Symmetrical Contralaterally Controlled Functional Electrical Stimulation Enhanced Cortical Activity and Synchronization of Stroke Survivors

Rui Xu, Haichao Zhang, Xinyu Zhao, Zhuoyue Zhao, Lin Meng, and Dong Ming, *Senior Member, IEEE*

***Abstract*— Contralaterally controlled functional electrical stimulation (CCFES) is a rehabilitation method whose efficacy has been proved in several randomized controlled trials. Symmetrical CCFES (S-CCFES) and asymmetrical CCFES (A-CCFES) are two basic strategies of CCFES. The cortical response can reflect the instant efficacy of CCFES. However, it is still unclear of the difference on cortical responses of these different strategies. Therefore, the aim of the study is to determine what cortical response CCFES may engage. Thirteen stroke survivors were recruited to complete three training sessions with S-CCFES, A-CCFES and unilateral functional electrical stimulation (U-FES), in which the affected arm was stimulated. The electroencephalogram (EEG) signals were recorded during the experiment. The event-related desynchronization (ERD) value of stimulation-induced EEG and phase synchronization index (PSI) for resting EEG were calculated and compared in different tasks. We found that S-CCFES induced significantly stronger ERD at affected MAI(motor area of interest) in alpha-rhythm (8–15Hz), which indicated stronger cortical activity. Meanwhile, S-CCFES also increased intensity of cortical synchronization within the affected hemisphere and between hemispheres, and the significantly increased PSI occurred in a wider area after S-CCFES. Our results suggested that S-CCFES could enhance cortical activity during stimulation and cortical synchronization after stimulation in stroke survivors. S-CCFES seems to have better prospects for stroke recovery.**

***Index Terms*— Stroke, electrical stimulation strategy, brain activation, cortical synchronization.**

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I. Introduction

THERE are about 5.5 million people suffering from stroke each year [1]. Motor dysfunction with hemiplegia is the main consequence of stroke [2]. Approximately 65% of stroke survivors cannot incorporate their affected upper limbs into their daily lives, which seriously affects the survivors' ability to live independently [3]. Advanced rehabilitation techniques can improve upper limb motor functions in stroke survivors.

Bilateral upper-limb training has been widely used to restore motor function for survivors with neurological diseases such as stroke and spinal cord injury (SCI) [4], [5], [6]. It has been proven that, compared with unilateral upper-limb movements, bilateral upper-limb movements activate additional brain circuits, especially the supplementary motor area (SMA), which could affect motor relearning and neuroplasticity [7], [8]. Bilateral training could better improve the motor function of paralyzed survivors [5], [9]. However, the lack of motor ability makes paralyzed survivors unable to complete bilateral training well. Therefore, some assisted bilateral training was widely used for hemiplegia survivors. Recently, contralaterally controlled functional electrical stimulation (CCFES), which allows the hemiplegia survivors control the functional electric stimulation (FES) of the affected limb according to the movement of the unaffected limb, has been proposed by Knutson et al. [10]. It has been proven that CCFES improved manual dexterity, active range of motion of wrist extension and functional behavior for stroke survivors more than unilateral FES [11], [12], [13], [14].

It is worth noting that neuroplasticity changes during stroke rehabilitation, and cortical response can reveal the mechanism of the change which is essential for neural rehabilitation of stroke. The electroencephalogram (EEG) signals are often used to validate some rehabilitation training methods, as they can reveal the neuroplastic changes during or after training. One of the most commonly used indexes is the event-related desynchronization (ERD), which reflects the strengthen of brain activation. For example, Muller et al. [15] and Qiu et al. [16] found that the ERD value at the parietal areas during FES-induced movements and the ERD pattern of stimulated movements were similar to that of active movements. Tangwiriyasakul et al. found that the ipsilesional ERD one month after stroke was significantly strengthened compared with that at stroke onset, and the motor function was also significantly improved. Their research suggested that ERD in acute stroke may assist in prognostication and rehabilitation [17]. Bethel et al. found that ERD restored to normal level after BCI-FES. Muscle strength also significantly improved for both hands after BCI-FES. It indicated that the ERD variation was connected to the muscle strength recovery [18].

Additionally, brain function is determined by the neural network connections between neurons in different regions or across regions of the brain [19]. The phase synchronization index (PSI), which represents synchronized brain activity, is a parameter for neural network analysis [20], [21]. EEG phase synchronization showed that there was a correlation between large-scale phase synchronization level of brain activity and clinical symptoms [22]. Kawano et al. found PSI was inversely related to the National Institutes of Health Stroke Scale (NIHSS) in stroke survivors [23]. Cunningham et al. suggested that CCFES reduced interhemispheric inhibition (IHI) when compared with unilateral FES [24]. However, the CCFES-induced cortical responses is still unclear.

CCFEFS is a therapy in which the paretic limb is stimulated to move symmetrically to the non-paretic limb, i.e., it creates symmetrical bilateral movements (S-BM). But CCFES could also be configured to create asymmetrical bilateral movement (A-BM), where the paretic limb is stimulated to move in the opposite direction as the paretic limb, as suggested for ankle rehabilitation by Knutson et Al. [25]. In addition, Knutson et al. also compared the effects of 6-week symmetrical CCFES (S-CCFES) and cyclic neuromuscular electrical stimulation (NMES) on motor function of stroke survivors, and found that S-CCFES produced greater improvement than cyclic NMES in motor ability [14]. Some studies also found bilateral symmetrical movement can activate the unaffected cerebral hemisphere, increase the activity of the affected cerebral hemisphere, and promote the movement control of the affected limb in stroke survivors [4], [26], [27]. In addition, Shih et al. found that, compared with S-BM, beta power of EEG signal decreases in older adults during A-BM [28]. It can be seen that the synchronization of bilateral upper limbs may affect cortical response.

Therefore, we sought to explore the differences in stroke survivors' cortical response of CCFES versus unilateral functional electrical stimulation (U-FES). We also investigated whether the symmetrical and asymmetrical CCFES (A-CCFES) could trigger different cortical responses. It was hypothesized that the S-CCFES may induce stronger cortical activities and brain synchronization related to a better rehabilitation. In this study, we designed experiments to test neurophysiological effects of S-CCFES, A-CCFES and U-FES by comparing the cortical responses for these three tasks. ERD occurs only in the task of motor or motor imagery, and there is no ERD phenomenon in simple resting tasks. Meanwhile, most studies have shown that resting PSI was correlate with stroke recovery, and the motor function improved after FES training, so we analyzed the resting PSI after FES. Therefore, the ERD was analyzed to reflect cortical activation during stimulation and the resting PSI was used to indicate cortical synchronization after stimulation.

TABLE I
CHARACTERISTICS OF STROKE SURVIVORS

ID	Age	Gender	Months after Stroke	Type	Dominant/Hemiplegic Side
1	69	Female	7	Ischemic	Right/Left
2	80	Female	18	Ischemic	Right/Left
3	51	Male	2	Ischemic	Right/Right
4	59	Male	2	Ischemic	Right/Left
5	49	Male	12	Ischemic	Right/Left
6	66	Female	3	Ischemic	Right/Right
7	65	Male	1	Hemorrhagic	Right/Right
8	67	Female	2	Ischemic	Right/Right
9	58	Male	5	Ischemic	Left/Left
10	69	Male	12	Ischemic	Right/Right
11	70	Female	24	Ischemic	Right/Left
12	60	Male	5	Hemorrhagic	Right/Right
13	63	Female	30	Ischemic	Right/Right

II. MATERIALS AND METHODS

A. Subjects

Seventeen stroke survivors were recruited from Tianjin Union Medical Centre, while four of them failed to complete the experiment. Table I showed the characteristics of thirteen stroke survivors (mean age $\pm$ standard deviation: 63.5 $\pm$ 8.3 years old, 6 females) who successfully participated in the study. The criteria for inclusion were (1) a first-ever ischemic or hemorrhagic stroke, (2) at least one-month poststroke, (3) Mini-mental State Examination (MMSE) score $>$ 24 (total score 30), (4) wrist extension elicited by FES without pain, and (5) the motor function of the unaffected upper limb is normal. All the subjects gave their written informed consent before the experiment. This study was approved by the Ethics Committee of Tianjin Union Medical Centre before the experiments.

B. Experimental Paradigm

There is a preliminary experiment and a formal one in this study. The details of the experiment arrangement were as follows.

1) Preliminary Experiment: Before the formal experiment, there were two parts in the preliminary experiment for each participant. The first one was performed to set the parameters for FES. The FES was applied using Rehastim2 (HASOMED GmbH, Magdeburg, Germany), which could be controlled through ScienceMode2 communication protocol. The stimulation pulses were a series of 300 μs biphasic symmetric pulses at 40 Hz. Two self-adhesive electrodes (4 cm × 4 cm) were placed on the Extensor Carpi Radialis (ECR) muscle belly of the affected arm to provide effective muscle contraction for wrist extension. The amplitude of the stimulation current was adjusted to each subject by increasing the current from 0 mA with 0.1 mA increments until a wrist extension was induced. These FES parameters were recorded and would be used to stimulate the affected limb muscle in the formal experiment. The second part was performed to train Support Vector Machine (SVM) classifier for movement onset recognition. Two wireless EMG sensor (Trigno Avanti Platform, DELSYS, USA), sampled at 2000 Hz, were placed in the direction of the muscle fibers of ECR and Flexor Carpi Ulnaris (FCU) of the unaffected arm. EMG signals were filtered using a fourth-order Butterworth band pass filter between 30Hz and 300 Hz and a notch filter with 50 Hz. Participants were asked to keep their unaffected wrist relaxed, extended and flexed for 20 s, respectively, during which EMG data was recorded. Then, the feature mean absolute value (MAV) was calculated with a 100-ms window. The formula was as follows:

$$MAV_i = \frac{1}{200}\sum_{k=0}^{199}|E_{i-k}| \tag{1}$$

where MAV_i is the MAV at the i^{th} frame of the EMG data, E_{i-k} is the preprocessed EMG at the $(i-k)^{th}$ frame. The sliding window was 50 ms. MAV of ECR and FCU were input to train the SVM classifier. The SVM output on/off orders for FES control based on EMG signals. This method was used to guarantee the synchronization of the bilateral movements.

