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Original Article

Observation of rehabilitative effects of repeated 1-Hz transcranial magnetic stimulation in patients with hand dysfunction after stroke

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Abstract: Objective: This study aimed to analyze the rehabilitative effects of repeated 1-Hz transcranial magnetic stimulation (rTMS) in patients with hand dysfunction after stroke. Methods: A total of 105 patients with hand dysfunction after stroke admitted to our hospital were selected as the research subjects for retrospective analysis, and divided into two groups according to the order of admission. Among them, Group B (n=52) received routine rehabilitation training and Group A (n=53) received 1-Hz rTMS in addition to routine rehabilitation training. The amount of rehabilitation was compared between the two groups. Results: Directly after rehabilitation and at 1, 2 and 3 months after rehabilitation, patients in Group A had significantly higher stages of the Brunnstrom Approach and grades of the Ueda 12-Stage Hemiplegic Function Test ($P<0.05$), significantly higher scores of grasping, griping, pinching and gross movement in Action Research Arm Test (ARAT) ($P<0.05$), and significantly higher scores of motor function and cognitive function in Functional Independence Measurement (FIM) ($P<0.05$) than those in Group B. At 3 months after rehabilitation, patients in Group A had better scores of independent, mildly dependent, moderately dependent and severely dependent daily lives ($P<0.05$) than those in Group B. Conclusion: Routine rehabilitation training in combination with 1-Hz rTMS can enhance the rehabilitative effect of patients with hand dysfunction after stroke, improve their hand function more significantly and strengthen their abilities of daily living.

Keywords: Stroke, hand dysfunction, repeated transcranial magnetic stimulation, 1-Hz, rehabilitation

Introduction

Stroke is a disease with high disability rate and high mortality rate throughout the world. The vast majority of stroke patients have different degrees of dysfunction, affecting the arm, wrist, face, hand and leg on one side of the patients' affected limb [1, 2]. Stroke patients with limb dysfunction, if they do not receive rehabilitation training in a timely manner for effective rehabilitation, are prone to limb use degredation and then disability [3].

Hands are important moving limbs in the body, and hand dysfunction is the most common type of limb dysfunction after stroke. The occurrence of hand dysfunction will directly affect the work and life of patients and significantly reduce their quality of life [4]. Hand dysfunction after stroke includes paresthesia, hemiplegia, shoulder subluxation, lack of isolated movements, shoulder pain, dystonia, etc. [5]. Previous study has shown that patients who have not recovered for after one year are prone to anxiety and a significant decline in subjective well-being due to the long-term impact on their lives [6]. Therefore, it is particularly important to do rehabilitation training.

The main objective of the rehabilitation of hand dysfunction after stroke is to improve patients' hand function and restore their gross and fine motor skills [7]. Although many rehabilitation methods are currently used in clinical practice, there is no sufficient evidence to prove that these methods can be used as daily training to improve patients' hand function [8, 9]. With the deepening of research, transcranial magnetic stimulation (TMS) has gradually become more widely used, since it can temporarily enhance or reduce the degree of cortical excitability, and repeated TMS (rTMS) can continuously improve the degree of cortical excitability in patients after repeated stimulation [10]. In this study, 105 patients with hand dysfunction after stroke were selected as the research subjects to explore the effects of rTMS on promoting rehabilitation in patients, so as to investigate more effective rehabilitation methods.

Materials and methods

Information

A total of 105 patients with hand dysfunction after stroke admitted to our hospital from June 2018 to May 2019 were selected as the research subjects, and divided into Group A (n=53) and Group B (n=52) according to the order of admission. This study has been approved by the Ethics Committee of the Second Affiliated Hospital of Hainan Medical University. All patients have signed the informed consent for this study. Inclusion criteria: those who met the diagnostic criteria for stroke formulated by the Chinese Society of Neurology of the Chinese Medical Association [11], and who were confirmed with hand dysfunction; those with first onset; those who were over 18 years old and under 80 years old; those with unilateral limb dysfunction; those who could communicate well and with normal comprehension. Exclusion criteria: those complicated with disturbance of consciousness, systemic disorders of heart, liver, kidney and lung, severe bleeding tendency or a history of epilepsy; those with progressive stroke; and those who were pregnant or lactating.

