Investigating the Effect of Different Types of Exercise on Upper Limb Functional Recovery in Patients with Right Hemisphere Damage Based on fNIRS

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Abstract

To investigate the effects of functional occupational therapy (FOT) combined with different types of exercise on upper limb motor function recovery and brain function remodeling in patients with right hemisphere damage (RHD) by analyzing functional near-infrared spectroscopy (fNIRS). Patients (n = 32) with RHD at Beijing Bo'ai Hospital were recruited and randomly allocated to receive either FOT combined with passive motion (N=16) or FOT combined with assisted active movement (N=16). The passive motion group (FOT-PM) received functional occupational therapy for 20 min and passive exercise for 10 min in each session, while the assisted active movement group (FOT-AAM) received functional occupational therapy for 20 min and assisted active exercise for 10 min. Both groups received conventional drug therapy and other rehabilitation therapy. Treatment was performed once a day, 5 times a week for 4 weeks. The recovery of motor function and activities of daily living (ADL) was assessed using Fugl-Meyer Assessment upper extremity (FMA-UE) and modified Barthel index (MBI) before and after treatment, and brain activation of the bilateral motor area was analyzed with fNIRS. The findings suggested that FOT combined with AAM was more effective than FOT combined with PM in improving the motor function of RHD patients' upper limbs and fingers, improving their ability to perform activities of daily living, and facilitating brain function remodeling of the motor area.

Introduction

Cerebral hemispheric damage can lead to sensory and motor dysfunction of the contralateral limbs[1,2,3], negatively affecting patients' motor control, mobility, and functional learning to various degrees[4] and therefore imposing heavy burdens on families and society[5]. For patients with right hemisphere damage (RHD), the speed of recovery is less

than satisfactory. However, in most RHD cases, the affected left limbs, being on the non-dominant side of the body, have received insufficient attention from the patient and the caregivers. Given that dysfunction of the upper limbs and hands seriously affects the ability to perform daily activities and quality of life, a more suitable method to improve the rehabilitation effect of upper limb function in RHD patients is needed[6,7,8,9,10].

Exercise therapy is an important method to help patients recover their limb function. For the early rehabilitation of patients with brain injury, passive movement (PM) and assisted active movement (AAM) training methods are usually used. AAM entails the activity of specific joints completed through a combination of their own muscle strength and outside assistance[11]. The key is for the patient to actively participate in assisted rehabilitation. The readiness of the human brain to activate can help stimulate and integrate the motor system in the cycle of motor control. Many studies have shown that AAM can induce neuroplastic changes, thereby leading to increased functional recovery in patients[12,13].

Functional near-infrared spectroscopy (fNIRS) is an imaging technique based on optical principles. According to the correlation between the attenuation of light in the tissue and the different concentrations of light-absorbing substances, fNIRS can quantitatively analyze concentration changes in oxygenated hemoglobin and deoxygenated hemoglobin in brain tissue, thereby monitoring the functional activity of the cerebral cortex[14]. Many studies have shown that fNIRS is an important means of monitoring brain oxygenation and energy metabolism after cerebral hemisphere injury[15,16,17]. Therefore, fNIRS might be a suitable monitoring method for studying cerebral cortex changes related to upper limb motor function recovery after cerebral hemisphere injury.

The motor signals produced by different sensory input methods and the adjustment states of the sensory cortex are different[18,19]. The sensory stimuli produced by passive and active movements are closely related to the stability of perception and the ability to build accurate representations of one's environment, which then guide one's behavior[20]. This study was designed to explore the effects of different modes of exercise on early upper limb rehabilitation and brain activation in patients with cerebral hemispheric injuries by analyzing fNIRS data and to provide scientific strategies for the comprehensive rehabilitation of patients in the future.

The purpose of this study was to investigate the effects of FOT combined with different types of exercise on upper limb function and brain remodeling in RHD patients. We hypothesized that FOT-AAM is more effective than FOT-PM in improving upper limb function and brain activation in RHD patients.

Protocol

This study was a single-blind randomized controlled trial and was approved by the Ethics Committee of the China Rehabilitation Research Center (CRRC-IEC-RF-SC-005-01) and registered with the Chinese Clinical Trials Registry (MR-11-23-023832).

