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The effect and mechanism of motor imagery based on action observation treatment on dysphagia in Wallenberg Syndrome: a randomized controlled trial

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ABSTRACT

BACKGROUND: The effect of motor imagery applied to dysphagia patients with Wallenberg syndrome has not yet been reported. AIM: This trial aimed to investigate the effect and mechanism of motor imagery based on action observation treatment in the rehabilitation of patients with dysphagia in Wallenberg syndrome.

DESIGN: A randomized controlled trial.

SETTING: The setting was in-patient.

POPULATION: Thirty patients with dysphagia of Wallenberg syndrome.

METHODS: The patients were divided into the experimental group and the control group. Both groups received conventional dysphagia treatment, and the experimental group underwent the addition of motor imagery based on action observation treatment to the control group once a day for 14 days. Overall swallowing function was assessed with specific scales before and after intervention. Meanwhile, the functional near infrared spectroscopy was used to detect changes in cerebral hemodynamics during the execution of volitional swallowing task and swallowing motor imagery.

RESULTS: The standardized swallowing assessment score (P=0.030), Murray secretion scale score (P=0.044) and swallowing quality of life score (P=0.011) of the experimental group improved better than those of the control group. In addition, multiple brain regions of the cortical presented extensive activation (P<0.05) during the execution of swallowing motor imagery. Moreover, there were significant differences (P<0.05) in brain regions pre-motor and supplementary motor cortex, right primary motor cortex, and right primary somatosensory cortex of the experimental group before and after treatment.

CONCLUSIONS: The present study indicated that motor imagery based on action observation treatment could improve swallowing function for patients with dysphagia of Wallenberg syndrome as an add-on training. As a top-down rehabilitation training, the mechanism of this therapy may be related to the selective activation of mirror neuron system.

CLINICAL REHABILITATION IMPACT: Motor imagery based on action observation treatment can be implemented as part of the therapeutic for dysphagia of Wallenberg syndrome.

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KEY WORDS: Lateral medullary syndrome; Deglutition disorders; Spectroscopy, near-infrared.

Wallenberg Syndrome is a clinical syndrome caused by damage to the nuclei and conduction tracts in the dorsolateral medullary region of the medulla oblongata, mostly due to thrombosis or occlusion of the posterior inferior cerebellar artery or the vertebral artery.¹ Since the central pattern generator that controls swallowing is located in the medulla oblongata, dysphagia is one of the five common clinical symptoms in patients with Wallenberg syndrome.² It is easy to cause choking, dehydration, malnutrition, aspiration pneumonia, and even respiratory distress and asphyxia. A series of comorbidities, poor prognosis, seriously reducing the quality of life of patients.³

Currently, the rehabilitation of swallowing function is based on the integrated treatment of swallowing organ function training, sensory facilitation training, therapeutic transoral feeding, physiotherapy, acupressure, acupuncture and moxibustion treatment and other methods.⁴ Among them, swallowing organ function training and sensory promotion training as the basic method of swallowing function rehabilitation training, its efficacy has been confirmed by a large number of clinical studies.⁵ But these two training methods are under the guidance of the therapist to carry out mechanical cooperative movement, the patient's lack of subjective initiative to swallow. Therapeutic transoral feeding, physiotherapy, acupressure, acupuncture treatment, etc. have certain demands on the practitioner's professional qualifications and equipment, and the promotion are limited. Dysphagia involves multiple levels and complex relationships from central processing to peripheral effects,⁶ therefore, exploring a more complete dysphagia rehabilitation strategy is still the focus of current research.

