Novel Approach to Transfer of Coordination Skills to the Paretic Hand by Improving the Efficiency of Cortical Network

Jinyi Long, Longbin Shen, Qiuwen Cai, Shan Xiao, and Zhuoming Chen

***Abstract*— We have previously shown that healthy subjects can transfer coordination skills to the unpracticed hand by performing a unimanual task with the other hand and visualizing a bimanual action using a game-like interactive system. However, whether this system could be used to transfer coordination skills to the paretic hand after stroke and its underlying neural mechanism remain unknown. Here, using a game-like interactive system for visualization during physical practice in an immersive virtual reality environment, we examined coordination skill improvement in the unpracticed/paretic hand after training in 10 healthy subjects and 13 chronic and sub-acute stroke patients. The bimanual movement task was defined as simultaneously drawing non-symmetric three-sided squares (e.g., U and C), while the training strategy was performing a unimanual task with the right/nonparetic hand and visualizing a bimanual action. We found large decreases in the intra-hand temporal and spatial measures for movement in the unpracticed/paretic hand after training. Furthermore, a substantial reduction in the inter-hand temporal and spatial interference was observed after training. Additionally, we examined the related cortical network evolution using EEG in both the healthy subjects and stroke patients. Our studies show that the cortical network became more efficient after training in the healthy subjects and stroke patients. These results demonstrate that our proposed method could contribute to the transference of coordination skill to the paretic/unpracticed hand by promoting the efficiency of cortical networks.**

***Index Terms*— Bimanual coordination, cortical network, virtual reality, EEG, stroke patients.**

Manuscript received 20 May 2022; revised 8 September 2022 and 31 October 2022; accepted 9 November 2022. Date of publication 16 November 2022; date of current version 31 January 2023. This work was supported in part by the National Natural Science Foundation of China under Grant 62276115, in part by the Outstanding Youth Project of Guangdong Natural Science Foundation of China under Grant 2021B1515020076, in part by the National Key Research and Development Program of China under Grant 2020YFC2005700, in part by the Guangdong Provincial Natural Science Foundation of China under Program 2019A1515012175, and in part by the Fundamental Research Funds for Central Universities. *(Corresponding authors: Jinyi Long; Zhuoming Chen.)*

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Digital Object Identifier 10.1109/TNSRE.2022.3221738

I. Introduction

IN DAILY life, many activities are performed using both hands, including riding a bike, eating with a knife and fork, and playing the piano. Inter-limb coordination is essential for these activities. However, stroke may cause muscle weakness or stiffness down one side of the upper extremity, leading to disruption of inter-limb coordination [1], [2]. Additionally, previous studies have shown that more than one-fifth of stroke patients cannot fully recover their paretic limb for cooperative movement control [2], [3], [4]. Therefore, it is critical to investigate the effect of bimanual training mechanisms to restore the coordinated function of the paretic hand.

Bilateral hand training is a promising approach to assist the stroke patients to improve the coordinated function of their paretic hand [5]. Bimanual coordination emerges as an active, task-specific assembling process where the limbs are constrained to act as a single functional unit by virtue of mutual coupling [6]. Bimanual training is expected to enhance the recovery of this interlimb coupling by entraining the impaired limb to the nonimpaired limb [7], [8], [9], a task that require to simultaneous use of both limbs in repetitive training [10], [11], [12]. However, it is challenging for bilateral hand training to perform the coordinated movements intensively using the paretic hand after stroke.

One approach for the paretic hand training of coordination skills is using the robot-assisted technique. For example, several studies have exploited the capabilities of robotics to assist the paretic limb in the movement trajectories predefined by the trajectory generator [31] or directed by the actual movements of the nonimpaired limb [7], [22], [26]. However, the robot-assisted technique is always limited to fixed movement trajectories and it is difficult to train fine movement of the fingers. Another approach to facilitate post-stroke training of the paretic hand is cross-limb transfer via visual feedback, i.e. the initial practice of unilateral motor tasks with one hand improves subsequent performance with the unpracticed/paretic hand [13], [14]. For example, practicing a motor task with one limb had been shown to improve performance with the limb opposite in a wide range of motor tasks including mirror tracing, pursuit tracking, sequential finger tapping, the serial reaction time task, and reaching while exposed to force perturbations [14], [15], [16]. Some of these improving was using the 3D virtual reality (VR) system to provide the real-time movement-based sensory feedback as if their unpracticed hand was training [16]. Furthermore, in our recent study, we examined the effect of visual feedback to the inter-manual coordination skill transfer through designing a bimanual task with simultaneously drawing non-symmetric three-sided squares (e.g., U and C) to learn limb coordination in a game-like interactive system under VR environments with the following training strategies: (1) performing a unimanual task with right hand and seeing a bimanual action; (2) not performing a task but seeing a bimanual action; (3) performing and seeing a unimanual task [32]. We demonstrated that the visual feedback can transfer coordination skill better to the untrained hand through practicing the coordinational task with one hand and seeing a bimanual action [32]. Therefore, we hypothesized that physical training with visual sensory feedback from the virtual hand could transfer coordination skills to the paretic hand after stroke. Therefore, we applied the same game-like scenario system to the stroke patients. Here, a virtual hand was designed to replace the unpracticed/paretic hand to perform a coordination task with the other virtual hand that is controlled by the practiced hand in an immersive environment.