2) Formal Experiment: The subjects were seated comfortably in an armchair at one-meter distance in front of a computer screen during the experiment. FES electrodes and EMG sensors were attached at the same location as the preliminary experiment. The FES parameters and SVM classifier determined in the preliminary experiment were used. Each subject had to perform three different tasks as shown in Figure 1(A), i.e. S-CCFES, A-CCFES and U-FES, and each task consisted of 20 trials. Three tasks were performed in random order among the participants. A 30-minute break between tasks was arranged in case of fatigue. The experimental paradigm was shown as Figure 1(B). The experimental interface was written by Labview 2017 (National Instruments, Texas, USA). Each trial (12 s) consisted of a stimulation period (4 s) and a rest period (8 s). There was a progress bar moving from left to right on the monitor. In the task of S-CCFES, participants were asked to extend their unaffected wrist to trigger the FES-induced extension of the affected wrist when the progress bar was red, and keep the extension for 4 s. There was an eight-second rest when the progress bar was blue. For the task of A-CCFES, it was similar with S-CCFES: participants were asked to flex their unaffected wrist to trigger the FES-induced extension of the affected wrist when the progress bar was red, and keep the extension/flexion for 4 s. In the task of U-FES, participants were asked to relax their unaffected wrist, only the affected wrist was cyclically stimulated through established procedures. The EEG data of each subject was recorded during the experiment. Meanwhile, the resting EEG of each subject was recorded for 30 s before and after the experiment. The electrode location of EEG and experimental tasks were shown in Figure 1(A). The scene of experiment was shown in Figure 2.

C. EEG Recordings and Preprocessing

EEG data were acquired by a 32-channel EEG acquisition system (Grael, Compumedics Ltd., Australia) with a sampling rate of 2048 Hz. The standard Ag/AgCl electrodes were placed on the scalp according to the international 10-20 system. This study focused on the sensorimotor cortex, where 15 selected electrodes (labeling F3, Fz, F4, FC3, FCz, FC4, C3, Cz, C4, CP3, CPz, CP4, P3, Pz, P4 as shown in Figure 1(A)) were selected for analysis. The reference electrode was placed in the middle of Cz and CPz and the ground electrode was placed on the forehead. All the signals were filtered to 0.5-100 Hz and notch filtered at 50 Hz. Then, the EEG data were downsampled to 256 Hz and processed by the common average reference. In order to split the EEG signal during the stimulation period, the data were labeled when FES was triggered or started. This was implemented based on an external circuit, which controlled and monitored the FES stimulator.

D. Data Processing

1) Event-Related Spectral Perturbation: The event-related spectral perturbation (ERSP) could reflect how the averaged event-related power changes in the view of time-frequency domain. ERSP could supply more details about ERD patterns of different tasks. ERSP was calculated according to the equation defined as follows:

$$ERSP\,(f,t) = \frac{1}{n}\sum_{k=1}^{n}\left(F_k(f,t)^2\right) \tag{2}$$

where $F_k\,(f,t)$ was the spectral estimation of the k^{th} trial at frequency f and time t. Short-time Fourier transform with a 256-point Hanning-tapered window was employed to perform time-frequency analysis of EEG data within EEGLAB. In order to normalize the ERSP, the mean power changes in a baseline period (0 s-1.5 s before the label) were subtracted from each spectral estimation. The ERSP in this paper referred to the baseline-normalized ERSP. In this work, the ERSP from three key electrodes C3, C4 and FCz at the area of SMA were displayed from -2 s to 6 s between 5 Hz and 30 Hz.

In order to investigate the difference in cortical electrophysiological activation during different tasks, alpha-ERD (8-15 Hz) and beta-ERD (15-29 Hz) were extracted at electrode C3, FCz and C4. ERD value can be calculated according to the equation defined as follows [16]:

$$ERD_{value,f_{low},f_{high}} = \min_{f_{low}\le p\le f_{high}}\left(\frac{1}{N}\sum_{f=p}^{p+4}\sum_{t=0}^{3}(ERSP\,(f,t))\right) \tag{3}$$

where N was the number of time-frequency bins in a 4-Hz wide frequency band, f_{low} and f_{high} were the upper and lower boundaries of the calculated frequency band, respectively. ERSP from 0 s to 3 s was used to calculate ERD.