1. Participants

1. Based on existing literature[21], use the reported Fugl-Meyer Assessment upper extremity (FMA-UE) scores of the experimental group and the control group after 4 weeks of treatment as the standard to calculate the sample size. For an estimated effect size of 0.28, a test

level (α) of 0.05, a two-sided distribution for the Z value, and a power of 0.8, the calculated sample size is 28. Assuming a dropout rate of 10%, the final necessary sample size is 32.

2. Recruit patients from the Occupational Therapy Department of the China Rehabilitation Research Center. Select patients according to the following inclusion criteria: diagnosis of first-onset right hemispheric injury (RHD); onset time within 3 months; age between 18 and 75 years; Mini-Mental State Examination (MMSE) score[22] > 20; Brunnstrom stage I or II[23] for the upper limb and hand; and right-handedness.
3. Exclude patients with obvious depression, anxiety or concurrent serious physical diseases and those who did not cooperate with the training were excluded.
4. Include only participants who sign an informed consent form before the study. The recruitment flow chart is shown in **Figure 1**.

2. Randomization and allocation

1. Randomly allocate the patients meeting the experimental criteria into the Experimental group (EG) and Control group (CG). Assign a therapist not involved in subject assessment or selection to perform the randomization procedure with a random data generator on a computer (https://www.randomizer.org/).

3. Intervention

1. Give both groups conventional drug therapy and conventional rehabilitation. Give all patients 20 min of functional occupational therapy (FOT) and 10 min of different types of upper limb exercise (EG performed active assisted movement and the CG performed passive movement) daily for a total of 30 min per day, 5 days per week for 4 weeks. To ensure the consistency of the intervention, select one therapist to perform all interventions and offer pre-research training to that therapist.
2. Functional occupational therapy (FOT):
   NOTE: The patient uses the metacarpophalangeal and interphalangeal joints of the affected finger to perform finger grasping movements driven by the glove on the healthy side.
   1. Have the therapist passively move the shoulder, elbow, wrist, thumb, and fingers of the affected limb for approximately 1 min.
   2. After the passive movements, instruct the patient to use the unaffected limb and hand to actuate the affected limb and hand to perform activities such as pushing a foam roller, lifting a wooden peg, lifting small wooden sticks, and holding a ball. Choose two to three activities for each training session according to the patient's condition.
3. Assisted active movement (AAM)
   1. Select a rehabilitation training device for the hand that will be trained. The device is designed to help the patient perform either passive or active movements. Select **Smart Mirror Mode** and set the **Time** to **10 min**. Ask the patient about their feelings and choose from levels **1-10** according to the patient's experience and tolerance. Then click the **Start** button.
   2. As the unaffected hand performs voluntary grasping, instruct the patient to observe the movement and to try to grasp with the affected hand with the assistance of the glove (**Figure 2A**).

3. As the unaffected hand is opened voluntarily, instruct the patient to observe the movement and to try to open the fingers of the affected hand with the assistance of the glove (**Figure 2B**)

   NOTE: When the unaffected hand grasps, the sensors on the unaffected glove cannot detect the blocked light signal, and the glove on the unaffected side will be triggered to grasp. When the unaffected hand opens, the sensors on the unaffected glove detect a light signal and trigger the glove on the unaffected hand to open.

4. Repeat the above process cyclically for 10 min, after which the equipment will end the training process automatically.

4. Passive movement (PM)

   1. Have the patient use the same device to perform passive grasping and hand opening. Place the corresponding glove on the affected hand. Select **Passive Mode**, set the **Time** to **10 min**, adjust the intensity from levels **1-10** according to the patient's sensations, and then click the **Start** button.

   2. Instruct the patient to remain relaxed and to close and open the affected hand with the aid of the glove (**Figure 2C**). Have the patient continue for 10 min, after which the device will end the training automatically.

4. Assessment

1. Have the clinical assessments performed by another therapist not blinded to group assignments. Have this therapist assess each patient twice: once before the intervention and once immediately after the 4 weeks of intervention.