Motor imagery (MI) originated from the "mental imagery" proposed by Hossack in 1950,7 which refers to the perceptual reproduction of specific action behaviors within the relevant regions of the brain without any obvious motor output, and its application is based on the theory of the central nervous system's remodelability. The theory suggests that the function of the cerebral cortex can be stimulated by external stimulation of it, facilitating intercortical responses and connections, and therefore repeated conscious and active training can stimulate changes in the structure of the cerebral cortex.8 Swallowing MI is an adjunctive therapeutic measure that has gradually gained attention in recent years, requiring the active cooperation and participation of patients, which is a supplementary means to a variety of passive stimulation therapies, allowing patients to internally and repeatedly imagine themselves executing similar swallowing actions without the presence of related actions.^{9, 10} It is known that MI can activate the corresponding mirror neuron system (MNS), causing cortical remodeling of the brain, thereby promoting recovery from dysfunction.¹¹ MNS is a group of neurons that fire both when performing specific actions and when observing others performing the same or similar actions.¹² In view of the plasticity and compensatory mechanism of the central nervous system, MNS is stimulated repeatedly during MI to induce its activation, which promotes the brain's training and learning of the original swallowing neural function, repairs the swallowing neural network, reactivates the topdown neural pathway, and restore the corresponding swallowing function.^{13, 14}

Swallowing MI is more complex than common limb MI, making it difficult to perform this imagery task out of thin air. In response to this issue, picture visual or action observation stimuli have been found at the clinical research level to ease the swallowing imagery task and thus improve efficacy.¹⁵ When patients are cognitively induced using swallowing-related action observation videos, the human visual and auditory senses are used to perceive and judge the color, taste, nature, and other characteristics of food and transmit them to the central nervous system for processing, which can enhance the patient's sense of the mental picture and improve the effectiveness of MI treatment. Functional near infrared spectroscopy (fNIRS) is a non-invasive brain imaging technique that captures changes in brain concentrations of oxygenated hemoglobin (HbO2), deoxygenated hemoglobin (HbR) and total hemoglobin (HbT), thereby reflecting the changes in cerebral hemodynamics.¹⁶ Compared with functional magnetic resonance imaging and electroencephalogram, fNIRS has the characteristics of strong resistance to body movement interference, portable and not limited by the environment, and can detect the brain function during various tasks.¹⁷ Currently, studies of fNIRS in swallowing function mainly focus on the changes of related functional brain regions during swallowing task in healthy subjects. Knollhoff et al.¹⁸ found that during swallowing, bilateral primary motor cortex (PMC), dorsolateral prefrontal cortex (DLPFC), inferior frontal gyrus (IFG), supplementary motor area (SMA), and primary somatosensory cortex (PSC) were all activated, and the activation was more prominent in the right M1 area.

The effect of MI applied to dysphagia patients with Wallenberg syndrome has not yet been reported. Therefore, this study will use MI based on action observation treatment to investigate the effect of its intervention on patients with dysphagia in Wallenberg syndrome. Moreover, fNIRS is applied to detect cortical activation of patients during the volitional swallowing task and the swallowing MI, so as to explore the mechanism of MI based on action observation treatment and provide the basis for the rehabilitation of patients with dysphagia in Wallenberg syndrome.

Materials and methods

Study design and participants

Ethical considerations

This study was performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments, was approved by the Ethics Committee of the First Affiliated Hospital of Zhengzhou University (2023-KY-0438), and was registered at ClinicalTrials.gov (NCT06224686). All patients received a full explanation of the experimental procedures, and they acknowledged their right to quit at any time during the study.

Subjects

This study was designed as a two-arm, randomized, prospective clinical trial. The participants were recruited from Wallenberg syndrome patients hospitalized with dysphagia in the Department of Rehabilitation Medicine, the First Affiliated Hospital of Zhengzhou University, between May 2023 and December 2023. All patients needed to meet the following inclusion criteria: 1) age ranged from 18-80 years and right-handed; 2) first onset, vital signs stable and conscious; 3) the dysphagia confirmed by videofluoroscopic swallowing study; 4) no cognitive impairment, the Mini-Mental State Examination (MMSE) Score: >17 for those with an illiterate education, >20 for those with an elementary education, and >24 for those with a secondary education and above; 5) good MI ability with kinesthetic and visual imagery questionnaire-10 (KVIQ-10) score \geq 25; 6) cranial integrity without craniotomy and/ or craniectomy; 7) patient and/or his/her relative agrees and signs written informed consent. The exclusion criteria were as follows: 1) combined ischemic foci at other sites; 2) presence of organic swallowing dysfunction or pre-existing dysphagia due to Parkinson's disease, dementia, and others; 3) severe cardiac, pulmonary, hepatic, and renal insufficiency and vital organ failure; 4) significant psychological disorders such as anxiety and depression; 5) infected or broken skin on the head; 6) poorly controlled epilepsy; 7) poor patient compliance. The shedding criteria included the following: 1) patients self-withdraw during the program; 2) patient develops a worsening condition or other complications during the trial that prevents continuation of this study.