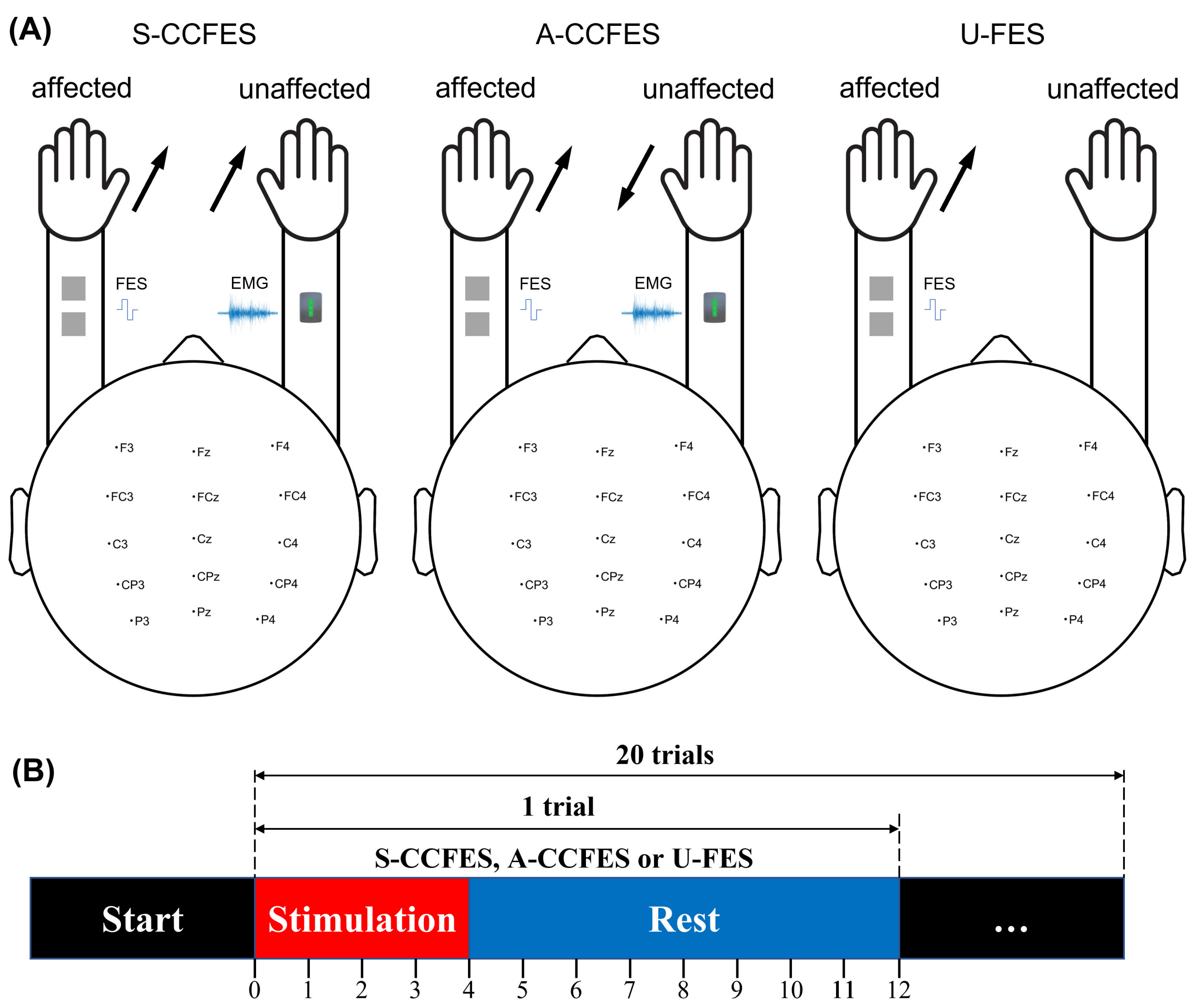

Fig. 1. (A) Experimental tasks. The left limb indicated the affected side with FES. The right limb indicated unaffected side and the EMG signal was recorded. (B) Experimental paradigm.

2) Phase Synchronization: The PSI of the resting EEG data was calculated to investigate the effect of cortical connectivity after each task [29]. PSI can describe the synchronization between neurons [30]. Firstly, for EEG signal $x(t)$, the Hilbert transform was used to calculate the instantaneous phase of EEG as follows:

$$\begin{cases} \tilde{x}(t) = \frac{1}{\pi} P \cdot V \int_{-\infty}^{+\infty} \frac{x(t)}{t-\tau} d\tau \\ A_x^H(t) e^{j\phi_x^H(t)} = x(t) + j\tilde{x}(t) \end{cases} \tag{4}$$

where $P \cdot V$ refers to the integral taken in the sense of the principal value of Cauchy, $A_x^H(t)$ and $\phi_x^H(t)$ represent the instantaneous amplitude and instantaneous phase of the signal, respectively. For another EEG signal $z(t)$, its instantaneous phase ϕ_z^H can also be calculated. If $\phi_{xz}^H(t) = \left|n\phi_x^H(t) - m\phi_z^H(t)\right| \leq const$, where $const$ is a constant and m and n are positive integer, $x(t)$ and $z(t)$ can be described as $n : m$ phase synchronization. Since 1:1 phase synchronization is the case for most neurophysiological activities [31], PSI can be calculated according to equation defined as follows:

$$\begin{cases} \phi_{xz}^H(t) = \left|\phi_x^H(t) - \phi_z^H(t)\right| \\ PSI = \sqrt{\left\langle \cos\left(\phi_{xz}^H(t)\right)\right\rangle_t^2 + \left\langle \sin\left(\phi_{xz}^H(t)\right)\right\rangle_t^2} \end{cases} \tag{5}$$

where $\langle \cdot \rangle$ represents the averaging operation over a period of time. PSI is a real number between 0 and 1. When PSI $= 1$, the two signals are completely synchronized. Since the affected sensorimotor cortex was corresponded to the movement of the affected upper limb, the mean PSI within the affected hemisphere (intra-PSI) and the mean PSI between the affected and unaffected hemispheres (inter-PSI) were calculated.

E. Statistical Analysis

One-way repeated measures analysis of variance (ANOVA) was used to analyze the effect of stimulation strategy on the ERD value and on the PSI between electrodes, intra-PSI and inter-PSI. These tests were made with SPSS 26 (IBM SPSS Inc., Chicago, IL, USA) in this paper.