Electrophysiological and neuroimaging studies have shown increased engagement within the lesioned hemisphere and brain connectivity plasticity after the completion of an upper extremity rehabilitation program [18], [19]. Therefore, we also examined the neural plasticity after training by testing the cortical network reconfiguration with EEG.

In summary, our main contributions are showing that the approach of performing a unimanual task while visualizing a bimanual action could transfer coordination skill to the untrained/paretic hand and demonstrating that this transference of coordination skill may be contributed with the efficiency of cortical networks.

This paper is organized into five sections. The methodologies, including the subjects, equipment, experimental tasks and procedures, behavioral performance measures, and cortical network analysis, are presented in Section II. The results are described in Section III, further discussion provided in Section IV, and Section V concludes the paper.

II. Methods

A. Subjects

Ten healthy right-handed volunteers (7 males, 23.7±3.9 years old) and 13 chronic and sub-acute stroke patients (8 males, 53.9±12.2 years old), were recruited for the study. The inclusion criteria for the healthy volunteers were that they do not have cognitive deficits or neurological problems that would impact the performance of upper limb movements. The inclusion criteria for stoke volunteers include: (1) volunteers present ischemic or hemorrhagic stroke learning from patients' medical history; (2) the Fugl-Meyer (FM-UE) assessment score regarding upper-extremity portion is larger than 35, and ability to draw a circle with the index finger of the paretic hand; (3) no other neurologic or orthopedic disorders. The exclusion criteria take discomfort and felling pain during tasks into consideration as well. All the subjects provided written informed consent prior to the study, which was approved by the local ethics committee of Jinan University. The study was performed in accordance with the guidelines of the Declaration of Helsinki.

TABLE I
Characteristics of the Stroke Patients

Patient	Gender	Age (years)	Diagnosis	Paretic side	Months PS	FM-UE
S1	M	40	H	L	19	36
S2	F	64	H	R	20	50
S3	M	68	I	R	33	56
S4	F	40	I	L	3	52
S5	M	41	I	R	6	48
S6	F	72	H	R	46	58
S7	F	67	H	L	14	48
S8	M	52	H	R	4	46
S9	M	57	I	R	3	50
S10	F	58	H	R	3	48

Months PS = months post-stroke; FM-UE = upper-extremity portion of the Fugl-Meyer (out of 66); M = male; F = female; H = hemorrhagic; I = ischemic; L = left; R = right.

Finally, 10 stroke patients were recruited for further analysis because the other 3 stroke patients felt discomfort during the experiment. Table I shows the clinical motor, functional outcome measurements, and demographic characteristics for the stroke group.

B. Equipment

Subjects wore an HTC Vive head-mounted display (HMD) in all trials (see Fig. 1A). The HMD display provides a resolution of 960*1080 pixels (per eye), a refresh rate of 60 Hz and field of view of vertical 60 degrees and horizontal 90 degrees. Subjects sat in front of a desk. The figure movements of both hands were recorded using Hi5 VR gloves (Noitom; sampling rate 100 Hz).

The virtual environment was composed of a table which was aligned spatially with the real table in front of the participant. The subjects would visualize the environment from a first-person point of view. Additionally, there were two virtual hands whose finger movements could be yoked in real-time to the subjects' actual finger movements (virtual hands were based on a model available in Hi5 VR gloves toolbox). The environment can be visualized in Fig. 1A.

During the experiment, the EEG data were acquired from 32 scalp sites (extended 10-20 system) using a cap with active Ag/AgCl electrodes (quickcap32). Wet electrodes were used in the cap, and the electrode impedance was modulated to less than 5 KΩ. The reference electrode was on the bilateral mastoid. A Neuroscan Synamps2 amplifier amplified the EEG signal. The sampling rate of the EEG signal was 1 kHz. The band pass filtering range was 0.5-30 Hz with a 50-Hz notch filter. In the preprocessing stage, we performed the Infomax independent component analysis (ICA) algorithm using the EEGlab tool-box [20]. After visual inspection of