   1. Collect basic patient information, including age, sex, and type of injury.

   2. Assess upper extremity motor function before and after intervention using the Fugl-Meyer Assessment for the upper extremity (FMA-UE)[24]. Additionally, use the wrist-hand component of the FMA (FMA-WH) to assess the hand function of patients.

   3. Assess the ability to perform daily activities using the modified Barthel index (MBI)[25].

   4. Monitor the activation of primary motor areas during passive motor tasks using fNIRS.

   5. Functional near-infrared spectroscopy data acquisition

      1. Obtain a research-type near-infrared brain functional imaging system with which to collect the fNIRS data. Such a system uses three wavelengths of near-infrared light (780, 805, and 830 nm) to monitor changes in the concentration of oxyhemoglobin (Δ[Oxy-Hb]) and deoxyhemoglobin (Δ[Deoxy-Hb]) and the total hemoglobin concentration (Δ[Hb]); its sampling rate is 13 Hz.

      2. According to the international 10-20 system, place 4 light source emitters and 4 detectors on the bilateral primary motor cortex (M1), with a total of 20 channels. See **Figure 3** for the specific positions.

   6. Task procedure

      1. Conduct the fNIRS evaluation in 5 consecutive trials in a modular paradigm (rest [15 s]-task [30 s]-rest [15 s]), as described in steps 4.1.6.2-4.1.6.9 (see **Figure 4**).

2. Open the fNIRS computer interface and enter the patient's basic information. Then, choose the optode arrangement **2X4(R), 2X4(L)**. Choose the **15-30-15** task paradigm, and set the assessment time to **5**.
3. Place the near-infrared system device on the patient according to the layout of the optodes. Adjust the positions of the emitters and detectors, and carefully remove the hair so that the optodes are in close contact with the scalp. After the adjustment is complete, click the **OK** button.
4. Go to the system's automatic signal adjustment interface, click **Standby**, and adjust all channels to display green (good signal).
5. Place the glove on the affected hand of the patient. Select the **Passive Exercise** mode. Since the training frequency will change with the strength, select the average strength, that is, **5** gears, for each subject during the test.
6. Click the **Start** button on the fNIRS computer interface. Perform the task in 3 phases. Measure an initial resting phase of 15 s, counting down from 15 s until 0 s. During this process, instruct the patient to sit quietly in the chair, keep still, and try not to think about other things so that the brain is in a relaxed state.
7. When the time counts down to 0 s, click the **Start** button of the hand device. The patient's affected hand will begin passive grasping and opening movements with the aid of the glove. At this time, the computer will start to count down from 30 s, which is the duration of the passive movement. When the countdown reaches 0 s, click the **Stop** button of the hand device to end the exercise. The frequency of grasping and opening is set by the device; 3 cycles of grasping and opening will be completed 3 times during the 30 s task.
8. Begin another 15 s rest period as described before. When this interval has passed, the first rest-task-rest test is over.
9. Repeat the above rest-task-rest test 5 times, and then end the fNIRS test.

7. Near-infrared data analysis:
    1. For this analysis, use the data analysis software installed in the fNIRS system, as described below.
    2. Eliminate the outlier data caused by severe motion artifacts in all channels and the dropped data.
    NOTE: When this protocol was performed, 1 outlier in the EG, 1 outlier in the CG, and 2 cases of dropped data in the CG were eliminated.
    3. Discard any channels with obvious motion artifacts.
    4. Conduct overlay averaging of the left and right channels (10 channels per side) separately.
    5. Use a bandpass filter (0.01-0.08 Hz) to remove noise components with obvious periodic fluctuations in the signal, including mechanical noise and physiological noise. Types of physiological noise that must be eliminated include heart rate (approximately 1 Hz), respiration (approximately 0.2-0.3 Hz), Mayer

waves (approximately 0.1 Hz), and extremely low-frequency physiological fluctuations (<0.01 Hz).

6. Take the 15 s before and after the start of the experimental task as the baseline, and take a block (rest [15 s]-task [30 s]-rest [15 s]) as the test unit. Superimpose the five blocks and take the average.
7. Use the Savitzky-Golay method for smoothing. Set the number of smoothing points to 5 and the number of smoothing times to 1[26].
8. After preprocessing, calculate the integral and centroid values.
9. Use the Shapiro-Wilk test (Shapiro-Wilk, SW) to test the normality of the centroid values, the integral values, and their differences before and after intervention in the two groups; consider the data normally distributed if the resulting *P* value is >0.05.
10. Use the independent-sample t-test to compare the data between the two groups before and after the intervention. Use the paired-sample t-test to compare the centroid values and integral values within the two groups before and after the intervention.

5. Statistics

1. Use SPSS for the statistical analysis.
2. Test the normality of the data using the SW test.
3. Compare the general data of the patients in each group using Fisher's exact test or an independent-sample t-test.
4. Behavioral data were compared between groups and within groups using repeated ANOVA and described as mean ± standard deviation.

Representative Results

Baseline

From October 2021 to June 2023, we recruited 35 patients, 32 of whom ultimately completed the study; no patients experienced any adverse events during the trial.

Regarding the clinical symptoms of the two groups of patients (**Table 1**), the average ages of the EG and the CG were 53.19 ± 10.72 and 55.88 ± 12.32 years (P = 0.515), respectively. There were no significant differences in gender, disease type, FMA-UL scores, or MBI scores (P > 0.05). Before the intervention, the FMA-WH scores of all patients in both groups were 0 points.

FMA-UL has high clinical significance and can effectively and reliably assess upper limb involvement in patients with brain injury. The FMA-UL has a total of 33 upper limb assessment items, and each unidirectional score is assigned as 2 points for full completion, 1 point for partial completion, and 0 points for no completion. The total possible upper limb movement score is 66 points. As a subcategory of the FMA-UL, the wrist-hand scale (FMA-WH) has 12 items, with a total possible score of 24 points.

The results of repeated measures analysis of variance showed that the main effect of the group on FMA-UL score was significant, F = 5.564, p = 0.030, $\eta^2 p$ = 0.214; the main effect of time was significant, F = 34.716, p < 0.001, $\eta^2 p$ = 0.831; the interaction effect of group and time was significant, F = 5.554, p = 0.030, $\eta^2 p$ = 0.256. (**Table 2**)

The main effect of the group on the FMA-WH score was significant, F = 8.817, p = 0.006, η^2p = 0.227; the main effect of time was significant, F =13.357, p = 0.001, η^2p = 0.308; The interaction effect between time and group was significant, F = 8.817, p = 0.006, η^2p = 0.227. (**Table 2**).

The modified Barthel index is widely used to assess the ability to perform daily activities and measures a person's ability to perform ten such basic activities. The total possible score on the Barthel index is 100 points, and the higher the score is, the stronger the patient's ability to perform activities of daily living.

The main effect of the group on the MBI score was significant, F = 8.512, p = 0.007, η^2p = 0.221; the main effect of time was significant, F = 588.559, p < 0.001, η^2p = 0.952; the interaction effect between group and time was significant, F = 10.425, p = 0.003, η^2p = 0.258. (**Table 2**).

The integral value is the integral of the blood oxygen signal during the execution of the task and reflects the magnitude of the hemodynamic response during the task. The centroid value is the time (s) shown by the vertical line of the center of the blood oxygen signal change area during the entire task period and is an indicator of time-course changes throughout the task, representing the speed of the hemodynamic response[27].

There was no significant difference in the integral or centroid values between the two groups before (**Figure 5A**) the intervention (P > 0.05). After the intervention, the integral value of the right hemisphere of the subjects in the CG was 0.20 ± 0.32, the integral value of the right hemisphere of the subjects in the EG was -0.06 ± 0.24, and there was a significant difference in the overall means of the two groups (t=-2.489, d=0.92, P = 0.020, P < 0.025 is considered statistically significant) (**Table 3**). After the intervention, the integral value of the left hemisphere of the subjects in the CG was 0.18 ± 0.32, the integral value of the left hemisphere of the subjects in the EG group was -0.04±0.26, and there was no significant difference in the overall means of the two groups (t=-1.975, P=0.059, d=0.75). There were no significant differences in the centroid values between the two groups after the intervention (P > 0.025) (**Figure 5B**).

