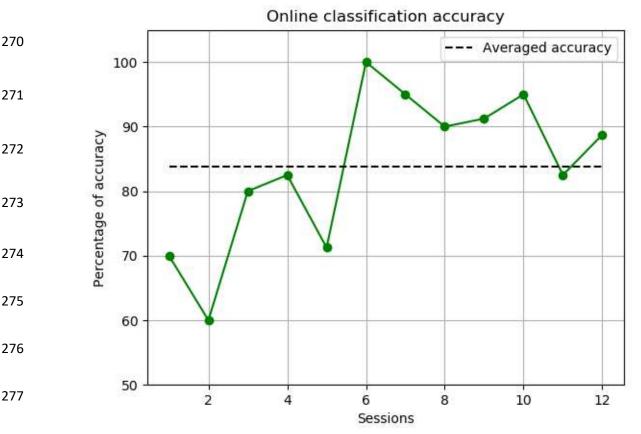


Figure 5. The percentage of online classification accuracy in each training session, and the averaged classification accuracy was 83.85 percentage.

Discussion

The objective of the current case study was to support the concept of applied AOMI-based BCI training for stroke rehabilitation, and our results demonstrated that AOMI-based BCI training with FES feedback could improve upper extremity function in a chronic stroke patient who experienced a stroke 12 years prior. FMA-UE was improved from 34 to 46 points, and the AROM of left wrist extension was increased from 0 degrees to 20 degrees after receiving 12 training sessions, consistent with the results from previous studies (22, 23); however, our method and

training paradigm were different from those of previous studies. In addition, the participant did not receive any conventional physical therapy during this intervention.

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There may be many factors that explain why our intervention improved motor function in the participant. First, the benefit from AOMI practice. It is well known that MI is a mental practice that can access or activate the brain areas associated with motor execution, including the supplementary motor area, premotor cortex, primary motor cortex, inferior/superior parietal lobule, basal ganglia, and cerebellum, without physical movement (29), but its drawback is that it is difficult to perform and depends on the cognitive ability of the patient. While AO is easier than MI to practice, it can also provoke brain regions involved in physical movement (21). However, it rarely activates the primary motor cortex (29), which is important for the recovery of motor function (30). Thus, AOMI may play a crucial role in fixing these problems; moreover, previous studies have shown that AOMI can activate corticomotor areas to a greater extent than MI or AO alone (31-33). In this study, we provided video-guided movement, which showed movement of the wrist and finger extension to the participant while he was executing MI. The video-guided movement may have made him focus on kinesthetic MI more easily and required a lower cognitive demand to perform the task; therefore, he could perform the cognitive task effectively corresponding to the averaged classification accuracy was 83.85 percentage, which might contribute to improving motor function.

Second, the EEG-based BCI with a neurofeedback system; although AOMI practice could promote the activation of the brain areas relating to an actual movement, it still lacks feedback, which is a key factor in the motor learning process (34). To solve this problem, we combined a BCI and knowledge of machine learning to monitor and classify EEG data while the participant was performing AOMI to provide real-time feedback represented by the FES backward to him to

inform his performance. We selected the FES as neurofeedback because it is able to provoke the activity of the brain regions associated with motor function (35) and may re-establish the sensorimotor feedback loop affected by stroke (36, 37).

Third, our strategy included repetitive practice with real-time feedback that may facilitate neural plasticity. In this study, the participant received 12 training sessions, and at each session, he was asked to attempt AOMI for 80 trials. It is known that repetition of a simple movement can induce use-dependent plasticity, leading to reorganization of the neural structure associated with motor function (38), and a recent study demonstrated that repetitive MI could promote use-dependent plasticity (39); therefore, repetitive AOMI could enhance use-dependent plasticity. Moreover, attempted AOMI with the given feedback is similar to Hebbian learning, which is the process used to strengthen the synaptic connection between neurons (37, 40). The activation of the brain regions related to motor function during AOMI coincided with FES feedback, which indicated that wrist extension might strengthen the synaptic connection in the neural pathways regarding upper limb function. In conclusion, these factors might be the causes why AOMI-based BCI training with FES feedback could improve upper limb function in this participant.