Sample size calculation

The sample size was estimated by G*Power 3.1.9.7, and a minimum sample size of 30 (15 individuals per group) was needed with the following parameters: effect size (1.07), 1 - β =0.80, α =0.05, and allocation ratio (1:1). Since there was no study examining the efficacy of MI therapy to patients with dysphagia in Wallenberg syndrome, the effect size was based on the between-group difference in SSA scores from previous trial applying this therapy to patients with dysphagia in ischemic stroke.¹⁹ We increased the sample size to 17 individuals per group to take into account the 10% possible attrition.

Randomization and masking

The patients were randomly allocated (1:1) to the experimental group and the control group. Randomization was performed by an independent person who did not participate in the implementation or evaluation of the trial using a pseudorandom number generated by a computer. Opaque, sealed envelopes were used to mask the randomization tables and they contained a paper labeled with a random identification number. Due to the particularity of the MI intervention in this study, the therapist performing the intervention and patients were aware of the treatment condition. However, in order to minimize bias, the outcome evaluator was masked to the treatment condition. The Consolidated Standards of Reporting Trials (CONSORT) was used to guide the reporting of this study.

Intervention

Both groups received conventional dysphagia treatment, and the experimental group underwent the addition of MI based on action observation treatment to the control group once a day for 14 consecutive days. Conventional dysphagia treatment included oropharyngeal muscle movement training, orofacial alternating hot and cold stimulation, Masako swallowing training, Mendelssohn swallowing training, therapeutic ingestion training, intermittent oralesophageal tube feeding, and low-frequency electrical stimulation of swallowing neuromusculature, etc., for 30 min each time. MI based on action observation treatment: first, the therapist explained the purpose and principle of the intervention method to the patient, keeping the surrounding environment quiet and comfortable to avoid the patient's mood fluctuations due to external interference. Then start the treatment, the video recorded in advance was given to the patient to watch, the playback device is an iPad. The content includes lip and tongue muscle relaxation exercises, healthy people eating, chewing, swallowing, drinking and other images. At the same time, the guidance was played, which was consistent with the content in the video. The patients were asked to concentrate on watching the video and use all their senses to fully imagine the food and eating images in the video. After the end, the patients were instructed to close their eyes while relaxing the whole body at the same time, guiding their attention back to the surrounding environment, and asked about the content and their feelings of the imagination to determine the quality of the patient's imaginations. The video was played 3 times consecutively for 30 min each time.

Outcome measurements

Patients' swallowing function was assessed before treatment and after 14 days of intervention. The primary outcome measure were the changes in standardized swallowing assessment (SSA) score before and after treatment. The SSA was used to assess the improvement of overall swallowing function, it has a maximum score of 46 and a minimum score of 18, with lower scores indicating better swallowing function.²⁰ In addition, cortical activation during volitional swallowing was measured with fNIRS before and after the intervention to assess neural imaging variation of patients. Also, real-time changes in cerebral hemodynamics during the execution of complete swallowing MI were detected during the patients' first MI treatment.

