Bilateral Repetitive Transcranial Magnetic Stimulation Combined with Intensive Swallowing Rehabilitation for Chronic Stroke Dysphagia: A Case Series Study

Ryo Momosaki Masahiro Abo Wataru Kakuda

Department of Rehabilitation Medicine, The Jikei University School of Medicine,
Tokyo, Japan

Key Words

Cardiovascular disease · Deglutition · Noninvasive brain stimulation

Abstract

The purpose of this study was to clarify the safety and feasibility of a 6-day protocol of bilateral repetitive transcranial magnetic stimulation (rTMS) combined with intensive swallowing rehabilitation for chronic poststroke dysphagia. In-hospital treatment was provided to 4 poststroke patients (age at treatment: 56–80 years; interval between onset of stroke and treatment: 24–37 months) with dysphagia. Over 6 consecutive days, each patient received 10 sessions of rTMS at 3 Hz applied to the pharyngeal motor cortex bilaterally, followed by 20 min of intensive swallowing rehabilitation exercise. The swallowing function was evaluated by the Penetration Aspiration Scale (PAS), Modified Mann Assessment of Swallowing Ability (MMASA), Functional Oral Intake Scale (FOIS), laryngeal elevation delay time (LEDT) and Repetitive Saliva-Swallowing Test (RSST) on admission and at discharge. All patients completed the 6-day treatment protocol and none showed any adverse reactions throughout the treatment. The combination treatment improved laryngeal elevation delay time in all patients. Our proposed protocol of rTMS plus swallowing rehabilitation exercise seems to be safe and feasible for chronic stroke dysphagia, although its efficacy needs to be confirmed in a large number of patients.

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Prof. Masahiro Abo, MD, PhD
Department of Rehabilitation Medicine
The Jikei University School of Medicine
3-25-8, Nishi-Shinbashi, Minato-Ku, Tokyo 105-8461 (Japan)
E-Mail abo@jikei.ac.jp

Introduction

Dysphagia is a common complication in stroke patients, with a reported incidence of approximately 55% during the acute phase of a stroke. Dealing with dysphagia is clinically important because it can affect the activities of daily living, quality of life, and prognosis of stroke patients. Using rehabilitation as treatment for dysphagia is a relatively recent development, and at present, effective techniques are limited to the Shaker exercise [1], lingual exercise, pronunciation training, and expiratory muscle strength training [2], among others.

Recent studies have described the usefulness of repetitive transcranial magnetic stimulation (rTMS) for poststroke paralysis and neurobehavioral impairment [3] as well as intervention research reports on dysphagia (table 1). The effectiveness of high-frequency rTMS [4, 5], low-frequency rTMS [6], and comparison of the two techniques [7] for unilateral supratentorial stroke dysphagia have been reported.

Recently, the effectiveness of low-frequency rTMS applied to the unaffected cerebral hemisphere in poststroke dysphagia has been reported [8]. However, the study had certain limitations with regard to interventional difficulties in targeting cerebral lesions of either hemisphere, cerebellum or brain stem. On the other hand, Khedr and Abo-Elfetoh [9] described a generalized technique of high-frequency rTMS, which is applied to the entire cerebral area, implementing it for dysphagia during the acute phase of brain stem and medulla oblongata infarctions (within 6 months of stroke), and reported the effectiveness of their method in improvements of swallowing. To our knowledge, there is no report that describes the effectiveness of this technique for stroke patients in the chronic phase (after 6 months).

Based on our experience, the application of rTMS alone without rehabilitation is not sufficiently effective. For this reason, we devised a protocol that combines rTMS with intensive rehabilitation for treatment of upper limb paralysis [3]. However, there are no studies that used the combination of rTMS applied to both cerebral hemispheres and rehabilitation for treatment of chronic stroke dysphagia.

The main hypothesis tested in the present study was that bilateral rTMS combined with an intensive swallowing rehabilitation program is safe and feasible for chronic stroke dysphagia caused by bilateral cerebral lesions.

Methods

Subjects

The subjects were 4 patients with dysphagia associated with chronic cerebral infarction (table 2). They included 2 females and 2 males, aged 56–80 years at the time of intervention. The time between onset of stroke symptoms and intervention ranged from 24 to 37 months. MRI taken within 30 days was used to determine the type and location of the stroke: all patients had bilateral cerebral infarctions.

The criteria used for inclusion in this protocol were: (1) 20–80 years of age; (2) greater than or equal to 6 months since the appearance of dysphagia; (3) epilepsy waveforms not present on the electroencephalogram; (4) a single digit score on the Japan Coma Scale; (5) ability to respond to verbal commands; (6) absence of infection requiring medical treatment; (7) willingness to participate in rehabilitation; (8) ability to sit for 2 h or more, and (9) not requiring major assistance to perform activities of daily living. The exclusion criteria were based on the guidelines related to rTMS safety [10]: history of an epileptic seizure in the past

year, and the use of intracranial metal (e.g., clips), or cardiac pacemakers. In addition, tracheostomy, use of oxygen, depression, and artificial dialysis were additional exclusion criteria used in this study. Subjects who had severe dysphagia (with repeated salivary aspiration) and subjects who had only mild dysphagia (with possible normal diet intake) were also excluded. Food intake ability was scored on the Functional Oral Intake Scale (FOIS; explained below); the scale in our patients ranged from levels 5–6.

The combination of the rTMS and rehabilitation program was approved by the University Ethics Review Committee, and informed consent was obtained from the patients or their families.

Treatment Schedule and Protocol

The treatment schedule is described in [fig. 1](#). Treatment was applied over 6 days as hospitalization therapy. Treatment sessions began in the afternoon on the day of hospitalization and were repeated twice daily thereafter every morning and afternoon. They consisted of 10 min of rTMS followed by a 20-min session of individualized swallowing rehabilitation.

rTMS Protocol

We used the MAGPRO R30 magnetic stimulator and 70-mm radius figure-of-eight coil (Magventure; