

Efficacy of functional magnetic stimulation in improving upper extremity function after stroke: a randomized, single-blind, controlled study

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Abstract

Objective: To clarify the efficacy of functional magnetic stimulation (FMS) in improving hemiplegic upper extremity function in patients with sub-acute stroke.

Methods: In this randomized controlled trial, 40 sub-acute stroke patients with hemiplegia were recruited from inpatient wards in the Department of Rehabilitation and randomly assigned to two groups. In the FMS group, magnetic stimulation was applied to extensor muscle groups of the affected upper extremity. In the low-frequency repetitive transcranial magnetic stimulation (LF-rTMS) group, stimulation was applied to the contralesional primary motor cortex. All patients received occupational therapy. Hand and upper extremity motor function was evaluated using the Fugl–Meyer Assessment for upper extremity (FMA-UE), and the Barthel Index (BI) evaluated daily living abilities.

Results: The FMA-UE and BI scores were significantly increased in both groups following stimulation. Furthermore, a significant between-group difference was observed in both FMA-UE and BI scores after 2 weeks of therapy. In the FMS group, 6 of 19 patients regained wrist and finger extension abilities, but only 2 patients regained equivalent motor skills in the LF-rTMS group.

Conclusions: FMS improves paretic upper extremity function and leads to better recovery of motor activity than LF-rTMS. FMS may be a novel modality to improve motor function.

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Keywords

Functional magnetic stimulation, repetitive transcranial magnetic stimulation, hemiplegia, upper extremity, randomized controlled trial, Fugl–Meyer Assessment, Barthel Index

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Introduction

Stroke survivors often have varying degrees of motor function impairment, especially in the upper extremities, which can lead to long-term disability and poor quality of life.¹ Several methods have been proposed for the rehabilitation of hemiplegic upper extremities;^{2–4} however, it remains the most common deficit following a stroke.

Repetitive transcranial magnetic stimulation (rTMS) is a non-invasive brain stimulation technique in which magnetic stimulation is delivered by a coil over the scalp, to generate an electric field within the brain.⁵ Low-frequency rTMS (LF-rTMS, ≤ 1 Hz) suppresses cortical excitability, while high-frequency rTMS (HF-rTMS, ≥ 5 Hz) enhances cortical excitability.⁶ Both types of rTMS are reportedly effective for improving upper extremity function after stroke,^{7,8} although a meta-analysis revealed that LF-rTMS may be more effective than HF-rTMS for regaining motor function.⁹ However, contraindications such as seizures and metal implants limit the application of rTMS, especially in stroke patients.¹⁰ Thus, studies have recently begun to develop novel modalities of magnetic stimulation. It has been reported that, when delivered peripherally, magnetic stimulation can generate electrical stimulation of selected nerves or muscles; this technique is usually known as functional magnetic stimulation (FMS).¹¹ Although it is similar to functional electrical stimulation, FMS has a deeper reach and generates less pain.¹¹ Reports have demonstrated the beneficial role of FMS in improving swallowing and respiratory functions after

stroke,^{12,13} but to our knowledge, no study has yet investigated its role in motor dysfunction. Therefore, this study aimed to explore the efficacy of FMS on upper extremity function in stroke patients.

Methods

Participants

We enrolled first-time stroke patients with upper extremity dysfunction who were admitted to the Department of Rehabilitation Medicine of The First Hospital of Jilin University between 4 July 2017 and 29 December 2017. All patients met the following inclusion criteria: 1) sub-acute stroke patients (cerebral infarction) with upper extremity hemiparesis; 2) 18 to 65 years old; and 3) able to follow the therapist's instructions. The exclusion criteria were as follows: 1) cerebral hemorrhage; 2) a history of epilepsy or recent administration of anti-epileptic drugs; 3) medically unstable, such as a severe cardiopulmonary situation, severe liver and kidney dysfunction, or malignant tumor; 4) severe cognitive dysfunction or aphasia with mental illness; 5) severe visual and auditory problems; 6) electronic and/or magnetic implants; and 7) spasticity of the affected upper extremity, with Modified Ashworth Scale > 2 . Basic patient information was collected, including sex, height, weight, handedness, and stroke characteristics (side and location).

This project is registered with chictr.org.cn (ChiCTR1800019757). The study protocol was reviewed and approved by the local

ethics review committee of the First Hospital of Jilin University (protocol no. 2107-343). All of the patients signed written informed consent for this study. The therapy procedure did not harm the patients and they could stop at any time if they felt uncomfortable.