The secondary outcome measures were Murray Secretion Scale (MSS) score, Yale Pharyngeal Residual Severity Rating Scale (YPR-SRS) score, Rosenbek Penetration-Aspiration Scale (PAS) score, and Swallowing Quality of Life (SWAL-QOL) Score. The severity of MSS was measured using a grade of 0-3, patients without obvious saliva accumulation are scored as MSS grade 0, whereas patients who had secretions in the laryngeal vestibule at the start of the exam were assigned grade 3.21 YPR-SRS scores were measured using a 5-point ordinal scale: I=none, II=trace, III=mild, IV=moderate, V=severe.22 The PAS was introduced to the field of dysphagia in 1996 and has become the standard method to describe and measure the severity of airway invasion during swallowing, and the highest PAS score is 8 and the lowest is 123, 24 (1=no entry of material into the airway; 2 - 5=penetration of material past the laryngeal additus into the supraglottic space and traveling as far as the true vocal folds; 6 - 8=tracheal aspiration of material below the true vocal folds). SWAL-QOL has a score range of 44-220, with lower scores indicating poorer swallowing function and poorer quality of life.²⁵

fNIRS data acquisition

We used a 39-channel fNIRS system (Nirsmart, Danyang Huichuang Medical Equipment Co., Ltd., China) to record the concentration changes of HbO2 and HbR to simultaneously assess changes in cortical activation of patients.²⁶ The acquisition headcap was designed based on the international 10-20 system consisting of 16 sources and 16 detectors. The montage placements of probes are presented in Figure 1. The signals of two different wavelengths of near-infrared light (760 and 850 nm) were recorded in the form of a continuous-wave at a sampling rate of 11 Hz. The cortical sensitivity of each channel was displayed on the headcap using AtlasViewer. The distance between the transmitting and receiving probes was 30 mm, and the brain area below the midpoint of each channel (the midpoint of the line connecting the transmitting and receiving probes) was the main detection area of the channel, which was used as the criterion for calibrating the brain area of the channel. The coordinate information of the detection area was determined on a standard head model by a 3D



Figure 1.—A) Placement of the probes; B) volitional swallowing procedure; C) swallowing MI procedure.

digitizer (Patriot, Polhemus, USA), and the corresponding brain area was found according to the corresponding Montreal Neurological Institute (MNI) coordinate and Talairach coordinate, and the Brodmann area contribution was calculated in each channel. The patients sat in a quiet treatment room for the fNIRS evaluation to minimize the influence of noise and to facilitate the detection of cortical activation during the patient's performance of a complete swallowing MI. The volitional swallowing procedure used in this study consisted of 30-s resting period and 30-s swallowing period, and the swallowing period required the patients to swallow saliva continuously in response to computerized voice commands. The specific procedures are presented in Figure 1.

Statistical analysis

SPSS26.0 software was used to statistically describe and statistically analyze the study data. The control group and the experimental group were compared by mean±standard deviation description and two-sample *t*-test if they were quantitative data obeying normal distribution, or by median and quartile (M, P₂₅-P₇₅) description and Mann-Whitney U Test if they did not obey normal distribution. In case of qualitative data, comparisons were made by frequency and percentage description and Chi-squared (χ^2) Test or Mann-Whitney U Test. Data measured at two time points between groups (pre-intervention, post-intervention) was compared using paired-sample *t*-test or Wilcoxon signed-rank test. In all comparisons, P<0.05 indicated statistical significance.

The fNIRS data was processed and analyzed using Nir-Spark software package. The data was preprocessed first: 1) extracting data segments to ensure that all data was of the same length; 2) automatically removing irrelevant motion artifacts (using a method based on moving standard deviation and spline interpolation); 3) converting the initial light intensity (Int) data to optical density (OD) data; 4) utilizing a bandpass filter between 0.01 and 0.2 Hz to reduce the effect of physiological fluctuations (respiration, heart rate, etc.); 5) transmitting the filtered OD data into relative changes in HbO2 concentration. After preprocessing, hemodynamic time series in task blocks were analyzed using general linear modeling to assess the activation of each channel in participants. The channels that were significantly activated during the task state compared to the resting state were calculated as follows: the beta value indicates the level of cortical activation of the channel, one-sample t-test was used for the analysis of cortical activation during the swallowing MI, and two-sample *t*-test was used to compare the differences in cortical activation between the two groups before and after the treatment, with a set threshold for significance (P < 0.05). The above data analysis was conducted by a research assistant blinded to the study.

Results

Baseline characteristics of the patients

In this study, 37 eligible patients were screened, 3 of whom refused to participate in the trial, 34 patients were randomized to either the experimental group (N.=17) or the control group (N.=17). During the course of treatment, 2 patients in the experimental group were unable to continue the trial after several interventions due to their own recurrent dizziness, 1 patient in the control group refused to participate in the post-intervention assessment due to discomfort with the flexible endoscopic examination of swallowing (FEES) and 1 patient withdrew due to changes in condition. The remaining patients (N.=30) completed treatment and assessment as expected, including 15 in the experimental group and 15 in the control group (Figure 2). No serious adverse events were reported during the study.

Comparing the gender, age, educational level, lesion side and duration after onset of the two groups, the results showed no statistically significant differences (P>0.05). For the function assessment at baseline, there were no



Figure 2.—Participant flow diagram.

TABLE I.— Demographics and Clinical Characteristics of the patients.

	Experimental group (N.=15)	Control group (N.=15)	P value
Gender (M)	12 (80.0)	12 (80.0)	1.000a
Age(years)	64.73±6.67	63.53±8.12	0.662 ^b
Education			
illiterate	3 (20.0)	2 (13.3)	0.463°
elementary	4 (26.7)	3 (20.0)	
secondary	8 (53.3)	10 (66.7)	
Lesion side (L)	6 (40.0)	8 (53.3)	0.715ª
Duration after onset (days)	23 (12-42)	42 (8-49)	0.519c
MMSE score	25.20±2.46	25.87±2.48	0.465 ^b
KVIQ-10 score	35.27±2.82	35.67±3.56	0.735 ^b
SSA	34.73±1.71	35.53±1.51	0.185 ^b
MSS			
0	1 (6.7)	0 (0.0)	0.436c
1	2 (13.3)	2 (13.3)	
2	5 (33.3)	4 (26.7)	
3	7 (46.7)	9 (60.0)	
YPR-SRS (vallecula)			
Ι	0 (0.0)	0 (0.0)	0.270c
II	0 (0.0)	0 (0.0)	
III	2 (13.3)	1 (6.7)	
IV	6 (40.0)	4 (26.7)	
V	7 (46.7)	10 (66.7)	
YPR-SRS (pyriform sinus)			
Ι	0 (0.0)	0 (0.0)	0.173°
II	0 (0.0)	0 (0.0)	
III	4 (26.7)	1 (6.7)	
IV	5 (33.3)	5 (33.3)	
V	6 (40.0)	9 (60.0)	
PAS	6.47±1.19	6.13±1.30	0.470 ^b
SWAL-QOL	112.07±4.71	111.40±5.53	0.725 ^b

Quantitative data are presented as the mean±SD or median (interquartile range),

Quantitative data are presented as the mean±SD or median (interquartile range), qualitative as percentage ^aChi-squared (χ^2) Test; ^bStudent's *t*-test; ^cMann-Whitney U Test. MMSE:Mini-Mental State Examination; KVIQ-10: Kinesthetic and Visual Imagery Questionnaire-10; SSA: standardized swallowing assessment; MSS: Murray Secretion Scale; YPR-SRS: Yale Pharyngeal Residue Severity Rating Scale; PAS: Penetration-Aspiration Scale; SWAL-QOL: Swallowing-Quality of Life

significant differences in the scores of MMSE, KVIQ-10, SSA, MSS, YPR-SRS, PAS and SWAL-QOL among the two groups (P>0.05), indicating that the data of the two groups of study subjects were comparable. For details, see Table I.