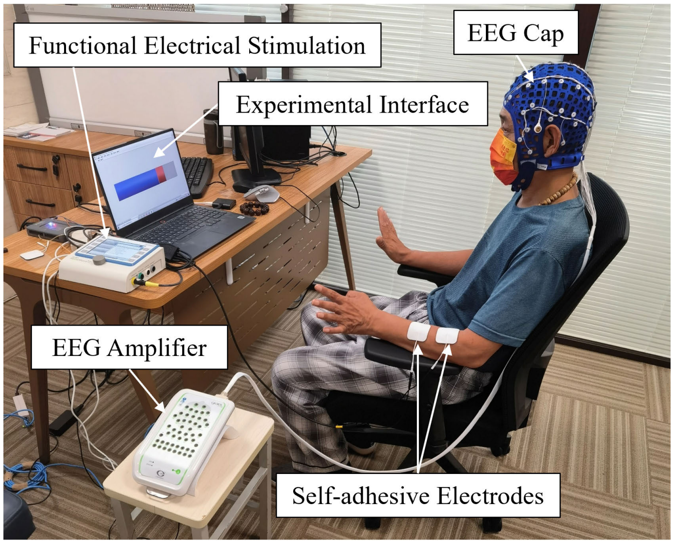

Fig. 2. The scene of experiment. The figure showed the scene at the S-CCFES task.

III. Results

A. The Effect of Stimulation Strategy on ERSP

First of all, the area where electrode C3 or C4 was located was named as motor area of interest (MAI) in this paper. Figure 3 showed the averaged ERSP at affected MAI, FCz and unaffected MAI during S-CCFES, A-CCFES, U-FES. The stimulation time of FES was 0-4s. It can be seen that, with the onset of the FES, an ERD phenomenon (blue color) was found in the alpha and beta bands for all tasks. The ERD phenomenon was strongest for the S-CCFES task.

The result of one-way repeated measures ANOVA showed that the alpha-ERD and beta-ERD values at affected MAI were significantly different in different FES strategies. Figure 4(A) showed that the alpha- and beta-ERD values during S-CCFES were significantly lower than those during A-CCFES and U-FES (S-CCFES vs. A-CCFES: $p = 0.014$ for alpha-ERD, and $p = 0.035$ for beta-ERD; S-CCFES vs. U-FES: $p = 0.009$ for alpha-ERD, and $p = 0.048$ for beta-ERD; A-CCFES vs. U-FES: $p = 0.692$ for alpha-ERD, and $p = 0.532$ for beta-ERD). Similarly, the alpha-ERD values at FCz were significantly different in different FES strategies, while there was no significant difference in beta-ERD. Figure 4(B) showed that the alpha-ERD value during S-CCFES was significantly lower than those during A-CCFES and U-FES (S-CCFES vs. A-CCFES: $p = 0.014$, S-CCFES vs. U-FES: $p = 0.016$, A-CCFES vs. U-FES: $p = 0.219$). However, there was no significant difference in the alpha and beta band at unaffected MAI in different FES strategies as shown in Figure 4(C).

In addition, the topography of mean ERD in alpha- and beta-rhythm bands were shown in Figure 5. To be noted, the topography of the survivors with the left hemisphere affected was flipped left-right symmetrically. Thus, the left side of the brain topography referred to the unaffected hemisphere, and the right side referred to the affected hemisphere. Compared to A-CCFES and U-FES, S-CCFES task induced stronger alpha-ERD at MAI (near electrode C3 & C4) and SMA region (near electrode FCz).

B. The Effect of Stimulation Strategy on PSI

In order to analyze the intensity of synchronization of the brain, Figure 6 showed intra-PSI and inter-PSI for resting EEG signal before and after stimulation. Both intra-PSI and inter-PSI after S-CCFES were significantly higher than those before stimulation, after A-CCFES and U-FES (intra-PSI: after S-CCFES vs. before experiment: $p = 0.008$; after S-CCFES vs. after A-CCFES: $p = 0.029$; after S-CCFES vs. after U-FES: $p = 0.048$. inter-PSI: after S-CCFES vs. before experiment: $p = 0.001$; after S-CCFES vs. after A-CCFES: $p = 0.001$; after S-CCFES vs. after U-FES: $p = 0.012$). Therefore, the intensity of synchronization was significantly enhanced after S-CCFES.

In order to analyze the area of significantly increased synchronization of the brain, Figure 7 showed the significant changes of PSI between any two of all electrodes after S-CCFES, A-CCFES and U-FES tasks, compared to that before stimulation. The figures were also flipped left-right symmetrically as above. The PSIs of EEG between the two electrodes connected with the green line indicated a significant increase after stimulation, while there was no significant decrease. It was obvious that there was a wider spread of the significantly increased PSI after S-CCFES (F4-FC4: $p = 0.008$, FC4-Fz: $p = 0.015$, Fz-Pz: $p = 0.006$, C3-CP3: $p < 0.001$). It can be seen from the figure that PSI increased in a wider area after S-CCFES.

IV. Discussion

This study compared the neural oscillations and cortical synchronization of stroke survivors using different strategies of CCFES and U-FES. To our knowledge, no previous reports have discussed the effect of CCFES on EEG response in real time. It was clear that the ERD value at affected MAI during S-CCFES was significantly stronger than those of other tasks in alpha-rhythm and beta-rhythm, and the ERD value at electrode FCz during S-CCFES was significantly stronger than those of other tasks in alpha-rhythm. Furthermore, there were more electrode pairs with significantly increased PSIs after S-CCFES. The intra-PSI and inter-PSI after S-CCFES were also the highest among these three tasks. Overall, the result illustrated that S-CCFES strengthened the cortical activity and cortical synchronization for stroke survivors.

