

## Research Article

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# Efficiency of Rehabilitation Robotic Gloves Combined with Mirror Therapy on Functional Recovery of Hemiplegic Upper Limbs

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**Abstract**

**Background:** Mirror therapy (MT) is an effective method to promote functional recovery after stroke.

Robot-assisted gloves (Yisheng SY-HR06), as a new treatment method, has been widely used in hospitals at all levels. The purpose of this study is to investigate the effect of the combination of robot gloves and MT as adjuvant therapy for stroke patients by using the "central-peripheral-central" closedloop rehabilitation theory, and to compare the results of the combination with the results of conventional treatment, and to clarify the neural mechanism of the effect of combination therapy on the brain network.

**Methods:** This will be a multicenter, double-blind, randomized controlled trial in which 60 patients will be randomly divided into three groups of 20 in each group: the control group will receive conventional mirror therapy, the glove group will receive the self-contained mirror mode, and the combination group will receive the robot glove combined with mirror therapy. Patients in each group will receive a 30 min intervention 5 days per week over 4 weeks. The primary outcome will be the Fugl-Meyer Upper Limb Motor Function Score (FMA-UE), Functional independence Rating (FIM), Brunnstrom grade seven assessment scale of upper limb and hand, secondary outcomes include MMSE, hand grip strength, FTHUE -HK.

**Discussion:** The results of this experiment will prove the synergistic effect of Robot-assisted gloves combined with mirror therapy on the recovery of upper limb dysfunction after stroke. In addition, whether Robot-assisted gloves and MT (combined or alone) are more effective than conventional treatment will also be determined.

**Ethics And Dissemination:** Ethics approval was granted by the Ethics Review Committee of Wuhan Wuchang Hospital on March 2, 2022 (2022003). We plan to submit the results to various journals and present them at conferences, rehabilitation forums and the public.

**Trial registration:** ChiCTR2200057613; Pre-registration.

**Keywords:** Mirror Therapy, Stroke, Upper Limb Dysfunction, Robot-Assisted Gloves, Combination Therapy

**Background**

Stroke is the second leading cause of premature death and secondary disability. There are approximately 62 million stroke patients worldwide, one third of whom are severely disabled [1]. Evidence shows that about 83% of stroke patients are able to walk again; 65% of stroke patients have paralysis of the upper limbs, especially the hands, which seriously affects the ability to exercise and reduces the quality of life [2]. However, only 5% to 20% of patients can achieve complete functional recovery of the upper limb, and the function of the upper limb tends to be fine, and the degree of recovery is affected by various factors, and there will be serious follow-up. Disorders such as shoulder pain, dislocation, etc [3-6]. Various studies have shown that the

recovery of upper limb function after stroke has always been the focus and difficulty of rehabilitation [7].

Mirror therapy was first proposed by Ramachandran et al. and applied to the treatment of limb hallucination pain [8]. Studies have found that the input of mirror optical illusion can activate the brain plasticity of the affected limb, and subsequently, MT has been widely used in the field of neurorehabilitation [9]. The Thieme et al. (2018) meta-analysis found moderate-quality evidence that MT helps improve motor dysfunction and activities of daily living [10]. So far, the related mechanistic hypotheses of MT mainly include the following three aspects: MT can activate the mirror neuron system, thereby inducing or enhancing motor

imagery; MT may also help recruit the ipsilateral corticospinal tract, and can be activated by mirroring the illusion enhances the attention of the affected side, thereby activating the motor network of the affected brain region [11-15]. However, due to the small sample size of patients and the large heterogeneity (Including the location and side of brain injury, the level of motor and cognitive impairment, sensory function, and even age, etc.), the clinical efficacy and related mechanisms of MT still need further research Analyze [16]. In recent years, the "central-peripheral-central" closed-loop regulation model formed by combining MT as a central intervention method with other peripheral intervention methods has become a research hotspot to further improve this technology. Some MT studies have combined it with EMG biofeedback, functional electrical stimulation, repetitive transcranial magnetic stimulation, robotic-assisted therapy and other interventions [17-20]. These results suggest that combination therapy has the potential to improve moderate to severe upper extremity dysfunction after stroke. In the past, some studies just stacked MT and other interventions sequentially such as MT with acupuncture, transcranial direct current, and failed to form MVF synchronized with other peripheral interventions to achieve central-peripheral closed-loop measures [21, 22]. Therefore, it is necessary to explore better MT synchronization intervention modes and combined treatment modes to further improve the effect of closed-loop regulation.

In our study, the upper limb rehabilitation robot glove (Yisheng SY-HR0 6) was used, and the flexible pneumatic bionic muscle was used as the power source to drive the bionic muscle on the glove to expand and contract through repeated inflation and pumping, thereby driving the glove to pull. The fingers complete the flexion and extension movements of the finger joints, based on bilateral hand movement intervention in patients with hand dysfunction after stroke. There are four modes, passive training, boost training, resistance training and contralateral mirror training. In the contralateral mirror training, the unaffected hand is equipped with a sensor glove for normal grasping, while the affected hand is equipped with an exoskeleton robotic glove, which controls the passive grasping of the affected hand through the movement of the healthy hand, imitating the unaffected hand. The principle is to let the sensing glove record the normal movement of the healthy hand, and input the data into the exoskeleton robot glove to guide the simulated movement of the affected hand [23].

What we use is to add a mirror to the contralateral mirror training, and the patient can observe the movement of the healthy hand from the mirror. This intervention approach may be related to four underlying principles of neural remodeling. First, based on the principle of mirror therapy, the patient looks at the mirror under the influence of vision and illusion, and imagines that the affected hand produces the same movement as the healthy hand, which can activate the primary motor cortex and mirror neuron system on the affected side [24]. Second, based on the theory of motor control and motor learning, training the affected hand through the healthy hand can speed up the blood flow of the hand, deepen the memory of the limbs, prevent muscle contraction, and also enhance the proprioceptive input by moving the

affected hand, thereby activating the corresponding primary sensory cortex and establish effective "peripheral" stimulus feedback to the "central" [25, 26]. Third, based on the principle of bilateral training, the soft robotic glove realizes a bilateral movement training mode through the joint action of the affected hand, which is beneficial to the normalization of cortical inhibition between the cerebral hemispheres. Several studies have shown that bilateral training is superior to neurodevelopmental therapy and unilateral robotic-assisted training in improving upper extremity motor function after stroke [27-31]. Fourth, the linkage device of the robotic glove can easily realize the repetitive motion of the affected hand, continuously provide positive feedback to the central nervous system through peripheral motion (each 30 minutes, can complete 150-200 grasps), strengthen the neuronal circuit, thereby promoting neural remodeling of the affected brain. The beneficial effects of high-repetition task practice are considered to be an effective intervention [32, 33]. Overall, the rehabilitation robotic glove can provide active and effective "peripheral" stimulation, while MT is based on the mechanism of motor imagery and mirror neuron generation of central regulation. If they are combined with synchronous intervention, a complete and powerful "central-peripheral-central" closed-loop regulation can theoretically be formed. However, whether it leads to better clinical outcomes and its mechanism remain unclear. Therefore, on the basis of previous research, we put forward the topic of research on the efficacy of rehabilitation robot gloves combined with mirror therapy on the functional recovery of hemiplegic upper limbs, hoping to explore the most suitable treatment mode through scientific and rational design and implementation.