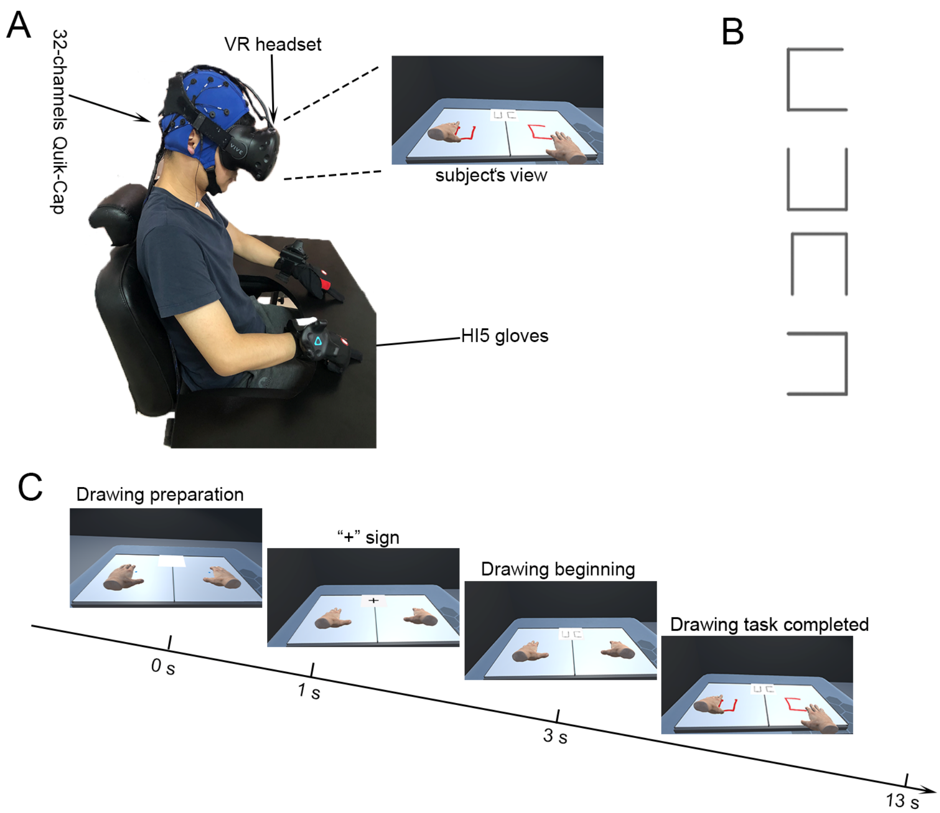

Fig. 1. Experimental setup. A, Subjects wore an HTC Vive HDM over the EEG cap and sat in front of a desk. Online visual sensory feedback was consisted of a drawing display by two virtual hands whose finger movements could be yoked in real-time to the subjects' actual finger movements (virtual hands were based on a model available in Hi5 VR gloves toolbox). The virtual environment was spatially consistent with the real environment. B, Four three-sided squares for each hand. The stimulus set was constituted by combining these four patterns for the left and right hand to create 16 patterns. C, Schematic illustration of one trial during a bimanual drawing task.

the scalp map and of the time-course of the activation in each component, we eliminated the components clearly related to eye blinks. The EEG data were back-projected with the remaining components for further analysis.

C. Experimental Tasks and Procedures

The experimental tasks and procedures were similar to our previous conference paper [32]. A 3D virtual environment was employed for stimulus presentation and online visual sensory feedback (Fig. 1A). Stimuli were presented directly on the virtual table. The stimulus shape for each hand was a three-sided square, with four patterns consisted of the open side facing right, left, up, or down (Fig. 1B). The length of each side spanned 10 cm. Hence, a set of 16 patterns could be created by combining those four patterns for the left and right hand, which were consisted of six pairs of congruent patterns and ten pairs of incongruent patterns.

Before the experiment, we created a training set and a test set. The training set was consisted of eight patterns (randomly selected 3 congruent and 5 incongruent), while the other eight patterns composed of the set for the pre-training and post-training tests. The subjects draw these patterns on the surface of the table.

During the test experiments, the start of each trial was indicated by the appearance of two circles (5-mm diameter), located 35 cm in front of the subject and separated by 40 cm (Fig. 1C). When seeing the starting circles, the subjects moved their index fingers into them and were required to hold this position. After holding 1 s, a "+" sign was appeared between the two starting circles to attract the subjects' attention. Then, after holding an additional variable time of 1-2 s, the subject was presented with the target pattern, which was two white and three-sided squares appeared 40 cm in front of the starting circles and indicated the target shape for each hand.

When the expected imperative signal appeared, the subjects were asked to produce the target shapes by moving their index fingers along the surface of the table "simultaneously" as accurately and quickly as possible.

The subjects were required to produce the shapes. However, we did not specify which endpoint of the three-sided square was to serve as the starting point, which means the subjects can start from any endpoint. When the drawings were completed, the end point of the shapes was that the subjects lifted their fingers off the table. Subjects were not instructed on how to properly coordinate their limbs. The drawing time was limited to 10 s. If the participants could not complete the drawing within this time, this trial would be discarded. The inter-trial interval was 3-5 s.

Additionally, during the training experiment, the strategy was performing a unimanual task while visualizing a bimanual action. This means that the drawings were completed with the right hand in healthy subjects and with the non-paretic hand in stroke patients using the similar experimental procedures to the test experiments. However, the other stimulus was drawn with the virtual hand of which strategy was predefined by computer progress, then coordinating with the drawing hand of subjects to provide the online visual sensory feedback as if both hands were drawing.

Note that the aim of this study was also to examine the neural plasticity after the coordination skills improvement of the upper extremity. Thus, we collected the EEG data during the experiment in the stroke and healthy subjects for further cortical network analysis.

Each subject was required to perform the experiment in three phases including the pre-training, training, and post-training. In the training phase, the subject completed 5 practice blocks. Each block consisted 32 trials where the eight patterns were presented four times each. Additionally, the pre-training and post-training phases comprised a 32-trial block each.