Experimental model

Patients were randomly assigned to either the FMS or the LF-rTMS group. Randomization was performed using a random number table by a researcher blinded to patient details. The researcher who enrolled the patients and the occupational therapist and doctor who evaluated the patients were unaware of the

randomization results. The trial flow diagram is shown in Figure 1. Clinical features and demographic data were collected. During hospitalization, patients received occupational therapy after FMS or LF-rTMS; each patient received one session per day, with a total of 10 sessions over 2 weeks.

Application of FMS and LF-rTMS

For the FMS group, stimulation was delivered via a parabolic coil (MMC-140 coil, Magpro R30 stimulator, Magventure, Farum, Denmark), at a frequency of 30 Hz, and with an intensity of approximately 20% to 40% of its maximal output without generating local pain. The extensor

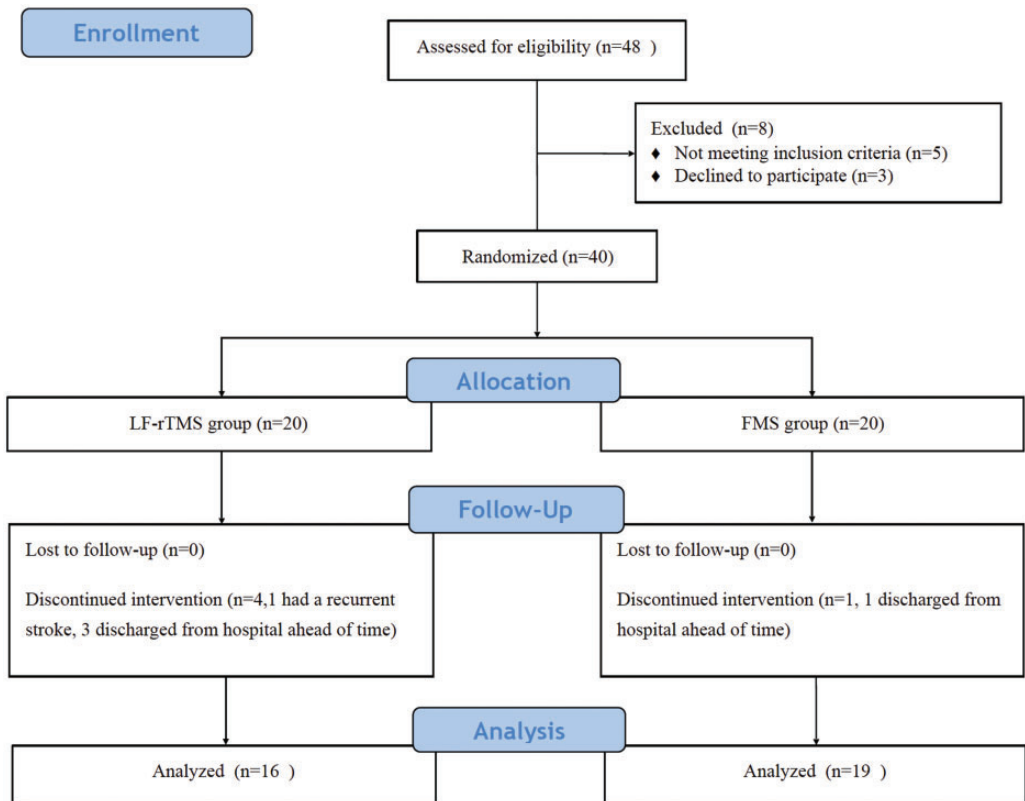


Figure 1. Flow diagram of the study design. LF-rTMS, low-frequency repetitive transcranial magnetic stimulation; FMS, functional magnetic stimulation.

muscles of the upper extremity and shoulder muscles were sequentially stimulated while patients simultaneously contracted; this was repeated five times for each site. Occupational therapy was conducted immediately after FMS. For the LF-rTMS group, stimulation was delivered via a slightly bent butterfly coil (MCF-B70 Butterfly Coil, Magventure) on the contralesional M1 area, at 45° to the sagittal direction, at an intensity of 90% of the resting motor threshold (RMT), with 1 Hz frequency and 1,500 pulses in total. The RMT was evaluated before therapy using a previously reported method.¹⁴ Briefly, the electromyography signal was monitored using disposable Ag/AgCl electrodes. The active electrode was attached to the skin overlying the contralesional abductor pollicis brevis, while the reference electrode was placed over the adjacent joint. The RMT was determined as the minimum TMS intensity that generated at least five motor evoked potentials of $\geq 50 \mu\text{V}$ peak-to-peak amplitude per 10 consecutive stimuli.