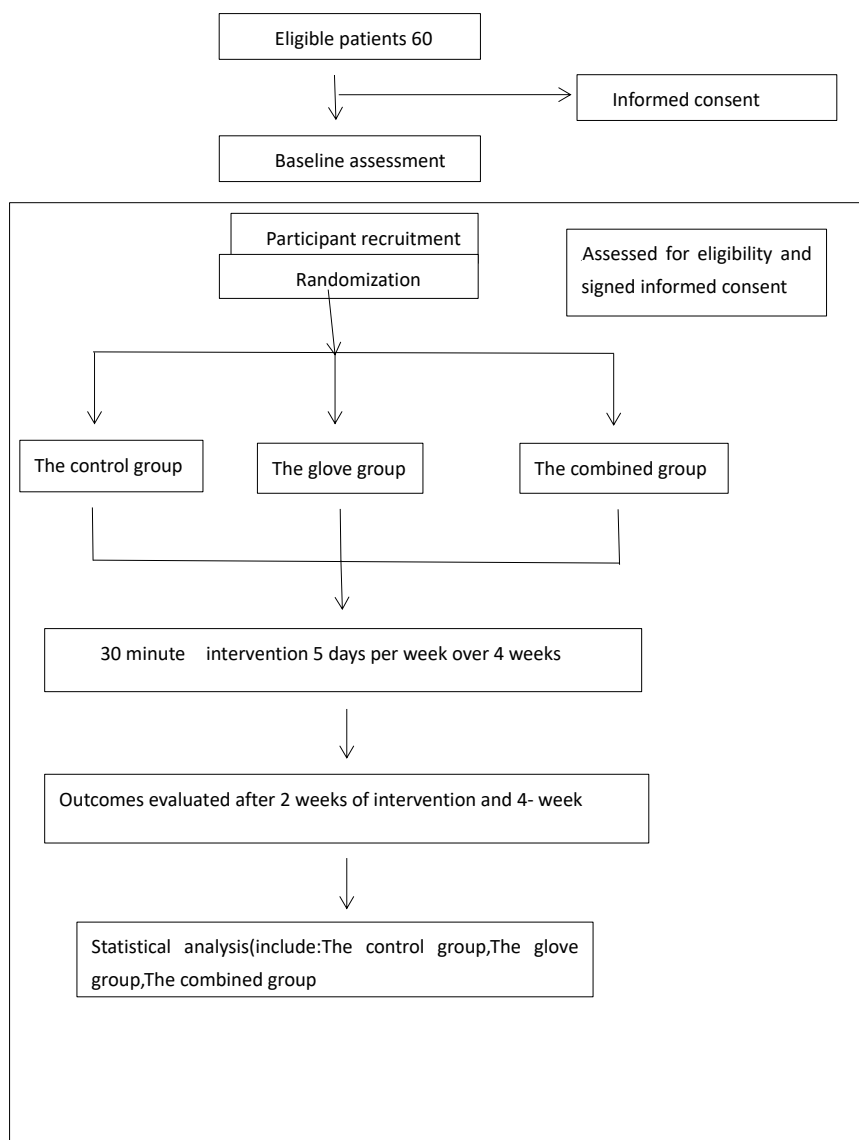
## Objectives And Methods

### Participant

Patients with subacute stroke who were admitted to the Department of Rehabilitation Medicine, Wuchang Hospital Affiliated to Wuhan University of Science and Technology from April 2022 to April 2023 were selected as the research subjects. A total of 60 stroke patients were selected and randomly divided into three groups by SPSS, with 20 people in each group, (1) control group, (2) glove group, (3) combined group, double-blind. This study was approved by the Ethics Committee of Wuchang Hospital (document batch number: 2022003), and all patients signed informed consent. It was approved by the Chinese Clinical Registry (No.: ChiCTR2200057613).

Inclusion criteria: (1) The first onset was unilateral stroke, and the imaging diagnosis was subcortical injury; (2) The disease was stable without serious complications; (3) The age was 30-80 years old, and the disease course was 7 days to 6 days after the onset of the disease. moon. (4) There is hand movement dysfunction.

Exclusion criteria: (1) craniocerebral injury; (2) severe cognitive impairment unable to cooperate with the researcher; (3) severe heart, lung, liver, kidney and other important organ failure; (4) pregnant patients; ( 5 ) The modified Ashworth scale of the extensor and flexor muscles of the hand is divided into muscle tension > 1+ grade.



**Withdrawal Criteria and Management: Patients were allowed to withdraw if:**

- (1) Serious breach of the agreement;
- (2) Disease progression or other mental disorders
- (3) The occurrence of adverse events related to MT
- (4) The patient requests to withdraw from the experiment

Items	Before enrollment 2-1(week)	Intervention period 1-4(week )	Outcome assessment 2(week)	Outcome assessment 4(week)
Inclusion criteria	×			
Exclusion criteria	×			
Informed consent	×			
Baseline	×			
Randomization and allocation	×			
intervention		×		
Fugl-Meyer assessment upper extremity	×		×	×
Function independent Measure	×		×	×
Brunnstrom	×		×	×

Mini-Mental State Examination Scale	×		×	×
Seven-level evaluation scale of upper limb function for hemiplegia	×		×	×
Hand grip strength	×		×	×
Adverse events		×		
Reasons of drop-out and withdrawals		×		

## Procedures And Experimental Tasks

All the recruited subjects were asked to perform three different visual feedback tasks, the treatment parameters were 30min each time, 1 time/day, 5 times/week, continuous treatment for 4 weeks, a total of 20 treatments. All three groups of patients received Stroke clinical routine drug treatment, while receiving comprehensive rehabilitation limb training, including good limb positioning, exercise therapy, occupational therapy, physical factor therapy and traditional rehabilitation therapy, etc. [34-37]. All treatments are completed by therapists and doctors with more than three years of work experience.

The mirror surface adopts a reversible plane with an area of 60 cm × 70 cm. Upper limb rehabilitation robot gloves (SY-HR06, Shanghai Siyi Intelligent Technology Co., Ltd., China), before the test, the robot gloves should be calibrated to ensure the accuracy of the experiment.

## The Control Group

The control group received conventional mirror therapy on this basis, as shown in Figure 1. The specific method is as follows: in a relatively quiet room, the patient sits upright in front of the mirror, with both hands on the treatment table, and the therapist is between the patient's upper limbs. Place a flat mirror perpendicular to the table, let the patient's unaffected hand on the front of the mirror and the affected hand on the back of the mirror. According to the therapist's demonstration, the patient looks at the moving image of the unaffected upper limb in the mirror, and conducts task guidance. Training, such as wiping the table, flexion and extension of the wrist joint, hand grasping and placing the ball, finger to palm, etc. At the same time, the affected limb is required to do the same movements as the unaffected upper limb as much as possible. Imagine that the affected limb is also mov-

ing smoothly and in a full range of joints at the same time. speed.

## The Glove Group

On this basis, the glove group adopts the mode of the healthy hand that comes with the rehabilitation robot glove equipment to drive the affected hand, as shown in Figure 2. The specific method is as follows: the patient sits and remains relaxed; selects the "mirror therapy" mode and wears the unaffected hand on the unaffected hand. Sensing gloves, the affected hand wears gas-driven soft gloves, and the rehabilitation robot screen will reflect the movement of the patient's hand in real time. The patient watches the screen to perform "clenching fist-relaxation" training, and the affected hand will perform mirror motion synchronously with the unaffected hand.

## The Combined Group

The combined group underwent rehabilitation robot glove therapy combined with mirror therapy, as shown in Figure 3. The specific method is as follows: wear rehabilitation robot gloves on the affected hand, place it behind the mirror, place the healthy hand in front of the mirror, and place the healthy hand in front of the mirror as prompted by the machine. "Tighten-release" activities, the patient stares at the mirror, and can be equipped with balls, wooden blocks, wooden sticks, and cups for training.

All patients received a rehabilitation assessment before treatment and after 4 weeks of treatment. The assessors were rehabilitation therapists who received standardized training in rehabilitation assessment. The basic information of patients was evaluated once before treatment, and the content of the evaluation included gender, age, stroke type, disease course, hemiplegia side, educational background, etc.



Figure 1: The control group



Figure 2: The glove group



Figure 3: The combined group



**Table 2: Groups and intervention allocation**

Groups	Interventions
The control group	Conventional treatment+MT
The glove group	Conventional treatment+rehabilitation robot glove
The combined group	Conventional treatment+MT+rehabilitation robot gloves

### Primary Outcomes

(1) Fugl - Meyer assessment upper extremity (FMA-UE) is widely used in motor function assessment and can reflect the functional level of stroke patients. It can differentiate motor function levels even in the early stages of functional recovery. The upper body has a maximum score of 66 points and is divided into three parts, namely shoulder-arm (36 points), wrist-hand (24 points), and coordination (6 points). The FMA-UE is a universal scale for evaluating upper extremity motor function after stroke. It is often used as the gold standard for testing, has good reliability and validity, and is sufficiently sensitive [38-40]. (2) Functional independence measure (FIM): to evaluate the activities of daily living of patients, 18 sub-items, with a total score of 126 (motor function score 91 points, cognitive function score 35 points), the higher the score, the stronger the activities of daily living; (3) Brunnstrom classification of upper limbs and hands: it is divided into grades 1 to 6, with grade 1 being completely immobile and grade 6 being normal motor function [41]. (4) Hand grip strength: It reflects the muscle strength level of the affected side of the fist. The higher the value, the greater the muscle strength of the patient's related muscles [43].

### Secondary Outcomes

(1) Mini-Mental State Examination Scale (MMSE): the total score is 30 points, which reflects the cognitive level of patients. The higher the score, the better the cognitive function [44]. (2) Seven-level evaluation scale of upper limb function for hemiplegia: it is the mainland version of the seven-level classification of hemiplegia in Hong Kong, which is more suitable for Chinese people. Divided into 1 to 7 levels, 1 level is no response, 7 level is to use the key to unlock the head, control chopsticks (strong hands), clips (non-strong hands), the higher the level, the better the function.

### Safety Assessments

All studies reported no adverse effects from MT. During the course of the study, any accidental injuries and sudden illnesses were recorded. The extent of symptoms, time of onset, duration, and treatment were recorded on the observation sheet. Serious adverse events will be reported immediately to the Ethics Committee.

### Data Collection and Management

Data is entered into a well-designed spreadsheet and uploaded to the ResMan Data Management Center, while a paper version is printed. Project evaluators will be responsible for quality control during data collection, and project leaders will be responsible for initial data cleaning, identification, coding, and conversion to appropriate data analysis formats. In addition, an independent data and safety monitoring committee will be established to monitor the safety of the trial. All forms must be noted. Project leaders

will have access to the data, which will be treated with a high degree of confidentiality and provided anonymously to anyone other than those involved in the management of the experiment. To facilitate dissemination of our findings, our research will be published in relevant journals.

### Quality Control of Statistical Analysis

Missing reports are not allowed, especially the main indicators must be clearly recorded. If the missing data is missing after checking the original data, we need to complete the missing part. If there is a serious deviation in the data, the experimental object will be removed, and all statistical analysis should be completed by professional statistical analysis experts, and the whole process will be transparent and open.

### Statistical Analysis

Statistical analysis was performed using SPSS 25.0 software. Measured data conformed to a normal distribution and were expressed as mean  $\pm$  standard deviation; count data were expressed as ratios or composition ratios. One-way analysis of variance was used to compare the measurement data of multiple groups, which was in line with normal distribution and homogeneity of variance, and the least significant difference method was used for comparison between groups.

### Discussion

The incidence of upper limb dysfunction caused by stroke is as high as 66% [45]. Every year, about 70-80% of stroke victims lose their ability to work to varying degrees and are unable to take care of themselves, placing a heavy burden on patients, families and society. Upper limb motor dysfunction is a major challenge and problem in stroke rehabilitation [46]. We earnestly study and study the experience of our predecessors, and hope to produce more, better and higher-quality treatment methods to help patients restore upper limb motor and sensory functions to the greatest extent, so that patients' lives will be more dignified and meaningful. Minimize disability and disability as much as possible.

A meta-analysis of mirror therapy suggests that mirror therapy can at least be used as an adjunct to routine rehabilitation in patients with upper extremity motor dysfunction and activities of daily living after stroke [10]. Relatively few studies are lacking related mechanisms Lee et al [47, 48]. (2017) studied 30 stroke patients and found that bilateral upper extremity exercise training was more effective than traditional occupational therapy in improving upper extremity function in stroke patients [49]. The contralateral repetitive training drives the remodeling of the cranial nerves on the affected side. MT can be viewed as a special kind of bilateral movement in which MT uses an optical illusion to replace the actual movement of the affected side compared to

traditional bilateral movement. The combination of MT and Rehab Robotic Gloves just makes up for this shortcoming. Synchronized movements of the bilateral upper extremities generated by the rehabilitation robot can reduce the inhibition between the cerebral hemispheres, and proprioceptive feedback on the affected side also facilitates the connection between motor control and the primary motor cortex due to the synchronous movements of the bilateral upper extremities. Promotes sensorimotor integration. Activation of sensory and motor areas showed a synergistic gain effect. The upper limb rehabilitation robot glove and the bilateral motion caused by the MT optical illusion are perfectly combined to realize the "central-peripheral-central" closed-loop central control correlation. This mechanism is critical for post-stroke patients, especially those with moderate to severe upper extremity motor dysfunction [29]. This is the theoretical support for our research. In clinical practice, there are few types of upper limb rehabilitation treatment methods. Proposing new and rich types of treatments can improve patients' desire and enthusiasm for rehabilitation and improve patient satisfaction. This is the actual clinical demand for our research.

However, this study lacks long-term follow-up observations and evaluations. The 4-week intervention cycle reflects its application in actual clinical practice and is sufficient to test whether rehabilitation programs are effective in the short term. However, the longer the intervention, the better the effect, which is worth our further exploration. This experiment has no follow-up, follow-up, and investigation of the continuation of the curative effect, and the follow-up will continue to improve. In addition, the evaluation methods we use are subject to a certain degree of subjectivity. If conditions permit, we can use magnetic resonance imaging, EEG, motor evoked potentials, and near-infrared spectroscopy to make more accurate indicators.

In conclusion, the results of this study are expected to elucidate the synergistic effect of the upper extremity rehabilitation robotic glove and MT on post-stroke upper extremity dysfunction. In addition, the findings are expected to confirm whether the upper limb rehabilitation robotic glove and MT combined or alone are more effective than conventional therapy in the treatment of post-stroke upper limb dysfunction.

### **Trial status**

Ongoing recruitment.

### **Abbreviations**

MT: Mirror Therapy; MT: Mirror Therapy; MMSE: Mini-Mental State Examination Scale; FMAUE: Fugl-Meyer Assessment for Upper Extremity; MBI: Modified Barthel index; FIM: Functional independence measure;

### **Acknowledgements**

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### **Funding**

Without fund support, it is completed by relying on the existing human, material and financial resources of the rehabilitation medicine department.

### **Availability Of Data and Materials**

Not applicable.

### **Ethics Approval and Consent to Participate**

This study is followed the Declaration of Helsinki exactly. All participants will be completely informed the study, and will sign the informed consent before participation. This trial is approved by the Ethics Review Committee of Wuhan Wuchang Hospital on March 2, 2022 (2022003).

### **Consent For Publication**

That all authors have reviewed the final version of the manuscript and approve it for publication. The manuscript by the authors has not been published elsewhere or is being considered for publication elsewhere.

### **Competing interests**

The authors declare that they have no competing interests.