D. Behavioral Performance Measures

The target shape for each hand was a three-sided square. Hence, it needed to segment the drawing traces for the behavioral performance measures. First, we calculated the X- and Y-axis changes and defined the larger value as the principal heading. At each sampled finger position, the principal heading of each hand was established after smoothing over three successive samples. If one new principal heading was identified in three consecutive samples, these points were recorded as changes in the heading. Trials were scored as correct if they had only three expected principal heading transitions (including the initial principal heading), and each matches the relevant target shapes. Only those correct trials were used for the behavioral performance measurements.

Here we calculated a set of spatial and temporal variables to assess the subjects' behavioral performance including the reaction time, total time to complete the drawings, inter-hand temporal measurement and intra-hand spatial measurement. The reaction time referred to the amount of time that used to initiate a response to the stimulus. Here, it was defined as the amount of time taken to increase the hand velocity larger than 5% of the maximum velocity of the first line segment after the stimulus presented. The end of this segment was marked as the time point when the hand velocity decreased below 5% of the maximum velocity. The similar velocity criteria were used to define the onset and offset times of the other two segments. Thus, we could calculate the intersegmental pause time prior to the initiation of the second and third segments based on the onset and offset times of each segment. The time between the onset and offset of each of the three segments were summed to quantify movement time. The total time was defined as the sum of the reaction time, pause time, and movement time.

In order to evaluate the effect of temporal coupling, the asynchrony in temporal between hands is calculated, which was represented as the difference of onset time between hands in each of the given three segments and averaged within the blocks of trials.

In order to evaluate the intra-hand spatial measurement of unpracticed/paretic hand, we calculated the angle between two successive segments. Note that when perfect performance was achieved, a 90° change in the principal heading would occur at each transition. Regarding the inter-hand spatial measurement, we calculated the angle deviation between the unpracticed and practiced hands depended on the absolute angular difference between the corresponding segments generated by both given hands and averaged within the blocks of trials.

E. Cortical Network Analysis

The preprocessed EEG data from 30 electrodes (FP1, FP2, F7, F3, FZ, F4, F8, FT7, FC3, FCZ, FC4, FT8, T3, C3, CZ, C4, T4, TP7, CP3, CPZ, CP4, TP8, T5, P3, PZ, P4, T6, O1, OZ, and O2) were used for cortical network analysis. For each recording session (i.e., pre- and post-training) and subject, all the correct trials were used to construct the cortical networks. To analyze the network properties, we first performed coherence analysis to measure the functional connectivity between each pair of electrodes [21], [22]. For EEG coherence calculation, the data of each trial from a pair of electrodes were first processed by a fast Fourier transform (FFT) algorithm. Denoting the FFT of the ith trial of EEG in one electrode by $X_i(f)$ and in the other electrode by $Y_i(f)$, the coherence at frequency f was estimated as:

$$Coh(f) = \frac{\left|\sum_{i=1}^{L} X_i^*(f)Y_i(f)\right|^2}{\sum_{i=1}^{L} X_i(f)X_i^*(f)\sum_{i=1}^{L} Y_i(f)Y_i^*(f)} \tag{1}$$

where L is the number of trials, and $*$ denotes the complex conjugate. For each frequency f, the coherence value was expressed as a real number between 0 and 1. The weights of the edge between electrode j and electrode k (w_{jk}) were estimated by averaging the *Coh(f)* strength within a specific frequency band (i.e., alpha frequency band: 8–13 Hz; and beta frequency band: 14–30 Hz). Following the calculation of the edge weights between each pair of 30 electrodes, a 30×30 weighted connectivity matrix can be constructed to represent the interactions among the 30 electrodes. For each recording session (pre- or post-training) and subject, the cortical network was constructed by averaging the weighted connectivity matrices of those correct trials.

After the cortical network was constructed, the related network indexes were calculated based on graph theories: clustering coefficient (CC), local efficiency (LE), characteristic path length (CPL), and global efficiency (GE). The CC and LE reflect the capacity of local information processing in the brain network through functional segregation estimation between brain regions, while the CPL and GE represent the efficiency of global information processing in the brain network through functional integration estimation between brain regions.

Let S represent the set of electrodes, N represent the electrode number, and d_{jk} represent the shortest weighted path length between electrode j and electrode k. These four network indexes were defined as follows [22] and [23]:

$$CC = \frac{1}{N}\sum_{j\in S}\frac{\sum_{k,h\in S}(w_{jk}w_{jh}w_{kh})^{1/3}}{\sum_{k\in S}w_{jk}\left(\sum_{k\in S}w_{jk}-1\right)} \tag{2}$$

$$LE = \frac{1}{N}\sum_{j\in S}\frac{\sum_{k,h\in S,k\neq j}(w_{jk}w_{jh}\left[d_{kh}(S_j)\right]^{-1})^{1/3}}{\sum_{k\in S}w_{jk}\left(\sum_{k\in S}w_{jk}-1\right)} \tag{3}$$

$$CPL = \frac{1}{\mathrm{N}}\sum_{j\in S}\frac{\sum_{k\in S,k\neq j}d_{jk}}{\mathrm{N-1}} \tag{4}$$

$$GE = \frac{1}{\mathrm{N}}\sum_{j\in S}\frac{\sum_{k\in S,k\neq j}(d_{jk})^{-1}}{\mathrm{N-1}} \tag{5}$$

Thereafter, we statistically compared these network indexes using paired t-tests to investigate differences between the pre- and post-training recording sessions.