A novel finding of the present study was that the significantly stronger ERD at affected MAI for S-CCFES as compared to A-CCFES and U-FES in alpha-rhythm and beta-rhythm. The ERD value was used to indicate cortical activity and more negative ERD indicated higher cortical activation [32], [33]. Therefore, it can be inferred that the cortical activity at affected MAI during S-CCFES was higher. This may be related to the theory of interhemispheric inhibition, which holds that the cortical damage for stroke survivors may result in hyperexcitability of the unaffected motor cortex and the affected hemisphere may receive interhemispheric inhibition from the hyperexcitable unaffected hemisphere [34]. During S-BM, similar neural networks in both hemispheres were activated and the interhemispheric inhibition was reduced [35]. Therefore, the motor function of the non-dominant hand was

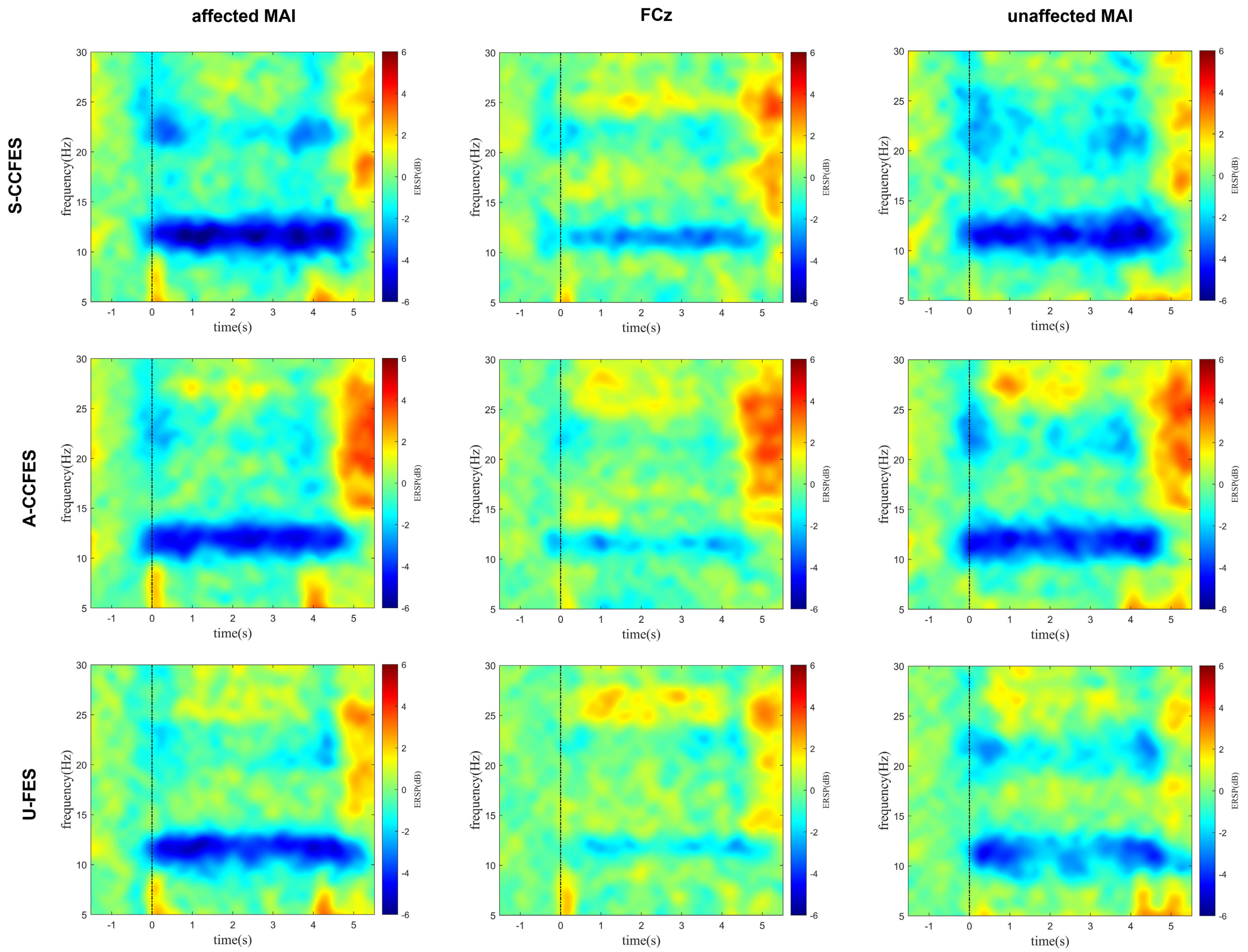

Fig. 3. Averaged ERSP across all participants at affected MAI, FCz and unaffected MAI. The dashed lines indicated the onset of FES.

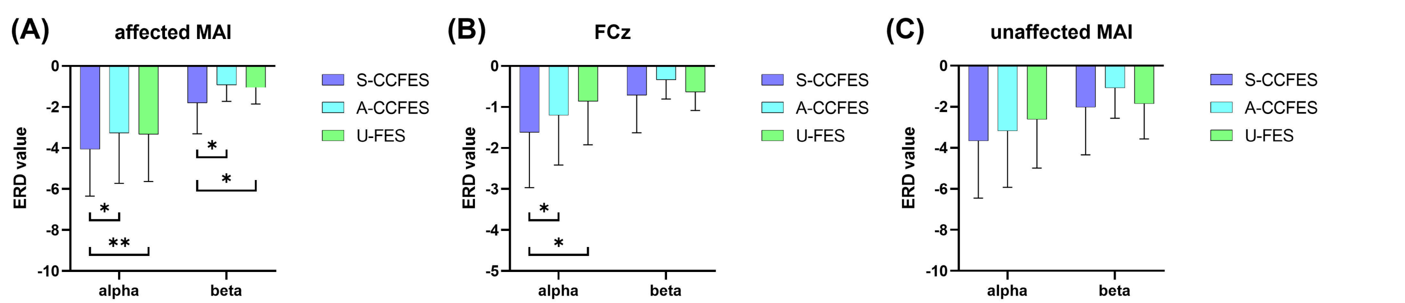

Fig. 4. (A) The ERD value at affected MAI. (B) The ERD value at electrode FCz. (C) The ERD value at unaffected MAI. *: $p < 0.05$, **: $p < 0.01$.