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### **References**

1. Pérez-Cruzado, D., Merchán-Baeza, J. A., González-Sánchez, M., & Cuesta-Vargas, A. I. (2017). Systematic review of mirror therapy compared with conventional rehabilitation in upper extremity function in stroke survivors. *Australian occupational therapy journal*, 64(2), 91-112.
2. Pollock, A., Farmer, S. E., Brady, M. C., Langhorne, P., Mead, G. E., Mehrholz, J., & van Wijck, F. (2014). Interventions for improving upper limb function after stroke. *Cochrane Database of Systematic Reviews*, (11).
3. Jaafar, N., Che Daud, A. Z., Ahmad Roslan, N. F., & Mansor, W. (2021). Mirror Therapy Rehabilitation in Stroke: A Scoping Review of Upper Limb Recovery and Brain Activities. *Rehabilitation Research and Practice*, 2021.
4. Haghighi, F. M., Yoosefinejad, A. K., Razeghi, M., Shariati, A., Bagheri, Z., & Rezaei, K. (2021). The effect of high-frequency repetitive transcranial magnetic stimulation on functional indices of affected upper limb in patients with subacute stroke. *Journal of Biomedical Physics & Engineering*, 11(2), 175.
5. Wu, J., Zhang, J., Bai, Z., Chen, S., & Cai, S. (2020). Predictive factors of upper limb motor recovery for stroke survivors admitted to a rehabilitation program. *European Journal of Physical and Rehabilitation Medicine*, 56(6), 706-712.
6. Ada, L., Preston, E., Langhammer, B., & Canning, C. G. (2020). Profile of upper limb recovery and development of secondary impairments in patients after stroke with a disabled upper limb: An observational study. *Physiotherapy theory and practice*, 36(1), 196-202.
7. Maeda, M., Mutai, H., Toya, Y., Maekawa, Y., Hitai, T., & Katai, S. (2020). Effects of peripheral nerve stimulation on paralysed upper limb functional recovery in chronic stroke patients undergoing low-frequency repetitive transcranial magnetic stimulation and occupational therapy: A pilot study. *Hong Kong Journal of Occupational Therapy*, 33(1), 3-11.