Methods

Group B received routine rehabilitation training, which was specific to guiding the passive and active movements of the hands and conducted operating training. (1) The passive and active movements of hands: The patients were guided to raise the affected hand with the healthy hand for the slow flexion and extension of the knuckles, wrist joints and elbow joints for 5 min each time and several times daily. After the passive movements could be successfully completed, the active movements were gradually increased. The patients were guided to make a fist directly with the affected hand, extend the palm, abduct the shoulder, and extend and flex the wrist and elbow joints without help. (2) Operating training: At first, the combined movements of the shoulder, elbow and hand were carried out, and then gradually transformed into single joint movements after adaptation. The single joint movements were mainly in the diagonal direction of rotation, and the line of sight was kept opposite to the fingers, which was beneficial to promote hand-eye coordination. Proximal exercises were first conducted, and then were turned to distal exercises, with the movement from simple to difficult and the time from short to long, gradually. The patients were instructed to perform delicate exercises such as flower pedal assembly and inlay, and gradually to perform exercises for the ability of daily living such as brushing teeth, going to the washroom, dressing, making the bed, and having meals by themselves. Each training session lasted for half an hour, performed once daily. The routine rehabilitation training was performed for 2 weeks.

Group A received 1-Hz rTMS combined with routine rehabilitation training. A neuromagnetic stimulator (Magstim rapid2, UK) was selected with a coil diameter of 7 mm and a maximum intensity of 0.8 T. SMA and PMC regions of the unaffected cerebral cortex were taken as magnetic stimulation regions. The magnetic stimulation parameters were set as follows: 1-Hz frequency, 1,000 pulses, and 90% of the motor threshold in the resting state. The center of the coil training plane was kept close to the training area of the healthy side of the brain during training. In order to ensure the safety of training, rehabilitation personnel urged the patients to lie flat, relax completely and keep their heads still. A family member could be allowed to accompany them, so as to prevent them from becoming excessively restless during training when they suffered from headache, temporary changes in hearing, and numbness in stimulatory areas. Each training session lasted for half an hour, performed once daily. The training was performed for 2 weeks.

After 2 weeks of rehabilitation training, the patients in both groups were followed up for 3 months to observe their rehabilitation.

Observational indicators

Hand motor function: The Brunnstrom Approach [12] and the Ueda 12-Stage Hemiplegic Function Test [13] were used to assess the hand motor function of patients. According to the former scale, the evaluators guided the patients to perform the extension, flexion, grasping and finger movements of hands, all of which were rated as 1-6 stages. A higher stage indicated a stronger hand motor function. The latter scale consisted of mass movements of fingers, isolated movements of wrist joints, isolated movements of hands and fingers, speed examination and associated reaction examination, with 12 grades in total. The assessment was conducted before, after, at 1 month, 2 months and 3 months after rehabilitation, respectively.

Upper limb motor function: The Action Research Arm Test (ARAT) [14] was used to assess the upper limb motor function of patients, mainly included grasping (6 items), griping (4 items), pinching (6 items) and gross movement (3 items). Each item was scored as 0-3 points. Zero points indicated no movement; 1 point indicated that the movement task could be partially performed; 2 points indicated that half of the movement task could be performed; 3 points indicated that the movement task could be normally performed. The total score of ARAT was 57 points, and the scores of the four movement tasks were 18 points, 12 points, 18 points and 9 points, respectively. The ARAT score was proportional to the upper limb motor function. The assessment was conducted before, after, at 1 month, 2 months and 3 months after rehabilitation.

Functional independence: The Functional Independence Measurement (FIM) [15] was used to assess the functional independence of patients, which included motor function and cognitive function. Motor function consisted of self-care (6 items), sphincter control (2 items), transfer (3 items) and locomotion (2 items), and cognitive function consisting of communication (2 items) and social cognition (3 items), with each item scored with 1-7 points. Seven points indicated complete independence; 6 points indicated modified independence; 5 points indicated supervision and preparation; 4 points indicated minimal assistance with a small amount of physical contact; 3 points indicated moderate assistance with physical contact; 2 points indicated maximal assistance with a large amount of physical contact; 1 point indicated complete dependence. The FIM score was 18-126 points in total (91 points for motor function and 35 points for cognitive function). The assessment was conducted before, after, at 1 month, 2 months and 3 months after rehabilitation.

Ability of daily living: The Barthel Index (BI) [16] was used assess the ability of daily living of patients, including feeding, bathing, decorating, dressing, control of bowels, control of bladder, going to the washroom by themselves, moving from wheelchair to bed and returning, walking on a level surface, and ascending and descending stairs (10 items in total). The total score of BI was 100 points. A score of 100 points indicated independent daily lives and complete self-care. A score of 61-99 points indicated mildly dependent daily lives and minimal assistance from others. A score of 41-60 points indicated moderately dependent daily lives and partial assistance from others. A score of ≤40 points indicated severely dependent daily lives and total assistance from others. The assessment was conducted before and at 3 months after rehabilitation.

Statistical analysis

Statistical analysis was conducted by SPSS 23.0. Measurement data were expressed as ($\bar{x} \pm s$) and compared by independent samples *t* test. Count data were expressed as [n (%)] and compared by chi-squared test. The comparison between multiple time points within groups was analyzed by analysis of variance (ANVOA) and conducted by F test. Figures were plotted by Graphpad Prism 8. When $P<0.05$, the difference was statistically significant.

Results

General information

There was no statistically significant difference between Groups A and B in the proportion of males to females, average age, average course of disease, the proportion of stroke types and the proportion of hemiplegia ($P>0.05$) (**Table 1**).

1 Hz rTMS improves the Brunnstrom stages

Before rehabilitation, the Brunnstrom stages were (1.02±0.39) in Group A and (1.05±0.42) in Group B. After rehabilitation, the Brunnstrom stages were (2.75±0.67) in Group A and (2.16±0.52) in Group B. At 1, 2 and 3 months

Table 1. Comparison of general information ($\overline{x}$ ± s)/[n (%)]

Information		Group A (n=53)	Group B (n=52)	t/X^2	*P*
Gender	Male	33 (62.26)	30 (57.69)	0.229	0.633
	Female	20 (37.74)	22 (42.31)		
Age (Years)		56.38±12.45	58.17±11.91	0.693	0.490
Course of disease (Months)		1.62±1.05	1.65±1.09	0.132	0.895
Types of stroke	Hemorrhagic	25 (47.17)	27 (51.92)	0.237	0.626
	Ischemic	28 (52.83)	25 (48.08)		
Hemiplegia	Left	26 (49.06)	25 (48.08)	0.010	0.920
	Right	27 (50.94)	27 (51.92)		

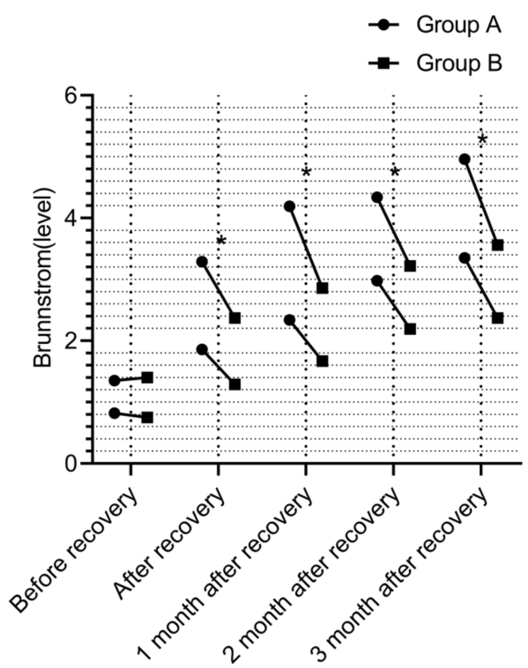

Figure 1. Comparison of results of the Brunnstrom Approach. Before rehabilitation, there was no significant difference in the Brunnstrom stage between Groups A and B (*P*>0.05). After rehabilitation and at 1, 2 and 3 months after rehabilitation, the Brunnstrom stages in Group A were significantly higher than those in Group B (*P*<0.05). * indicates the comparison between the two groups, *P*<0.05.

after rehabilitation, the stages were (3.51±0.73), (3.96±0.81) and (4.25±0.89) respectively in Group A, and (2.43±0.56), (2.84±0.62) and (3.02±0.65) in Group B, respectively. Before rehabilitation, there was no significant difference in the Brunnstrom stages between Groups A and B (*P*>0.05), while after rehabilitation and at 1, 2 and 3 months after rehabilitation, the Brunnstrom stages in Group A were significantly higher than those in Group B (*P*<0.05) (**Figure 1**).