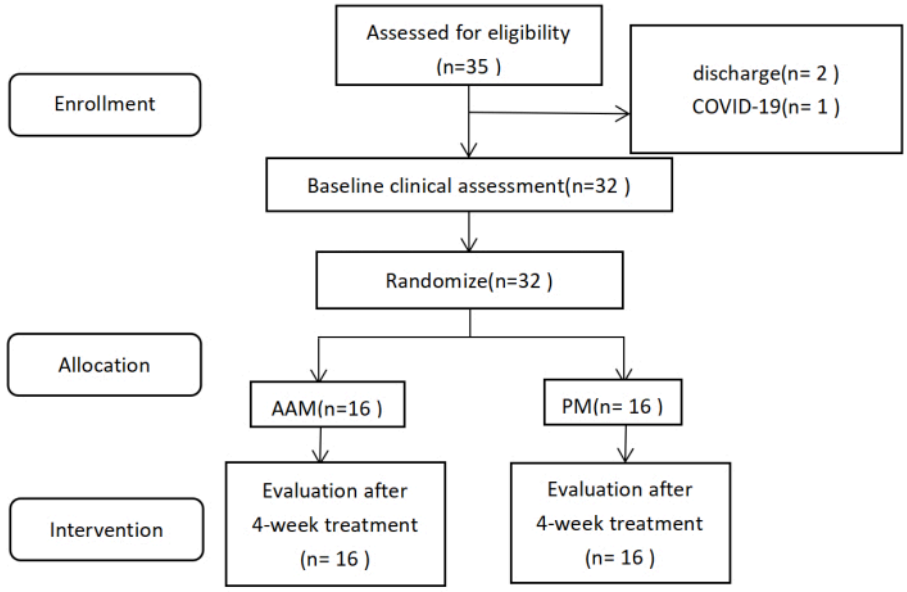

Figure 1: Recruitment flow chart. A total of 35 subjects were recruited, of which 2 subjects did not meet the requirements and 1 subject dropped out due to the epidemic, and 32 subjects were finally included. Please click here to view a larger version of this figure.

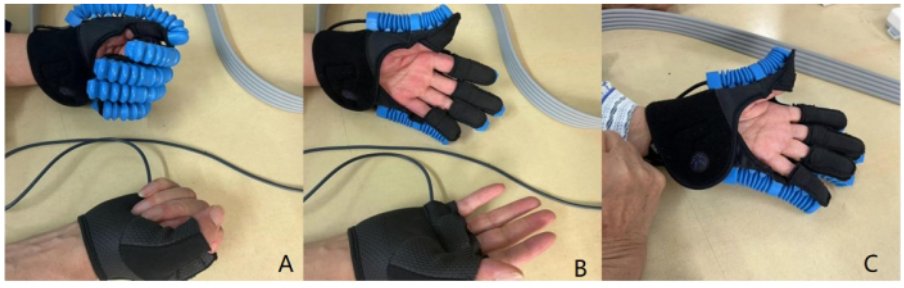

Figure 2: Upper limb rehabilitation training with different movement modes. (**A**,**B**) EG performing active hand rehabilitation training. (**C**) CG performing passive hand rehabilitation training. Please click here to view a larger version of this figure.

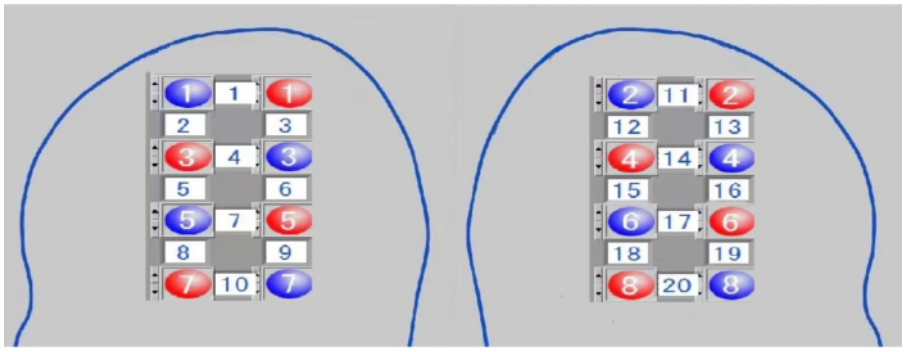

Figure 3: Arrangement and location of light beams. A red circle represents a light source, a blue circle represents a detector, and the path of the beam is shown between them. Please click here to view a larger version of this figure.