Swallowing function assessments

In comparison with the baseline characteristics, both groups improved in the post-treatment swallowing scale assessment compared with their respective pre-treatment periods (P<0.05, Figure 3). Comparing the post-treatment scale data between the two groups, it was found that the SSA score (P=0.030), MSS score (P=0.044) and SWAL-QOL score (P=0.011) of the experimental group improved better than those of the control group, and the difference was statistically significant. However, there were no significant differences in the post-treatment YPS-SRS scores (Pvallecula=0.319, Ppyriform sinus=0.090) and PAS score (P=0.168) of the two groups (Figure 3).

Cortical activation analysis of fNIRS measurements

Cortical activation during swallowing MI

During the execution of swallowing MI in the patients of experimental group, multiple brain regions of the cortical presented extensive activation, mainly including the premotor and supplementary motor cortex (PSMC), the PMC. the prefrontal cortex (PFC), the right PSC, and the right supramarginal gyrus (Figure 4). According to the beta values of each channel during the swallowing MI task in the patients of experimental group, 11 of the channels showed statistically significant beta values (P<0.05): Channel 1 (T=2.77, P=0.015), Channel 2 (T=2.52, P=0.024), Channel 8 (T=2.90, P=0.012), Channel 10 (T=3.18, P=0.007), Channel 15 (T=2.31, P=0.037), Channel 21 (T=3.19, P=0.007), Channel 31 (T=2.33, P=0.035), Channel 32 (T=2.75, P=0.016), Channel 35 (T=2.31, P=0.036), Channel 38 (T=3.30, P=0.005), Channel 39 (T=3.39, P=0.004). The associated brain areas of these 11 channels are shown in Table II.

Cortical activation during volitional swallowing task in subjects of two groups.

Cortical activation during the volitional swallowing task was compared between the two groups based on the beta values of HbO2. The results showed that the intergroup comparisons of beta value collection from each brain region between the experimental group and control group before and after the intervention demonstrated no significant differences (P>0.05). Nevertheless, there were significant differences (P<0.05) in brain regions PSMC, right PMC, and right PSC of the experimental group before and after treatment: channel 1 (T=2.40, P=0.031) and channel 39 (T=2.88, P=0.012), as shown in Figure 4.

Discussion

In this present study, we aimed to observe the efficacy of MI based on action observation treatment in treating patients with dysphagia in Wallenberg syndrome and to further investigate the mechanism of action of this therapy. The results of this study showed that after 14 consecutive days of treatment, MI based on action observation treatFigure 3.—The SSA (A), MSS (B), YPR-SRS (C, D), PAS (E), and SWAL-QOL (F) scores of preand post-intervention in the experimental and the control groups. The data are described as the mean±SD or percentage.

*P<0.05; **P<0.01; ***P<0.001.



ment improved swallowing scale assessment indexes as an add-on training. In addition, we used fNIRS to detect extensive activation of PSMC, PMC, PFC, PSC and other brain regions during the execution of swallowing MI.

Our study revealed that for the swallowing function assessment, there were statistical differences between the two groups before and after their respective treatments, demonstrating the effectiveness of both treatment protocols: conventional dysphagia treatment and MI based on action observation treatment combined with conventional dysphagia treatment. When comparing the two groups after treatment, there were significant differences in SSA, MSS, and SWAL-QOL scales, suggesting that MI based on action observation treatment can help to improve swallowing function, reduce secretion retention, and increase quality of life in patients. MI can promote the formation of normal swallowing neural reflex arc, which is equivalent to the effect of actual exercise on neural stimulation of the swallowing cortex.²⁷ MI is a special motor state in which motor memories are activated under the control of the motor center but there is no obvious motor output. According to the "psycho-neuro-muscular" theory, MI can consolidate and strengthen the motor "program" stored in the central nervous system of patients.9 This neural stimulus can be transmitted to the appropriate motor muscle receptors, forming a neuromuscular conduction pattern consistent with actual movement. Some studies in recent years have found that MI can improve swallowing function of stroke patients.^{28, 29} In this study, MI intervention was performed on patients with dysphagia in Wallenberg syndrome, which involved the muscle movements of mouth, lips, tongue, and pharynx, and promoted the formation of normal swallowing nerve reflexes during the imagery process, thus improving the swallowing function of patients. Patients with Wallenberg syndrome have insufficient epiglottis turnover and incomplete opening of the upper esophageal sphincter, resulting in increased risk of penetration/aspiration and more pharyngeal residue, 30, 31 whereas dysfunction of the