1 Hz rTMS improves the Ueda grades

Before rehabilitation, the Ueda grades were (2.74±1.02) in Group A and (2.81±1.05) in Group B. After rehabilitation, the grades were (4.51±1.36) in Group A and (2.99±1.12) in Group B. At 1, 2 and 3 months after rehabilitation, the grades were (4.94±1.52), (5.42±1.91) and (6.02±2.13) respectively in Group A, and (3.21±1.24), (3.69±1.36) and (3.85±1.44) respectively in Group B. Before rehabilitation, there was no significant difference in the Ueda grades between Groups A and B (*P*>0.05), while after rehabilitation and at 1, 2 and 3 months after rehabilitation, the Ueda grades in Group A were significantly higher than those in Group B (*P*<0.05) (**Figure 2**).

1 Hz rTMS improves ARAT

Before rehabilitation, there was no significant difference between Groups A and B in the scores of grasping, griping, pinching and gross movement (*P*>0.05). After rehabilitation and at 1, 2 and 3 months after rehabilitation, the scores in Group A were significantly higher than those in Group B (*P*<0.05) (**Figure 3**).

1 Hz rTMS promotes FIM

Before rehabilitation, there was no significant difference between Groups A and B in the scores of motor function and cognitive function (*P*>0.05). After rehabilitation and at 1, 2 and 3 months after rehabilitation, the scores in Group A were higher than those in Group B (*P*<0.05) (**Figure 4**).

1 Hz rTMS ameliorates BI

Before rehabilitation, there was no significant difference between Groups A and B in the

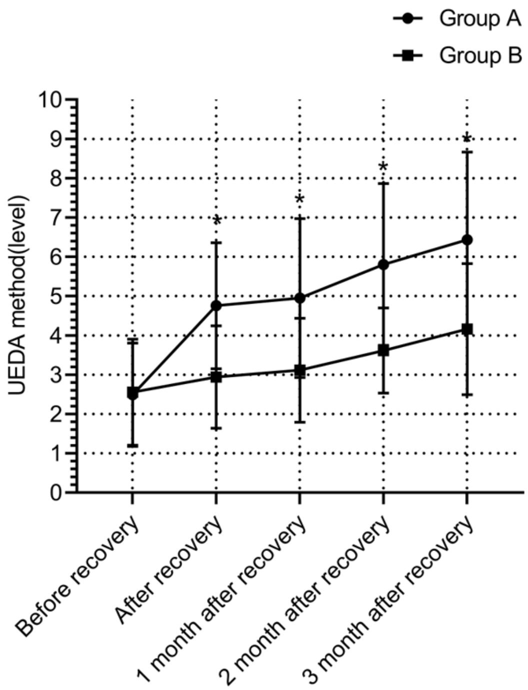

Figure 2. Comparison of results of the Ueda 12-Stage Hemiplegic Function Test. Before rehabilitation, there was no significant difference in the Ueda grade between Groups A and B ($P>0.05$). After rehabilitation and at 1, 2 and 3 months after rehabilitation, the Ueda grades in Group A were significantly higher than those in Group B ($P<0.05$). * indicates the comparison between the two groups, $P<0.05$.

scores of independence, mild dependence, moderate dependence and severe dependence ($P>0.05$). At 3 months after rehabilitation, the proportion in Group A was better than those before rehabilitation ($P<0.05$), but the proportion in Group B had no statistically significant difference from those before rehabilitation ($P>0.05$). At 3 months after rehabilitation, the proportion of independence and mild dependence in Group A were higher than those in Group B ($P<0.05$), and the proportion of moderate dependence and severe dependence in Group A were lower than those in Group B ($P<0.05$) (**Table 2**).