enhanced during S-BM [36]. Our results, combined with Cunningham et al [24], showed S-CCFES, similar to S-BM, may alleviate hemispheric inhibition and enhance the activation of the affected hemispheric motor cortex. The authors also suggested that S-CCFES induced the activation of homologous muscles, which may reduce muscle recruitment difficulty based on homologous coupling theory [37]. For A-CCFES and U-FES, although they induced similar ERSP patterns in affected hemisphere as S-CCFES, the cortical activity was significantly reduced. The ERD values of the unaffected MAI as shown in Figure 3 and Figure 4, and there was not any difference of ERD among the three tasks. It can be seen that although the unaffected side of the hand in the U-FES task was relaxed, there was also ERD phenomenon, which may be spread from the affected side. In addition, the ERD compared statistically was the minimum value within a certain frequency band and time period. The non-significance result only indicated there was no difference in the strongest strength

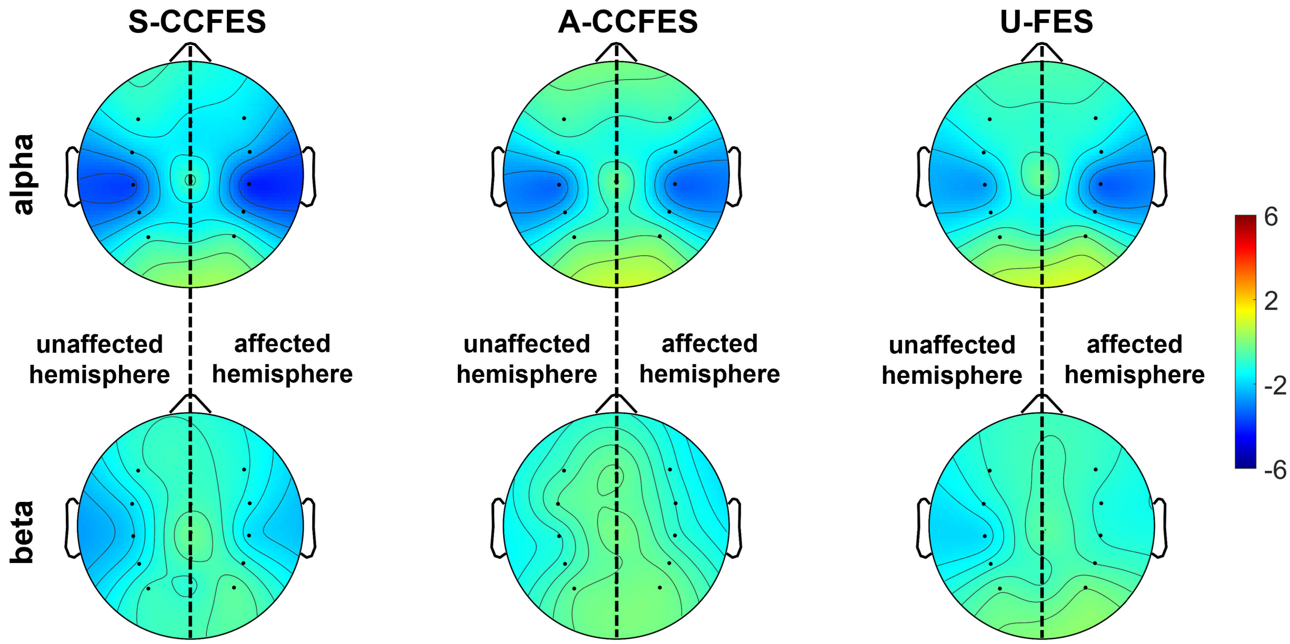

Fig. 5. The averaged ERD brain topography in alpha- and beta-rhythm bands.

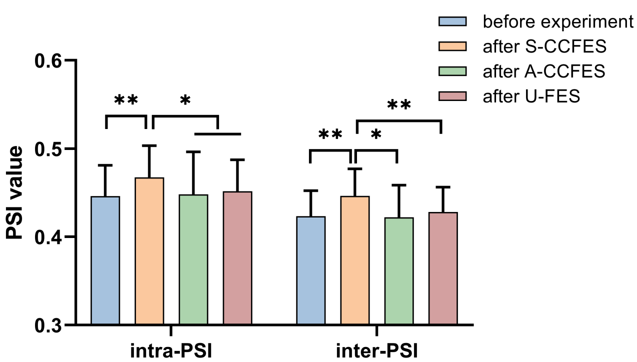

Fig. 6. Comparison of intra-PSI and inter-PSI. *: $p < 0.05$. **: $p < 0.01$.