F. Statistical Analysis

A paired t-test ($p < 0.05$) with a false discovery rate (FDR) correction was used to quantify the network topology differences between the pre- and post-training recording sessions per group and frequency band. Repeated measures two-way ANOVAs were conducted to determine the effect of subject group (healthy subjects and stroke patients) and test stage (pre-training and post-training) on the behavioral performance measures of total time, reaction time, temporal asynchrony, intra-hand angle deviation and inter-hand angle deviation. Repeated measures two-way ANOVAs were also performed to evaluate the effect of the network properties (CC, CPL, GE and LE) and test stage (pre-training and post-training) in the healthy subjects on the results at the alpha and beta frequency bands separately. The same analysis was completed in the stroke patients. Bonferroni Post Hoc correction was used to check for significant comparisons (significance level α of 0.05). A priori comparisons were made as specified. Normal distribution was tested by the Shapiro-Wilk test (all $p>0.05$). The significance degree was set at $p<0.05$ and group data were presented as mean ± SD in the text and as SEM in the figures.

III. Results

A. Behavioral Performance

Figure 2 shows the intra-hand measure results in temporal dimension for the unpracticed/paretic hand during the drawing experiment in healthy/stroke subjects. Figure 2 shows that the performance in both the healthy subjects and stroke patients was enhanced in planning and initiating their movements, and in performing the drawing tasks during training.

Repeated-measures ANOVA showed a remarkable effect of the subject group ($F(9,1) = 22.09$, $p = 0.001$), test stage ($F(1,9) = 59.61$, $p < 0.001$) and their interaction ($F(1,9) = 16.77$, $p = 0.003$) on the average total time. Post hoc analysis also showed that the average total time was reduced to perform the drawing task at the post-training compared with the pre-training experiment within the healthy subjects ($p = 0.004$), and the same significance was found within the stroke patients ($p < 0.001$; Fig. 2A). Additionally, we found that the total time for drawing was larger in the stroke patients than that in the healthy subjects within the pre-training stage ($p < 0.001$) and the post-training stage ($p = 0.005$; Fig. 2A).

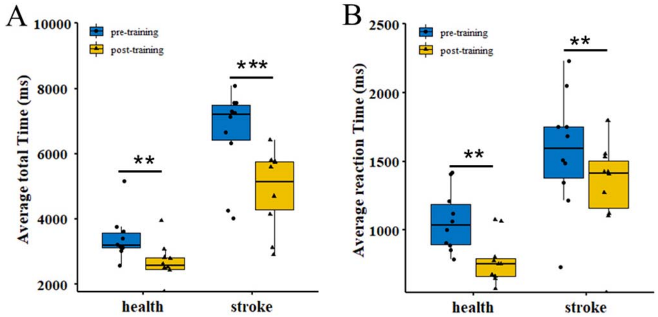

Fig. 2. Intra-hand measure results in temporal dimension for paretic/unpracticed hand during training. Average total time required to perform the drawings (A) and reaction time required during drawing (B) at pre-training stages (blue) and post-training stages (yellow) in the healthy subjects and stoke patients. Error bars indicate SEs. **$p < 0.01$ and ***$p < 0.001$.

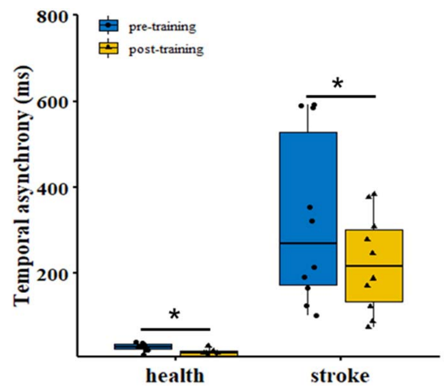

Fig. 3. Inter-hand temporal measure results for the unpracticed/paretic hand during training. Temporal asynchrony of the intra-hand angle deviation at the stages of pre-training (blue) and post-training (yellow) in the healthy subjects and stoke patients. Error bars indicate SEs. *$p < 0.05$.

A similar analysis was performed on the average reaction time of the unpracticed hand for the drawings during the experiment. This manifests a significant effect of the subject group ($F(9,1) = 12.46$, $p = 0.006$), test stage ($F(1,9) = 24.34$, $p < 0.001$) and their interaction ($F(1,9) = 26.54$, $p < 0.001$) on the reaction time during performing drawing. Post hoc analysis indicated that the reaction time was decreased at the post-training process compared with that at the pre-training experiment within the healthy subjects ($p = 0.008$), and the same significance was found within the stroke patients ($p = 0.002$; Fig. 2B).