Discussion

At present, due to the improvements in medical conditions and levels of diagnosis and treatment, the effective rate of treatment in stroke patients has been gradually improved, and the survival rate of patients has been significantly increased, but the disability rate has not been effectively elevated. Most of the patients still have varying degrees of dysfunction after treatment, which seriously affects their quality of life [17]. It takes a long time for functional rehabilitation of stroke patients, especially for patients with hand dysfunction, whose rehabilitation is the most difficult and the slowest. Therefore, in order to ensure the best rehabilitative effect, the selection of rehabilitation methods must be emphasized in addition to ensuring patients' good rehabilitation compliance [18].

Some previous rehabilitation methods were invasive and it was difficult to ensure patients' compliance, but the progress of current medical technology has led to the clinical emergence of non-invasive rehabilitation methods, which have been widely recognized by rehabilitation personnel and patients [19]. As a new neurological rehabilitation method specifically developed based on the theory of interhemispheric inhibition, rTMS has been shown to be effective in improving the motor function of stroke patients. The theory holds that the healthy brain inhibits the transmission of neurotransmitters in the affected brain through the corpus callosum after stroke occurrence, thereby leading to dyskinesia in the affected brain [20]. TMS includes high- and low-frequencies, of which high-frequencies one can stimulate the cerebral cortex and low-frequencies can reduce cerebral cortical excitability. Currently, no unified conclusion has been drawn as to whether TMS is better at high-frequency or low-frequency. Some studies indicated that that there is little difference between the application of high-frequency and low-frequency in the effect of rehabilitation, but some studies showed that high frequency can improve the quality of rehabilitation [21, 22]. In this study, low-frequency TMS at 1-Hz was applied to reduce the cortical excitability of the healthy brain via stimulation, so as to correspondingly improve the excitability of the affected brain. After rehabilitation and at 1, 2 and 3 months after rehabilitation, patients in Group A had significantly higher stages of the Brunnstrom Approach and grades of the Ueda 12-Stage Hemiplegic Function Test, and higher scores of grasping, gripping, pinching and gross movement in ARAT than those in Group B ($P<0.05$). This suggests that 1-Hz rTMS combined with routine rehabilitation training could significantly improve the patients' hand function, upper limb motor function and hand dexterity. It was shown in the study that