Figure 4.—The cortical activation maps based on analyzed HbO2 beta values: A) during performance of swallowing MI; B) during performance of volitional swallowing task of the experimental group before and after treatment. Only the areas corresponding to the significantly activated channels were shown. P<0.05 for significant activation. The redder the color, the smaller the P value. CH 38

CH 39

4 - Primary motor cortex

TABLE II.— <i>The associated brain areas of the activated channels.</i>			
Channel	Brodmann area	Percentage	
CH 01	1 - Primary somatosensory cortex	0.1533	
	3 - Primary somatosensory cortex	0.1707	
	4 - Primary motor cortex	0.2404	
	6 - Pre-motor and supplementary motor cortex	0.122	
	43 - Subcentral area	0.3136	
CH 02	1 - Primary somatosensory cortex	0.2715	
	2 - Primary somatosensory cortex	0.1753	
	40 - Supramarginal gyrus part of Wernicke's area	0.5533	
CH 08	10 - Frontopolar area	0.011	
	11 - Orbitofrontal area	0.989	
CH 10	10 - Frontopolar area	0.4324	
	11 - Orbitofrontal area	0.5676	
CH 15	4 - Primary motor cortex	0.3372	
	6 - Pre-motor and supplementary motor cortex	0.6628	
CH 21	10 - Frontopolar area	0.4431	
	46 - Dorsolateral prefrontal cortex	0.5569	
CH 31	6 - Pre-motor and supplementary motor cortex	1	
CH 32	6 - Pre-motor and supplementary motor cortex	1	
CH 35	6 - Pre-motor and supplementary motor cortex	1	

epiglottis and the upper esophageal sphincter is more efficacious when intervened with passive means (*e.g.*, balloon catheter dilation, botulinum toxin injections, etc.).³² It is difficult to achieve the same therapeutic effect in a short period of time with active MI, which may be the reason why there was no statistical difference in YPR-SRS scale and PAS scale scores between the two groups of patients after treatment. In addition, it is worth noting that this study design can only verify the effect of add-on MI training.

6 - Pre-motor and supplementary motor cortex

6 - Pre-motor and supplementary motor cortex

Cortical areas associated with swallowing primarily include the sensorimotor cortices, insular cortex, parietaltemporal cortex, and cingulate cortex,33 and several previous studies^{34, 35} have also identified the activated areas during swallowing task to be located in the PSC, PMC, cerebellum, insula, PSMC, and PFC. The results of the fNIRS Test showed that PSMC, PMC, PFC, right PSC, right supramarginal gyrus and other brain areas were activated during the patients' performance of MI. And after MI intervention, there were significant differences in the brain regions of the PSMC, the right PMC, and the right PSC before and after treatment of the patients in the experimental group, which suggests that the performance of MI can activate the cortical regions related to swallowing function. The primary sensorimotor cortex and the supplementary motor cortex play an important role in swallowing movements, which may be due to the involvement of the supplementary motor cortex in the planning and preparation of voluntary movements.³⁶ The PFC is thought

to be closely related to cognitive control in humans and other primates, and is responsible for coordinating actions and thoughts related to internal goals.³⁷ Besides, a previous study also showed that PFC microelectrode stimulation can cause the muscles responsible for swallowing movements to contract, and can generate the pharyngeal swallowing response by delivering more current.³⁸ The supramarginal gyrus is part of the inferior parietal lobule, located near the insula, which is associated with oral movements and sensation.³⁹ Moreover, Nishitani et al.⁴⁰ found that in humans, the Supramarginal gyrus was activated when observing lip movements. Ushioda et al.41 reported that the PSMC and the Supramarginal gyrus were excitably active in response to visual and auditory stimuli related to swallowing. This study further found that the brain regions of right PSMC, PMC, and PSC appeared to dominate in the swallowing task, which we speculate may be related to the lateralized pattern of cortical activation during swallowing.⁴² It has been shown that hemispheric dominance seems to differ in some subjects depending on the swallowing task.⁴³ Kober *et al.*²⁸ found that dysphagia patients with right hemisphere lesions are more likely to exhibit unilateral patterns of activity during swallowing. In addition, there was no statistical difference in fNIRS test results between the two groups after treatment, which may be due to the fact that the hospitalized patients included in this study were treated with MI for only 14 days.