Regarding temporal coupling, the expected drawing motions of these two hands are substantially synchronized after training (Fig. 3). Repeated-measures ANOVA manifested a significant effect of the subject group ($F(9,1) = 10.79$, $p = 0.009$), test stage ($F(1,9) = 36.23$, $p < 0.001$) and their interaction

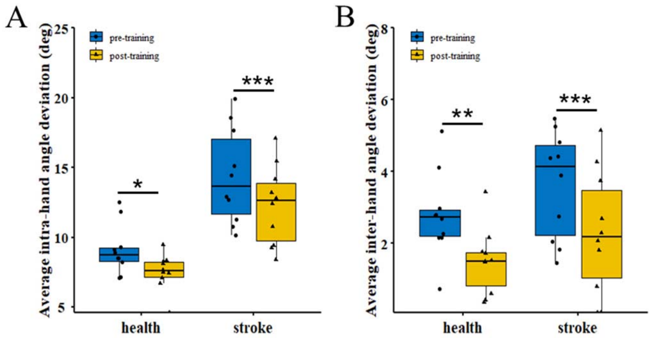

Fig. 4. Spatial measure results during training. (A) Average angle deviation of intra-hand between two successive segments generated by the unpracticed/paretic hand in healthy subjects and stroke patients at the stages of pre-training (blue) and post-training (yellow). (B) Average angle deviation of inter-hand between two corresponding segments generated by the two hands at the pre-training stage (blue) and post-training stage (yellow) in healthy subjects and stroke patients. Error bars indicate SEs. *$p < 0.05$, **$p < 0.01$ and ***$p < 0.001$.

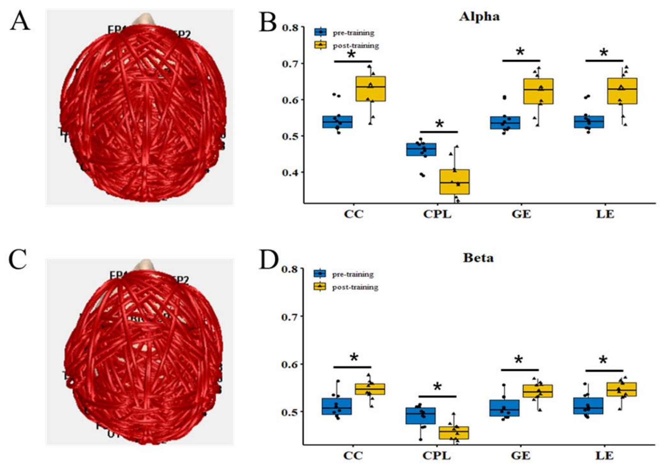

Fig. 5. Cortical network results in healthy subjects. Topological distributions with significant edges between pre-and post-training at the alpha (A) and beta (C) frequency bands. Cortical network properties at the alpha (B) and beta (D) frequency bands during pre-training (blue) and post-training (yellow) in healthy subjects. The error bars indicate SEs. *$p < 0.05$.

($F(1,9) = 26.25$, $p < 0.001$) on the intra-hand angle deviation. Post hoc analysis manifested that the degree of temporal asynchrony was decreased at the post-training stage compared with that at the pre-training state in healthy subjects ($p<0.05$) and stroke patients (Fig. 3; $p<0.05$). Additionally, we found that the intra-hand angle deviation during drawing was larger in the stroke patients than in the healthy subjects within the pre-training stage ($p < 0.05$) or the post-training stage ($p = 0.01$; Fig. 3).

Figure 4 shows the spatial measure results during the drawing experiment in the healthy subjects and stroke patients. Note that both the healthy subjects and stroke patients have better performance in heading transitions in drawing with the paretic/unpracticed hand over training. Furthermore, the spatial interference manifested between the practiced hand and the paretic/unpracticed hand can be eliminated during training.

Repeated-measures ANOVA manifested a significant effect of subject group ($F(9,1) = 144.08$, $p < 0.001$), test stage ($F(1,9) = 41.81$, $p < 0.001$) and their interaction ($F(1,9) = 13.12$, $p = 0.006$) on the intra-hand angle deviation. Post hoc analysis indicated that the intra-hand angle deviation was reduced during drawings at the post-training stage compared with that at the pre-training experiment within the healthy subjects ($p = 0.015$), and the same significance was found within the stroke patients ($p < 0.001$; Fig. 4A). Additionally, we found that the intra-hand angle deviation for drawing was larger in the stroke patients than in the healthy subjects within the pre-training stage ($p < 0.001$) or the post-training stage ($p < 0.001$; Fig. 4A).

Similarly, repeated-measures ANOVA identified a significant effect of the subject group ($F(9,1) = 68.65$, $p < 0.001$), test stage ($F(1,9) = 37.91$, $p < 0.001$) and their interaction ($F(1,9) = 24.21$, $p < 0.001$) on the inter-hand angle deviation. Post hoc analysis indicated that the inter-hand angle deviation was also reduced during drawings at the post-training stage compared with that at the pre-training experiment within the healthy subjects ($p = 0.008$), and the same significance was found within the stroke patients ($p < 0.001$; Fig. 4B).

B. Cortical Network Analysis Results

Figure 5 shows the cortical network properties at the alpha and beta frequency bands during the pre- and post-training in the healthy subjects. Note that the cortical network in these frequency bands shows improvements in the local information processing capacity and increased efficiency in global information processing after the RH-BH training.