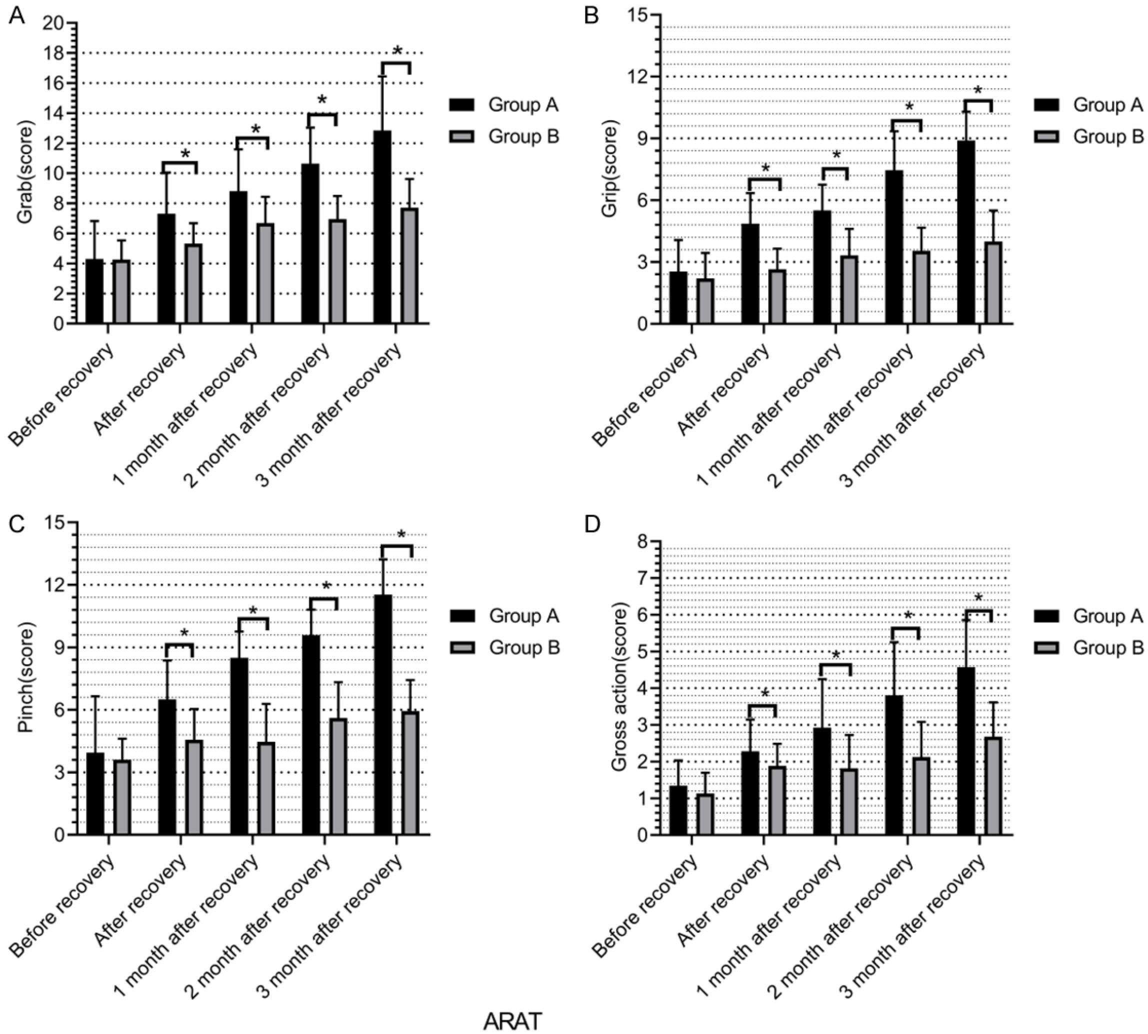

Figure 3. Comparison of ARAT results. Before rehabilitation, there was no significant difference in the scores of grasping (A), griping (B), pinching (C) and gross movement (D) between Groups A and B (*P*>0.05). After rehabilitation and at 1, 2 and 3 months after rehabilitation, the scores in Group A were significantly higher than those in Group B (*P*<0.05). * indicates the comparison between the two groups, *P*<0.05.

the motor function and ability of daily living of patients with rTMS were significantly improved after 3 months compared with those without rTMS (P<0.05) [23]. This is because rTMS has effectively improved the states of cerebral PMC and SMA regions, which are considered to be closely involved in learning and motor skills. The PMC region is mainly responsible for controlling the execution of motor function and actions, which can improve the visual motion process. The SMA region is responsible for transforming the actions from memory to actual activities while maintaining the plan of the actions [24]. The implementation of continuous rTMS can consolidate motor skills and sequences, improve the process of nerve reflex from cognition to actions, accelerate the rehabilitation of hand motor function, and enhance the fine motor ability of hand [25]. In our study, the scores of motor and cognitive function in Group A were higher than those in Group B after rehabilitation and at 1, 2 and 3 months after rehabilitation. At 3 months after rehabilitation, Group A had better a proportion of independent, mildly dependent, moderately dependent and severely dependent daily lives (*P*<0.05), which indicates that the application of 1-Hz rTMS can obtain better effects of the recovery in patients after stroke. It improves the motor function more clearly, improves the cognitive function, and enables patients to have stronger self-care ability, which is of great significance to