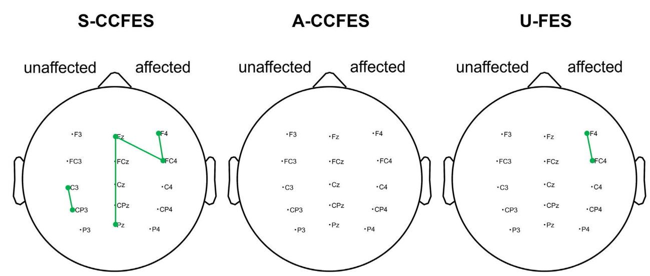

Fig. 7. Significant changes of PSI between any two electrodes. The green line represented a significant increase in PSI after stimulation.

of ERD for three tasks, but it is possible that the ERD range is different, which deserves further studies.

Another finding was that the PSI after S-CCFES was significantly higher than those of A-CCFES and U-FES and the significantly increased PSI spread to more electrode pairs. PSI has been used to examine the large-scale integration of neural activity [29]. Shi et al. proposed that there was a significant negative correlation between National Institutes of Health Stroke Scale (NIHSS) and PSI [30], indicating that the higher the PSI is, the better the motor function is. According to the changes of PSI of all electrode pairs for all tasks in Figure 7, some PSIs between electrodes were significantly increased after S-CCFES and U-FES. It seems that FES could not only affect the circuits within somatosensory cortex, but also alter the circuits within motor network [38], [39]. Manto et al. proposed that motor cortex could affect polysynaptic responses to peripheral stimulation from the intermediate cerebellum [40]. FES was thought to affect multiple regions of cerebral cortex. The synchronization increased only in affected hemisphere after U-FES, while it increased in both hemispheres after S-CCFES. It could be caused by the inhibition of interhemispheric crosstalk and synchronization tendency from other hemisphere [41]. The unaffected hemisphere can adaptively compensate the affected hemisphere by interhemispheric crosstalk during S-CCFES [42]. Our brain will reduce the crosstalk of each cerebral cortex during A-CCFES, which may weaken the connectivity between each cerebral cortex. This might be why there was no PSI significantly increased after A-CCFES. Biasiucci et al. demonstrated that EEG connectivity within affected hemisphere for stroke survivors increased after a period of BCI-FES treatment, while no significant changes were found in connectivity between the two hemispheres and within the unaffected hemisphere [43]. Our results showed that both intra-PSI and inter-PSI significantly increased after S-CCFES, which indicated S-CCFES better promoted inter-hemispheric connection.

It is interesting that the absolute ERD value at electrode FCz during S-CCFES was significantly higher than that of A-CCFES and U-FES in alpha-rhythm. EEG at FCz electrode reflected the activity of SMA. The activation of SMA might also be due to the presence of interhemispheric crosstalk, either enhancing or inhibiting [44].Grefkes et al. found that, compared with unilateral hand movements, the SMA region was significantly activated during symmetrical bilateral hand movement [8]. Dietz et al. also proved that SMA region was significantly activated during bilateral hand movements based on functional magnetic resonance imaging (fMRI) [6]. Our results showed that the symmetry of FES had different effects on the activation of SMA. It was deduced that S-CCFES was more conducive to the excitability of SMA than A-CCFES, thus more conducive to promoting motor learning and neural plasticity.

Our findings may provide the interpretation of the CCFES recovery mechanism. There are many studies focusing on the rehabilitation effect of motor function of CCFES. For example, Knutson et al. demonstrated CCFES could significantly improve the score of Box and Block Test (BBT) and Arm Motor Abilities Test (AMAT) for stroke survivors with chronic (>6 months) compared with U-FES after 12 weeks' treatment [12]. Zheng et al. proved that FES-BM could significantly improve the score of upper extremity function, the strength of extensor carpi and the activities of daily living for survivors with early-phase stroke (<15 days post-stroke) compared with U-FES after 2 weeks' treatment [45]. These studies analyzed the long-term effect of CCFES on motor performance, without considering the real-time neural activities during CCFES. The real-time EEG signal reflected immediate cortical response during different strategies of FES. Meanwhile, S-CCFES seemed to have better prospects for recovery.

A. Limitation

However, the study had some limitations. Firstly, it was proved that the interhemispheric inhibition was related to the degree of motor impairment [24]. Limited by the sample size, the relationship between cortical activity/synchronization and the degree of motor impairment was not analyzed. Secondly, the spatial resolution of EEG signal was relatively low. fMRI or functional near-infrared spectroscopy may further reveal more information about the brain functional responses of three different tasks. Thirdly, the FES strength was a pre-set constant value during the wrist extension. Therefore, our EMG-triggered FES is not likely to be as strong as CCFES in which the electrically stimulation is proportionally controlled by a command glove worn on the contralateral hand. This may probably discount the effect of CCFES.

V. Conclusion

In order to determine the effect of different electrical stimulation strategies on neural oscillations and cortical synchronization for stroke survivors, an experiment with S-CCFES, A-CCFES and U-FES was designed. The result showed the ERD values at affected MAI and FCz during S-CCFES were significantly stronger than those of A-CCFES and U-FES. It indicated that S-CCFES strengthened the activation of the affected motor area and SMA. Additionally, the intra-PSI and inter-PSI were both significantly larger after a short time S-CCFES, and there were more electrode pairs with significantly increased PSI. Therefore, the PSI intensity increased significantly and the area with significantly increased PSI became wider after S-CCFES. These results indicated that S-CCFES strengthened the cortical synchronization. This study verified the efficacy of the S-CCFES from the perspectives of the cortical activation and synchronization. This may also provide a better guidance for the development of CCFES in stroke rehabilitation.

Conflict of Interest

None of the authors have potential conflicts of interest to be disclosed.

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