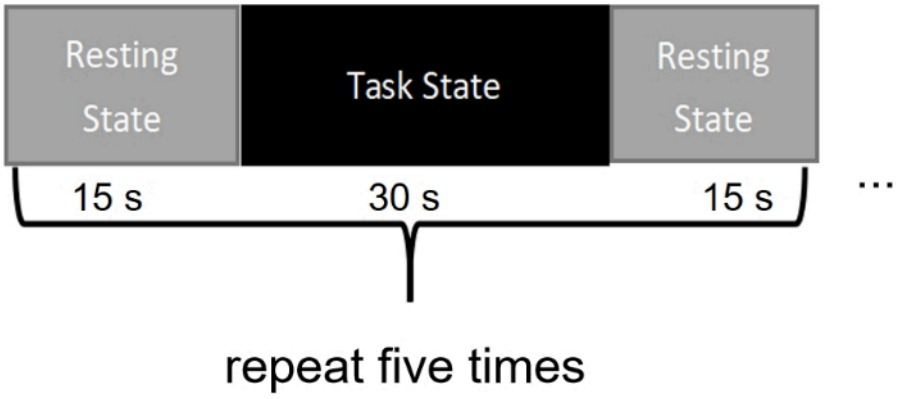

Figure 4: Task paradigm. A rest (15 s)-task (30 s)-rest (15 s) was used as a test unit and repeated 5 times in total. Please click here to view a larger version of this figure.

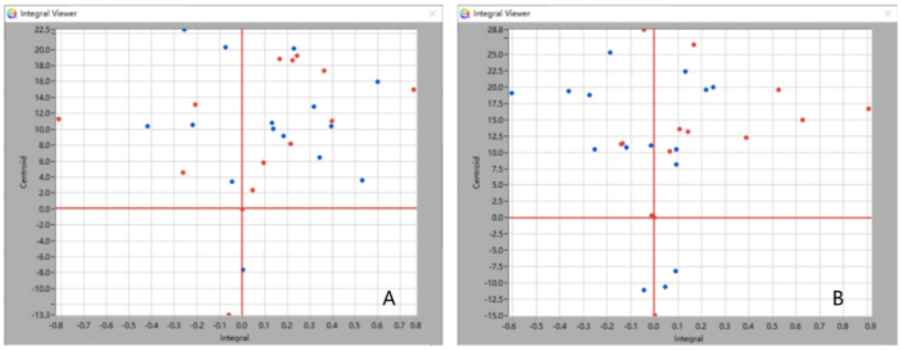

Figure 5: Scatter plots showing the distributions of the centroid values and integral values of the right hemisphere in the two groups of patients. (**A**) Before the intervention. (**B**) After the intervention. Please click here to view a larger version of this figure.

Variable	PM (n = 16)	AAM (n = 16)	p value
Gender (male/female)	9/7	8/8	1
Age in years (mean ± SD)	53.19 ± 10.72	55.88 ± 12.32	0.515
Type (hemorrhagic/ischemic)	9/7	6/10	0.479

Table 1: Subject characteristics. FMA: Fugl-Meyer Assessment; MBI: Modified Barthel Index; PM: passive motion; AAM: assisted active movement; FOT: functional occupational therapy.

Assessment Indicators	Main Effect (Group)			Main Effect (Time)			Interaction Effect (Group x Time)		
	F	P-values	η^2p	F	P-values	η^2p	F	P-values	η^2p
FMA-UL	5.564	0.03	0.214	34.716	<0.001	0.831	5.554	0.03	0.256
FMA-WH	8.817	0.006	0.227	13.357	0.001	0.308	8.817	0.006	0.227
MBI	8.512	0.007	0.221	588.559	<0.001	0.952	10.425	0.003	0.258

Table 2: Results of analysis of repeated two-way ANOVA conducted on GROUP, TIME, and interaction effect on FMA-UL, FMA-WH, and MBI.