After magnetic stimulation, all patients immediately received occupational therapy, which included muscle stretching, muscle strengthening exercises, and passive and active upper extremity movements. These movements included shoulder flexion, extension, and rotation; elbow extension and flexion; wrist extension, flexion, supination, and pronation; and thumb flexion. A repetitive task-oriented training approach was taken, using movements such as reaching and weight bearing, repetitive hand motor skills, and activities related to daily living (ADL). All therapies were performed by two occupational therapists who were trained to perform the same occupational procedures.

To evaluate improvements in upper extremity function and ADL performance, respectively, the Fugl-Meyer Assessment for upper extremity (FMA-UE)¹⁵ and the Barthel Index (BI)¹⁶ were performed

pre- and post-therapy. An experienced physician performed all evaluations in a blinded manner.

Statistical analyses

Statistical analyses were performed using IBM SPSS Statistics for Windows, version 22.0 (IBM Corp., Armonk, NY, USA). Data are presented as the mean (standard deviation [SD]) if they showed a normal distribution. The χ^2 test and independent t-test were used to compare baseline characteristics. Paired t-tests were used for pre- and post-therapy data comparisons within groups. To investigate changes between groups, an independent samples t-test was used. A P-value of less than 0.05 was considered to be statistically significant.

Results

The patients' clinical characteristics are displayed in Table 1. There were no significant differences in clinical and demographical characteristics between the two groups. The patients who completed this study were all right-handed, and lesion areas included the primary motor cortex, premotor cortex, supplementary motor cortex, basal ganglia, and brainstem. All patients underwent anticoagulant therapy and supportive care before admission to the Department of Rehabilitation. Of the 40 enrolled patients, one patient in the FMS group and four patients in the LF-rTMS group were excluded because they failed to complete the magnetic stimulation sessions (Figure 1). No adverse effects of therapy were reported.

There were no significant differences in FMA-UE or BI scores between the two groups before therapy. After 10 sessions of therapy, there were significant improvements in both FMA-UE and BI scores in both groups compared with the baseline values ($P < 0.05$, Table 2). Furthermore,

Table 1. Demographic features of the groups.

	FMS (n = 19)	LF-rTMS (n = 16)	P
Sex (male:female)	14:5	13:3	0.700
Age (years), mean (SD)	52.56 (11.65)	48.68 (14.11)	0.387
Height (m), mean (SD)	1.74 (0.07)	1.73 (0.07)	0.69
Weight (kg), mean (SD)	72.38 (6.95)	71.05 (9.68)	0.64
BMI (kg/m ²), mean (SD)	23.88 (1.61)	23.66 (2.43)	0.76
Side of stroke (left:right)	9:10	9:7	0.738
FMA-UE, mean (SD)	16.21 (14.54)	15.75 (12.73)	0.922
BI, mean (SD)	38.42 (22.43)	34.06 (19.08)	0.544

FMS, functional magnetic stimulation; LF-rTMS, low-frequency repetitive transcranial magnetic stimulation; SD, standard deviation; BMI, body mass index; FMA-UE, Fugl-Meyer Assessment for upper extremity; BI, Barthel Index.

Table 2. Evaluation of upper limb function after therapy.

	FMS group			LF-rTMS group			Between groups
	Pre-therapy, mean (SD)	Post-therapy, mean (SD)	P	Pre-therapy, mean (SD)	Post-therapy, mean (SD)	P	P
FMA-UE	16.21 (14.54)	31.42 (13.49)	0.002	15.75 (12.73)	26.25 (12.90)	0.027	0.003
BI	38.42 (22.43)	58.16 (19.66)	0.007	34.06 (19.08)	48.75 (19.62)	0.040	0.011

FMS, functional magnetic stimulation; LF-rTMS, low-frequency repetitive transcranial magnetic stimulation; SD, standard deviation; FMA-UE, Fugl-Meyer Assessment for upper extremity; BI, Barthel Index.

post-therapy FMA-UE scores were significantly higher in the FMS group than in the LF-rTMS group ($P < 0.05$, Table 2). Similarly, the post-therapy BI scores were significantly higher in the FMS group than in the LF-rTMS group ($P < 0.05$, Table 2). In the FMS group, 6 of 19 patients regained some motor activity in the upper extremity, such as wrist extension and finger extension. In the LF-rTMS group, only 2 of 16 patients regained the equivalent motor skills.