The topological distributions with significant edges at alpha band were shown in Fig. 5A, while those at beta frequency band were shown in Fig. 5C. Repeated two-way ANOVA with the factors of network properties (CC, CPL, GE and LE) and test stages (post-training and pre-training) was performed on the results at the alpha and beta frequency bands. This identified a significant effect of network properties ($F(3,30) = 58.33$, $p < 0.001$), test stages ($F(1,10) = 26.74$, $p < 0.001$) and their interaction ($F(3,30) = 26.87$, $p < 0.001$) on the results at the alpha frequency band. Thus, the network properties modulated how the brain network configuration changed with test stages. Tukey's *post hoc* tests showed that the results were reduced at post-training compared with that at pre-training in CPL ($p<0.05$) but were increased in CC ($p<0.05$), GE ($p<0.05$) and LE ($p<0.05$, Fig. 5B). Similar results can be found in the results at the beta frequency band with a significant effect of the network properties ($F(3,30) = 22.09$, $p < 0.001$), test stages ($F(1,10) = 21.79$, $p < 0.001$) and their interaction ($F(3,30) = 22.01$, $p < 0.001$). Tukey's *post hoc* tests showed that the results were reduced at post-training compared with those at pre-training in CPL ($p<0.05$), but were increased in CC ($p<0.05$), GE ($p<0.05$) and LE ($p<0.05$, Fig. 5D).

Figure 6 illustrates the cortical network properties at the alpha and beta frequency bands during pre- and post-training in the stroke patients. Similar to the results in healthy subjects, we also found that the cortical networks in these frequency bands show improvements in the local information processing capacity and increased efficiency in global information processing after training. The average network with significant

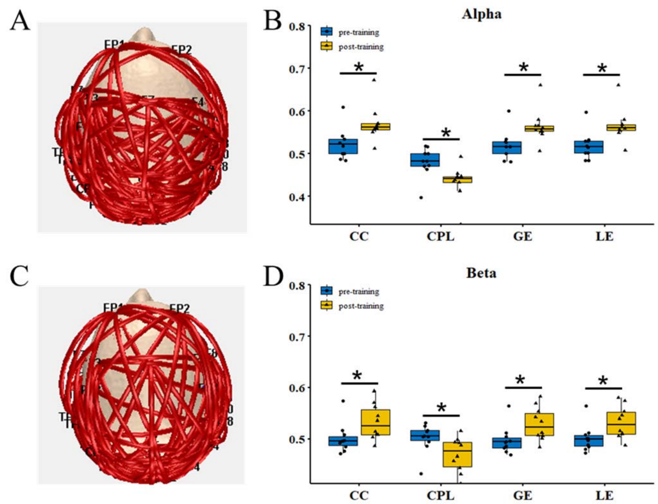

Fig. 6. Cortical network results in stroke patients. Topological distributions with significant edges between pre-and post-training at the alpha (A) and beta (C) frequency bands. Cortical network properties at the alpha (B) and beta (D) frequency bands during pre-training (blue) and post-training (yellow) in the stroke patients. The error bars indicate SEs; $^*p < 0.05$.

edges at alpha band was shown in Fig. 6A, while those at beta frequency band was shown in Fig. 6C. Repeated two-way ANOVA taking network properties (CC, CPL, GE and LE) and test stages (post-training and pre-training) as factors was performed on the results at the alpha and beta frequency bands. This identified a significant effect of the network properties ($F(3,27) = 14.27$, $p < 0.001$), test stages ($F(1,9) = 67.21$, $p < 0.001$) and their interaction ($F(3,27) = 68.53$, $p < 0.001$) on the results at the alpha frequency band. Thus, the network properties modulated how the brain network configuration changed with the test stages. Tukey's *post hoc* test showed that the results were reduced at post-training compared with those at pre-training in CPL ($p<0.05$), but were increased in CC ($p<0.05$), GE ($p<0.05$) and LE ($p<0.05$, Fig. 6B). Similar results were obtained at the beta frequency band with a significant effect of the network properties ($F(3,27) = 3.17$, $p = 0.04$), test stages ($F(1,9) = 11.98$, $p < 0.001$) and their interaction ($F(3,27) = 12.52$, $p < 0.001$). Tukey's *post hoc* test showed that the results were reduced at post-training compared with those at pre-training in CPL ($p<0.05$), but were increased in CC ($p<0.05$), GE ($p<0.05$) and LE ($p<0.05$, Fig. 6D).

IV. Discussion

Coordination skills between hands are essential for everyday activities. Here, we applied a game-like interactive system for visual feedback during unilateral physical practice as if both hands were coordinated movement in an immersive environment. We proposed that unilateral physical training with one hand through visual sensory feedback as if both hands coordinated training in immersive VR environment could transfer coordinated skills to the paretic/unpracticed hand, which was accompanied by the neural plasticity.