		Assisted Active Movement Group	Passive Movement Group			
		mean ± SD	mean ± SD	t value	P value	Cohen's d
Integral value	Left	-0.04 ± 0.26	0.18 ± 0.32	-1.975	0.059	0.75
	Right	-0.06 ± 0.24	0.20 ± 0.32	-2.489	0.02	0.92
Centoid value	Left	13.03 ± 10.45	11.54 ± 9.13	0.396	0.695	0.15
	Right	11.04 ± 12.00	12.58 ± 10.98	-0.351	0.728	0.13

Table 3: Comparison of fNIRS data between the two groups after the intervention.

Discussion

In this study, by using near-infrared spectroscopy, we explored the effect of FOT combined with upper limb functional training in different exercise modes on the early rehabilitation of RHD patients. FOT helps the patient passively move the stiff upper limbs to facilitate subsequent training. The key is that the healthy hand leads the affected hand to perform purposeful, important, and practical functional tasks, use real-life objects, and simulate real scenarios as much as possible[28]. This can stimulate the patient's enthusiasm for treatment and maximize the patient's active movement. The most crucial point of AAM is that the patient's movement is driven by the unaffected limb and hand, while the affected limb and hand make a spontaneous active attempt, which is the most important feature that distinguishes it from passive movement. The rehabilitation devices give patients real-time visual and tactile feedback and complete a closed loop between the central nervous system and the periphery in rehabilitation training[29].

There are no complex techniques involved in training for the rehabilitation task, but there are numerous caveats to consider when evaluating patients with fNIRS. To ensure a good fNIRS signal and prevent motion artifacts from interfering with test results, we usually place a head holder on the table in front of the subject. We adjust the height of the table so that the subject's chin rests on the head holder without causing discomfort. This helps to reduce head sway during movement. In addition, skin oil on the scalp will affect the optical signal; accordingly, we wipe the oil from the patient's head with oil-absorbing paper before the experiment to ensure the signal quality. Based on previous experience, we have also found that reducing the influence of natural light and sound improves the collection of fNIRS signals; therefore, we collect all data in a dark and quiet environment[30].

Previous studies have shown that MT can effectively improve finger flexibility after stroke [31], especially for the upper limb rehabilitation of subacute patients[32], and therefore shows great promise in restoring motor function and improving the ability to perform daily activities after cerebral hemisphere damage[33,34,35,36]. When a patient moves their unaffected arm, an optical illusion formed by a mirror is considered by the patient to be the movement of their affected hand,

which increases the activity of their visual and somatosensory cortical areas, thereby enhancing the patient's attention and reducing the possibility of unilateral neglect[37,38]. In this way, the patient can consciously choose to use the affected limbs more often[39]. On the basis of traditional MT, we directly provide somatosensory stimulation and visual feedback to the affected limb through the AAM device, which reduces the unpleasant feeling caused by the asynchrony of proprioception of the affected hand and vision[40], thus demonstrating broader therapeutic potential than conventional MT. Our training equipment has a simple operating procedure and a strong safety profile, with the option to stop the training immediately by clicking the close button to avoid emergency situations that may occur during the test. In addition, some studies have demonstrated that MT can promote the normalization of hemisphere balance after stroke by regulating the excitability of M1. In follow-up studies, we will use fNIRS to evaluate the resting-state functional connectivity of the cerebral cortex to verify the cerebral hemisphere changes in RHD patients further after treatment[41].

This study has several limitations. First, the task paradigm chosen for the near-infrared spectroscopy test is passive, whereas brain activation may occur more in active movements. Thus, the task paradigm of active attempts may be more suitable than passive movement. Second, we monitored only the M1 area, but MT also increases neural activity in areas involved in attention allocation and cognitive control, which can promote the recovery of motor function by increasing the cognitive role in motor control[42]; therefore, monitoring prefrontal hemodynamics may also be necessary. In addition, due to the large number of treatment plans for the inpatients, only 10 min of hand rehabilitation training was performed every day. In the future, the training time should be extended to better explore the rehabilitative effect. Follow-up studies are needed to observe the long-term effect of this training. In the future, large-sample multicenter studies are expected to provide the most suitable rehabilitation strategies for early RHD patients.

Disclosures

The authors declare that the research was conducted in the absence of any commercial or financial relationship that could be construed as a potential conflict of interest.

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