8. Ramachandran, V. S., Rogers-Ramachandran, D., & Cobb, S. (1995). Touching the phantom limb. *Nature*, 377(6549), 489-490.
9. Herrador Colmenero, L., Perez Marmol, J. M., Martí-García, C., Querol Zaldivar, M. D. L. Á., Tapia Haro, R. M., Castro Sánchez, A. M., & Aguilar-Ferrándiz, M. E. (2018). Effectiveness of mirror therapy, motor imagery, and virtual feedback on phantom limb pain following amputation: A systematic review. *Prosthetics and orthotics international*, 42(3), 288-298.
10. Thieme, H., Mehrholz, J., Pohl, M., Behrens, J., & Dohle, C. (2012). Mirror therapy for improving motor function after stroke. *Cochrane database of systematic reviews*, (3).
11. Darbois, N., Guillaud, A., & Pinsault, N. (2018). Do robotics and virtual reality add real progress to mirror therapy rehabilitation? A scoping review. *Rehabilitation research and practice*, 2018.
12. RJOSK V, LEPSIEN J, KAMINSKI E, et al. Neural Correlates of Mirror Visual Feedback-Induced Performance Improvements: A Resting-State fMRI Study [J]. *Front Hum Neurosci*, 2017, 11: 54.
13. Neva, J. L., Vesia, M., Singh, A. M., & Staines, W. R. (2014). Modulation of left primary motor cortex excitability after bimanual training and intermittent theta burst stimulation to left dorsal premotor cortex. *Behavioural brain research*, 261, 289-296.
14. Casile, A. (2013). Mirror neurons (and beyond) in the macaque brain: an overview of 20 years of research. *Neuroscience letters*, 540, 3-14.
15. Calmels, C., Holmes, P., Jarry, G., Hars, M., Lopez, E., Pailard, A., & Stam, C. J. (2006). Variability of EEG synchronization prior to and during observation and execution of a sequential finger movement. *Human brain mapping*, 27(3), 251-266.
16. Luo, Z., Zhou, Y., He, H., Lin, S., Zhu, R., Liu, Z., ... & Zeng, Q. (2020). Synergistic effect of combined mirror therapy on upper extremity in patients with stroke: a systematic review and meta-analysis. *Frontiers in Neurology*, 11, 155.
17. Liu, M., Xu, L., Li, H., Chen, S., & Chen, B. (2021). Morphological and functional changes of the tibialis anterior muscle after combined mirror visual feedback and electromyographic biofeedback in poststroke patients: a randomized trial. *American Journal of Physical Medicine & Rehabilitation*, 100(8), 766-773.
18. Kim, D. H., & Jang, S. H. (2021). Effects of Mirror Therapy Combined with EMG-Triggered Functional Electrical Stimulation to Improve on Standing Balance and Gait Ability in Patient with Chronic Stroke. *International Journal of Environmental Research and Public Health*, 18(7), 3721.
19. Kim, J., & Yim, J. (2018). Effects of high-frequency repetitive transcranial magnetic stimulation combined with task-oriented mirror therapy training on hand rehabilitation of acute stroke patients. *Medical Science Monitor: International Medical Journal of Experimental and Clinical Research*, 24, 743.
20. Rong, J., Ding, L., Xiong, L., Zhang, W., Wang, W., Deng, M., ... & Jia, J. (2021). Mirror visual feedback prior to robot-assisted training facilitates rehabilitation after stroke: a randomized controlled study. *Frontiers in Neurology*, 12, 1093.
21. Xu, Y., Lin, S., Jiang, C., Ye, X., Tao, J., Wilfried, S., ... & Yang, S. (2018). Synergistic effect of acupuncture and mirror therapy on post-stroke upper limb dysfunction: a study protocol for a randomized controlled trial. *Trials*, 19(1), 1-9.
22. Liao, W. W., Chiang, W. C., Lin, K. C., Wu, C. Y., Liu, C. T., Hsieh, Y. W., ... & Chen, C. L. (2020). Timing-dependent effects of transcranial direct current stimulation with mirror therapy on daily function and motor control in chronic stroke: a randomized controlled pilot study. *Journal of NeuroEngineering and Rehabilitation*, 17(1), 1-11.
23. Haghsheenas-Jaryani, M., Patterson, R. M., Bugnariu, N., & Wijesundara, M. B. (2020). A pilot study on the design and validation of a hybrid exoskeleton robotic device for hand rehabilitation. *Journal of Hand Therapy*, 33(2), 198-208.
24. Fong, K. N., Ting, K. H., Zhang, J. J., Yau, C. S., & Li, L. S. (2021). Event-Related desynchronization during mirror visual feedback: a comparison of older adults and people after stroke. *Frontiers in Human Neuroscience*, 237.
25. Hamzei, F., Erath, G., Kücking, U., Weiller, C., & Rijntjes, M. (2020). Anatomy of brain lesions after stroke predicts effectiveness of mirror therapy. *European Journal of Neuroscience*, 52(6), 3628-3641.
26. Colomer, C., Noe, E., & Llorens Rodríguez, R. (2016). Mirror therapy in chronic stroke survivors with severely impaired upper limb function: a randomized controlled trial. *European journal of physical and rehabilitation medicine*, 52(3), 271-278.
27. Zhuang, J. Y., Ding, L., Shu, B. B., Chen, D., & Jia, J. (2021). Associated mirror therapy enhances motor recovery of the upper extremity and daily function after stroke: a randomized control study. *Neural Plasticity*, 2021.
28. Tai, R. Y., Zhu, J. D., Cheng, C. H., Tseng, Y. J., Chen, C. C., & Hsieh, Y. W. (2020). Cortical neural activity evoked by bilateral and unilateral mirror therapy after stroke. *Clinical Neurophysiology*, 131(10), 2333-2340.
29. Qiu, Y., Zheng, Y., Liu, Y., Luo, W., Du, R., Liang, J., ... & Lin, Q. (2022). Synergistic immediate cortical activation on mirror visual feedback combined with a Soft Robotic Bilateral Hand Rehabilitation System: a fNIRS study. *Frontiers in Neuroscience*, 52.
30. Li, Y. C., Wu, C. Y., Hsieh, Y. W., Lin, K. C., Yao, G., Chen, C. L., & Lee, Y. Y. (2019). The priming effects of mirror visual feedback on bilateral task practice: a randomized controlled study. *Occupational Therapy International*, 2019.
31. Al-Wasity, S. M., Pollick, F., Sosnowska, A., & Vuckovic, A. (2019). Cortical functional domains show distinctive oscillatory dynamic in bimanual and mirror visual feedback tasks. *Frontiers in Computational Neuroscience*, 13, 30.
32. Mane, R., Chouhan, T., & Guan, C. (2020). BCI for stroke rehabilitation: motor and beyond. *Journal of Neural Engineering*, 17(4), 041001.
33. French, B., Thomas, L. H., Coupe, J., McMahon, N. E., Connell, L., Harrison, J., ... & Watkins, C. L. (2016). Repetitive task training for improving functional ability after stroke. *Cochrane database of systematic reviews*, (11).
34. Tatsuno, H., Hamaguchi, T., Sasanuma, J., Kakita, K., Okamoto, T., Shimizu, M., ... & Abo, M. (2021). Does a combination treatment of repetitive transcranial magnetic stimulation and occupational therapy improve upper limb muscle paralysis equally in patients with chronic stroke caused by cerebral hemorrhage and infarction?: A retrospective cohort study. *Medicine*, 100(24).