A. Transfer of Coordination Skill to the Paretic Hand

Our study shows that the spatial and temporal accuracy of movements in the unpracticed/paretic hand can increase with unilateral physical training with one hand while receiving visual sensory feedback as if both hands coordinated training in immersive VR environment. This finding is consistent with previous studies showing that motor skills in unilateral task can be transferred across the hands through unilateral training with one hand [16], [24]. For example, training with mirror feedback had a positive effect on improving the performance of a simple skill in the unpracticed hand of healthy subjects [25] and accelerate the recovery of motor function in the paretic hand of stroke patients [26], [27]. This finding is also consistent with previous studies proposing that unilateral training with visual feedback can contribute to the transference of motor skills and strength across the hands for multiple unilateral motor tasks including mirror tracing, pursuit tracking, sequential finger tapping, the serial reaction time task, and reaching while exposed to force perturbations [14], [15].

The role of sensory feedback on the coordination skill transfer to the paretic hand during physical training with the other hand is unclear [32]. In our resent study on the healthy subjects, we have demonstrated that a game-like interactive system can result in a significant performance gain in the transference of coordination skill to the unpracticed hand during practicing a coordinational task using one hand to control one corresponding virtual hand with another virtual hand [32]. Due to paralysis of the unilateral limb, it is difficult for stroke patients to perform coordination tasks. Here, we expanded this game-like interactive system to the chronic and sub-acute stroke patients. Our data indicated that the coordination skills were impaired after stroke compared with that in the healthy subjects. However, we found that, for stroke patients, non-impaired limb training by providing visualizations in bimanual interacting training results in the paretic limb being incoporated to the practiced for better controlling interlimb coordination. This finding agrees with previous evidence showing that interlimb coordination can be enhanced after bimanual training in stroke patients [31], [33], [34]. Additionally, visual feedback can promote cognitive strategy to cause greater generalization of intermanual transfer [35]. Thus, our findings open the possibility that the visual feedback contributes to the transfer coordination skills to the paretic hand.

B. Improving the Cortical Network Efficiency

Neuroimaging studies have shown that the large-scale cortical network is involved in coordination tasks [27]. Our studies show that the cortical network indexes of CC, GE and LE increased while the CPL decreased after training by carrying out a unimanual task with the right/nonparetic hand and visualizing a bimanual action in both healthy subjects and stroke patients. This finding is consistent with previous studies suggesting that the cortical network is engaged during visuomotor practice [28], [29], [30] and the degree of inter-regional coupling is correlated with the subsequent performance gain in the unpracticed hand [16]. The CC and LE are related to the capacity of local information processing in the brain network through functional segregation estimation between brain regions, while the CPL and GE are involved in the efficiency of global information processing in the brain network through functional integration estimation between the brain regions [21], [22]. Previous studies have shown that efficient brain reconfiguration is essential for information processing during cognitive task [21] and motor tasks [22]. Furthermore, a previous study showed that a better performance in the hand-controlled modality of a tracking task by practicing in the eye-controlled version of such task was is supported by the motor cortex, the basal ganglia and the cerebellum, which is consistent with other effectors [36].Thus, we speculate that a higher cortical network efficiency may contribute to increased gains of transferring coordination skill with one hand and visual sensory feedback of a virtual hand that is controlled by the subject coupled with the opposite virtual hand during physical training.

C. Limitations and Future Works

In this study, there are still several limitations which need to be clarified in the future. One of the limitations in our design is low realistic feedback. Here, the same shape of realistic virtual hand was applied for each participant. However, the realism level of virtual hands would improve the training performance [32]. Hence, it would be helpful to improve the level of realism by adjusting the size of the realistic virtual hand for each participant. Additionally, it would be interesting to investigate whether the presence of a seated full-body avatar would provide even more performance improvements for an untrained/paretic hand in bilateral tasks than compared to a realistic hand in the future. Another way to affect the realistic level of feedback is the strategy of visual sensory feedback of unpracticed/paretic hand during the training period. Here, the system replayed the visual feedback using predefined computer progress, which cannot capture the subjective drawing characteristics to provide better realism, especially in the stroke patients. Further research can improve the realistic level of visual feedback by using the strategy recoded from the pre-training period. Second, it would be helpful to know how long the improvement of bimanual motor function can be reserved for the paretic hand in stroke patients. However, we only examined the immediate rehabilitation performance after training here. We would extend the study for longitudinal rehabilitation examination in the future. Third, the number of stroke patients used in this study is relatively small. In the future, it would be better to collect more subjects' data to examine the efficiency of our proposed method. Especially, it is helpful for the clinical applications to examine this efficiency for different stroke groups according to the post-stroke time. At the last, previous studies had been shown that the 3D environments require more brain resources and effort than 2D and might be more appropriate for rehabilitation tasks [37], [38]. Thus, it might promote the rehabilitative performance by performing our proposed method in the 3D instead of the 2D environments.

V. Conclusion

Bimanual coordination skills are critical for daily life in humans; however, for stroke patients, training with one hemiplegic hand is hard to establish. This paper studied the effect of visual feedback for the transference of coordination skills to the unpracticed/paretic hand and its related neural plasticity. Our studies show that the coordination skills could be transferred to the paretic/unpracticed hand after performing a short-term training for the other hand while collecting online sensory visual feedback as if both two hands were drawing. Furthermore, the training would contribute increasing efficiency of cortical network at the healthy subjects and stroke patients. These results open the possibility way to promote the rehabilitation of coordination skills of the paretic hand through physical training by performing a unimanual task and visualizing a bimanual action.

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