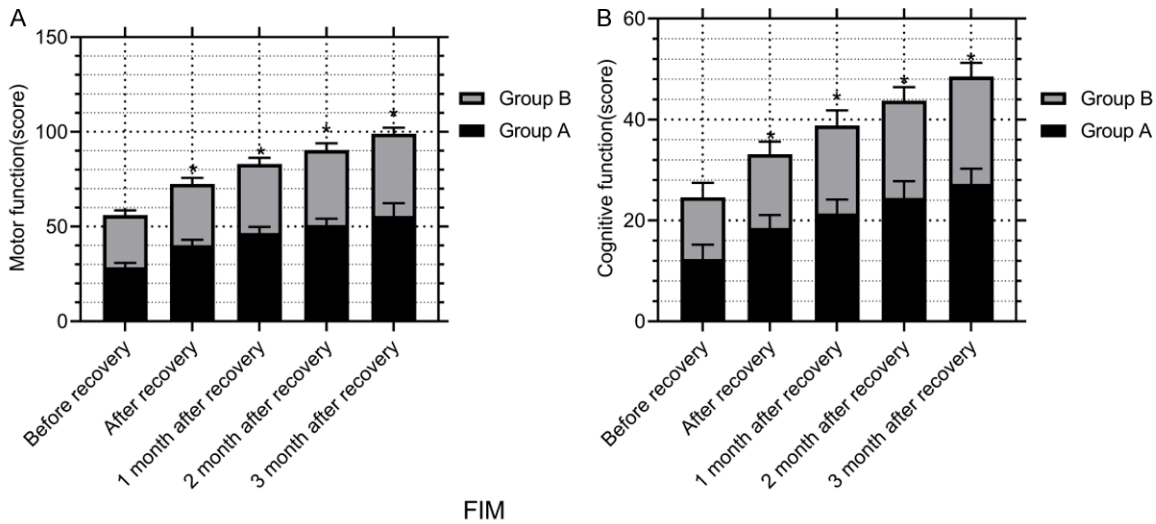

Figure 4. Comparison of FIM results. Before rehabilitation, there was no significant difference in the scores of motor function (A) and cognitive function (B) between Groups A and B ($P>0.05$). After rehabilitation and at 1, 2 and 3 months after rehabilitation, the scores in Group A were significantly higher than those in Group B ($P<0.05$). * indicates the comparison between the two groups, $P<0.05$.

Table 2. Comparison of BI results before and at 3 months after rehabilitation [n (%)]

Groups	Time	Independence	Mild dependence	Moderate dependence	Severe dependence
Group A (n=53)	Before rehabilitation	0 (0.00)	13 (24.53)	30 (56.60)	10 (18.87)
	Three months after rehabilitation	11 (20.75)	28 (52.83)	13 (24.53)	1 (1.89)
X^2		12.274	8.949	11.308	8.216
P		0.000	0.003	0.001	0.004
Group B (n=52)	Before rehabilitation	0 (0.00)	12 (23.08)	29 (55.77)	11 (21.15)
	Three months after rehabilitation	3 (5.77)	17 (32.69)	24 (46.15)	8 (15.38)
X^2		3.089	1.195	0.943	0.580
P		0.079	0.274	0.331	0.446
$X^2 1$		5.108	4.346	5.379	6.102
P1		0.024	0.037	0.020	0.014

Note: $X^2 1$ and *P1* are the comparative statistical values between the two groups at 3 months after rehabilitation.

improve the patients' quality of life and help them recover to their regular lives. It was found that magnetic stimulation on the basis of routine exercise rehabilitation accelerates the neural remodeling of motor areas of the brain, promotes the movement learning of patients, and obtains better rehabilitation functions [26]. The activity level of aminobutyric acid type B in the cerebral cortex is considered to be responsible for the partial cortical rest of spinal cord interneurons. The stage of cortical rest changes the activity level under magnetic stimulation due to cortical inhibition and the activation of spinal cord interneurons, thus improving the cortical excitability of the affected brain and the hand function of the patients [27].

In summary, routine rehabilitation training combined with 1-Hz rTMS can improve the rehabilitative effect of patients with hand dysfunction after stroke, improve their hand function more significantly and strengthen their abilities of daily living. This study has confirmed that 1-Hz rTMS can promote the rehabilitation of patients with hand dysfunction after stroke, but there are still some deficiencies, such as the absence of injury stratification for patients during magnetic stimulation rehabilitation, small selection of measurement indicators for efficacy evaluation, and no imaging examination before and after treatment to judge the rehabilitative effect. All of these have resulted in a lack of comprehensiveness of the obtained results and limited reference values for the selection of stroke rehabilitation methods. These should be further explored, so more extensive and comprehensive research is needed in future studies.

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Disclosure of conflict of interest

None.

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