35. Wang, F., Zhang, S., Zhou, F., Zhao, M., & Zhao, H. (2021). Early physical rehabilitation therapy between 24 and 48 h following acute ischemic stroke onset: a randomized controlled trial. *Disability and rehabilitation*, 1-6.
36. Mubeen, I., Ahmad, A., & Afzal, W. (2021). Effects of mental imagery technique in addition to conventional physical therapy to improve hand functions in chronic stroke patients. *Journal of the Pakistan Medical Association*, 71(8), 1944-1949.
37. Marques-Sule, E., Arnal-Gómez, A., Buitrago-Jiménez, G., Suso-Martí, L., Cuenca-Martínez, F., & Espí-López, G. V. (2021). Effectiveness of Nintendo Wii and physical therapy in functionality, balance, and daily activities in chronic stroke patients. *Journal of the American Medical Directors Association*, 22(5), 1073-1080.
38. Roman, N., Miclaus, R., Repanovici, A., & Nicolau, C. (2020). Equal opportunities for stroke survivors' rehabilitation: A study on the validity of the upper extremity fugl-meyer assessment scale translated and adapted into Romanian. *Medicina*, 56(8), 409.
39. Rech, K. D., Salazar, A. P., Marchese, R. R., Schiffino, G., Cimolin, V., & Pagnussat, A. S. (2020). Fugl-Meyer assessment scores are related with kinematic measures in people with chronic hemiparesis after stroke. *Journal of Stroke and Cerebrovascular Diseases*, 29(1), 104463.
40. Amano, S., Umeji, A., Takebayashi, T., Takahashi, K., Uchiyama, Y., & Domen, K. (2020). Clinimetric properties of the shortened Fugl-Meyer Assessment for the assessment of arm motor function in hemiparetic patients after stroke. *Topics in Stroke Rehabilitation*, 27(4), 290-295.
41. Bottemiller, K. L., Bieber, P. L., Basford, J. R., & Harris, M. (2006). FIM scores, FIM efficiency, and discharge disposition following inpatient stroke rehabilitation. *Rehabilitation Nursing*, 31(1), 22-25.
42. Huang, C. Y., Lin, G. H., Huang, Y. J., Song, C. Y., Lee, Y. C., How, M. J., ... & Hsieh, C. L. (2016). Improving the utility of the Brunnstrom recovery stages in patients with stroke: validation and quantification. *Medicine*, 95(31).
43. Yang, Y., Zhao, Q., Zhang, Y., Wu, Q., Jiang, X., & Cheng, G. (2018). Effect of mirror therapy on recovery of stroke survivors: a systematic review and network meta-analysis. *Neuroscience*, 390, 318-336.
44. Khaw, J., Subramaniam, P., Abd Aziz, N. A., Ali Raymond, A., Wan Zaidi, W. A., & Ghazali, S. E. (2021). Current update on the clinical utility of MMSE and MoCA for stroke patients in Asia: a systematic review. *International journal of environmental research and public health*, 18(17), 8962.
45. Mehrholz, J., Hädrich, A., Platz, T., Kugler, J., & Pohl, M. (2012). Electromechanical and robot-assisted arm training for improving generic activities of daily living, arm function, and arm muscle strength after stroke. *Cochrane database of systematic reviews*, (6).
46. Murray, C. J., Vos, T., Lozano, R., Naghavi, M., Flaxman, A. D., Michaud, C., ... & Haring, D. (2012). Disability-adjusted life years (DALYs) for 291 diseases and injuries in 21 regions, 1990–2010: a systematic analysis for the Global Burden of Disease Study 2010. *The lancet*, 380(9859), 2197-2223.
47. Inagaki, Y., Seki, K., Makino, H., Matsuo, Y., Miyamoto, T., & Ikoma, K. (2019). Exploring hemodynamic responses using mirror visual feedback with electromyogram-triggered stimulation and functional near-infrared spectroscopy. *Frontiers in Human Neuroscience*, 13, 60.
48. Bai, Z., Fong, K. N., Zhang, J., & Hu, Z. (2020). Cortical mapping of mirror visual feedback training for unilateral upper extremity: A functional near-infrared spectroscopy study. *Brain and Behavior*, 10(1), e01489.
49. Lee, M. J., Lee, J. H., Koo, H. M., & Lee, S. M. (2017). Effectiveness of bilateral arm training for improving extremity function and activities of daily living performance in hemiplegic patients. *Journal of Stroke and Cerebrovascular Diseases*, 26(5), 1020-1025.
50. Deconinck, F. J., Smorenburg, A. R., Benham, A., Ledebt, A., Feltham, M. G., & Savelsbergh, G. J. (2015). Reflections on mirror therapy: a systematic review of the effect of mirror visual feedback on the brain. *Neurorehabilitation and neural repair*, 29(4), 349-361.