Furthermore, we also assessed the alteration in the ERD/ERS pattern by analyzing LC values in each training session. For LC values in the alpha band, their values tended to be positive when comparing the values between the first and last training sessions. It may be inferred that ERD in the affected hemisphere was stronger than that in the unaffected hemisphere when the participant was performing the cognitive task. This pattern was similar to that in healthy subjects, in which the ERD pattern usually occurs strongly over the contralateral hemisphere with respect to the imagined limb (41). Hence, this result may imply that the alteration of brain function returned to normal, corresponding to an improvement in upper limb function. Nevertheless, the

trend of LC values in the beta band was opposite, and it seemed to be slightly negative over time. These results might also be explained by the automatization process in which the participant was used to the cognitive task due to performing it several times, so he may have required less effort to perform the task; consequently, neural activation in the contralateral hemisphere may have decreased (28). However, there was only one participant in this study. In future studies, the changes in LC values in the beta band should be investigated in a larger population of poststroke patients who receive an AOMI-based BCI with neurofeedback. Moreover, there were other limitations to this study in addition to one participant, such as the lack of a control group, in evaluating whether AOMI-based BCI training is superior to AO- or MI-based BCI training in terms of improvement of upper limb function. Next, we did not measure EMG to monitor the muscle activity of the left upper extremity while the participant performed the cognitive task; however, we used visual inspection to ensure that the participant did not use any signal artifacts from any part of the body movement to be the control signal in every trial. Finally, we did not know exactly which parts of the brain were damaged from the stroke because his stroke onset occurred 12 years ago, so his medical information was eliminated, and he felt inconvenient for MRI examination again.

Conclusions

we would like to support the concept of using an AOMI-based BCI for stroke rehabilitation, and our results have shown that it can improve upper limb function in chronic stroke patients. Additionally, because of its advantages, we believe it may be a promising strategy used to improve motor function in poststroke patients.

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Abbreviations

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356	MI: Motor imagery; AO: Action observation; AOMI: Combined action observation and motor
357	imagery; BCI: Brain-computer interface; FES: Functional electrical stimulation; FMA-UE: Fugl-
358	Meyer Assessment of Upper Extremity; AROM: Active range of motion; Lc: Laterality
359	coefficient; ADLs: Activities of daily living; CIMT: Constraint-induce movement therapy; EEG:
360	Electroencephalogram; ERD: Event-related desynchronization; fMRI: functional magnetic
361	resonance imaging; TMS: transcranial magnetic stimulation; MAS: Modified Ashworth scale;
362	MMSE: Mini-Mental State Exam; CAR: Common average reference; CSP: common spatial
363	pattern; FFT: fast Fourier transform; LDA: linear discriminant analysis; ICA: independent
364	component analysis; PSD: power spectral density

Ethics approval and consent to participate

- A participant provided written informed consent to participation that was granted approval by the
- Mahidol University Central Institutional Review Board (COA No. MU-CIRB 2020/097.3107),
- and the Thai Clinical Trial Registry identification number was TCTR20200821002.

369 Consent for publication

- A participant gave the written informed consent for publication that was granted approval by the
- Mahidol University Central Institutional Review Board (COA No. MU-CIRB 2020/097.3107).

Availability of data and materials

373 Not applicable

Competing interests

375 The authors declare that they have no competing interests.

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382	Authors' contributions
383	NR is responsible for design of the study, performed the experiment, acquired the EEG data,
384	evaluated the motor function of the subject, drafted the manuscript.
385	YW obtained funding for the study, designed the study, provided the input for the experiment,
386	reviewed the manuscript.
387	
388	Authors' information
389	NR is the physical therapist and PhD student; YW is the Prof. at the Department of Biomedical
390	Engineering, Mahidol University.
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