In our study, patients were allowed to watch the video corresponding to the swallowing task during MI, which on the one hand is to assist the smooth progress of the swallowing MI task, and on the other hand, it can also achieve the purpose of stimulating the excitation of the swallowing motor cortex and enhance the effect of MI training, which is in line with the MNS theory. The MNS is widespread in multiple brain regions and is a collection of neurons with specialized mapping functions that are involved to varying degrees in various high-level activities such as emotion, learning, language, and cognition in humans.⁴⁴ Current researches show that human MNS mainly include two mirror networks, a parieto-frontal mirror system consisting of the ventral premotor cortex, the posterior IFG, the inferior parietal lobule, the lower precentral gyrus, the supplementary motor area, etc., and a limbic mirror system composed of insula, amygdala, prefrontal cortex, etc.⁴⁵ It can be seen that MI based on action observation treatment is closely related to the parieto-frontal mirror system. The perception of MNS is largely dependent on sensory neurons and motor neurons.⁴⁶ Vision is the main source of information that the human perceives

0.129

0.871

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from the outside, so the sensory signal input mainly relies on visual mirror neurons as well as some auditory neurons, but of course, motor neurons also hold an important value in transmitting motor information.⁴⁷ Thus, the whole MI process would selectively activate the main motor areas, premotor areas and sensory areas. The storage of movement mechanisms in the brain as a motor memory reserve through observation and understanding, and then benefiting from the MNS's perception, comprehension, and imitation of motor skills that link the person who performed the act to the observer, are the basis for achieving movement reproduction.48 Therefore, MI based on action observation treatment is a top-down rehabilitation therapy by selectively activating the MNS and subsequently remodeling the neural circuits in the region, which leads to the reorganization of brain functions and the restoration of the corresponding functions.

Limitations of the study

There are some limitations to our study. First, the intervention period was short. As the participants included were hospitalized and were influenced by the length of stay in the hospital, only 14 days of intervention were conducted in this study. Second, no follow-up was conducted. Due to limited human resources, the swallowing function of patients after discharge was not followed up, and the maintenance effect of MI based on action observation treatment is unknown. Third, given the low morbidity of Wallenberg syndrome, the sample size included in this study was relatively small. Rehabilitation of swallowing function is a long-term process, and MI based on action observation treatment can achieve home rehabilitation. Therefore, future studies may carry out multicenter, large-sample randomized controlled trials, extend the intervention time, add follow-up after discharge, monitor the activation of brain regions in different time periods, and dynamically observe the changes of activated brain regions, to further explore the possible mechanisms of nerve function reconstruction.

Conclusions

The present study indicated that MI based on action observation treatment could improve swallowing function and quality of life for patients with dysphagia of Wallenberg syndrome as an add-on training. Moreover, as a top-down rehabilitation training, the mechanism of this therapy may be related to the selective activation of the MNS, especially to the activation of brain areas such as PSMC, PMC, PFC and PSC.

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Conflicts of interest

The authors certify that there is no conflict of interest with any financial organization regarding the material discussed in the manuscript.

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Authors' contributions

Xi Zeng, Heping Li and Liugen Wang conceived and designed the trial. Le Wang and Ruyao Liu were involved in the research conducting and data collection. Yongkang Yuan and Yunyun Song performed data sorting and analysis. Le Wang and Yi Li performed manuscript writing and editing. Xi Zeng and Wenjian Li supervised the study and modified the manuscript. All authors read and approved the final version of the manuscript.

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History

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