Discussion

The results of this study suggest that both FMS and LF-rTMS increase function in the paralyzed upper extremity and improve ADL performance in sub-acute stroke patients. LF-rTMS has previously been

reported to have a beneficial effect on upper limb function in stroke patients.^{17,18} Here, we aimed to investigate a new modality of non-invasive magnetic stimulation, so we used LF-rTMS as a control rather than using sham stimulation; thus, all patients received treatment during the ‘golden period’ of therapy.

Compared with the LF-rTMS group, patients in the FMS group gained better motor function and performance, as measured by FMA-UE scores, and greater improvements in ADL, as evaluated by BI scores. The underlying mechanisms for these improvements remain unclear. It has been reported that peripheral stimuli preferentially activate the proprioceptive afferents that carry information from mechanoreceptors, as well as muscle spindles and deep connective tissue sensors;

these in turn may enhance M1 excitability.¹⁹ Kumru et al.²⁰ demonstrated that peripheral magnetic stimulation of the extensor carpi radialis, followed by 1 Hz rTMS on the M1 area, increased corticospinal excitability and decreased intracortical inhibition. Furthermore, peripheral magnetic stimulation has also been revealed to increase sensory function in paretic limbs, which may also have a positive impact on motor recovery.^{21,22} Therefore, magnetic stimulation over muscles or nerves may help motor recovery by facilitating plastic changes in the M1 area, as well as by providing sensory input. In the present study, six patients in the FMS group reported that they were able to extend their wrist and fingers following treatment, which they had been unable to do before magnetic stimulation; in contrast, only two patients reported this improvement in the LF-rTMS group. This result suggests that FMS may be more beneficial for regaining motor performance in post-stroke patients.

FMS has been extensively used to treat urodynamic stress incontinence, constipation, and pain.²³⁻²⁵ One previous study reported that FMS improved dysphagia in stroke patients.¹² In addition, by conditioning the inspiratory and expiratory muscles, FMS has also been reported to improve voluntary respiratory functions.¹³ However, no studies have previously reported the impact of FMS on motor function in stroke. In the current study, FMS was effective in improving paretic upper extremity function. As well as the possible mechanisms mentioned in the previous paragraph, active muscle contractions may enhance the efficiency of proprioceptive afferent input transmission to the cortex.²⁶ We thus speculate that FMS during active muscle contractions may enhance synaptic connectivity in the proprioceptive projections, which leads to better motor performance in stroke patients. In addition, neuromodulation over direct nerve

stimulation may also improve these effects. However, further studies are needed to demonstrate the underlying mechanisms.

The present study has some limitations. Further studies should include a larger sample size, and should also have longer follow-up periods to observe how long the beneficial effects may last. Moreover, the lower extremities were not included in the current study, and should be considered in future studies. However, even with these limitations, we were able to observe the promising effect of FMS on motor function.

rTMS has many contraindications, including epilepsy and the presence of metal implants, which are very common in patients after stroke and traumatic brain injury. These contraindications greatly narrow the application of this non-invasive magnetic stimulation treatment. FMS, however, is expected to have wider applications for brain-injured patients. Future studies also need to investigate the optimal frequency and stimulating times to achieve the best therapeutic effects.

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Author contributions

Xiaowei Chen, Xuncan Liu, and Zhenlan Li contributed to the design and monitoring of the project. Xiaowei Chen wrote the manuscript. Xuncan Liu enrolled and managed the patients and decided on the analytical strategy. Yinxing Cui performed all evaluations in both groups. Guoxing Xu was responsible for the FMS and LF-rTMS delivery. Lu Liu carried out the occupational therapy. Xueru Zhang and Kun Jiang collected all data and performed the statistical analyses. All authors discussed the results and contributed to the final manuscript.

Clinical message

FMS can improve paretic upper extremity function and allow patients to regain hand function more efficiently than LF-rTMS.


Declaration of conflicting interest

The authors declare that there is no conflict of interest.

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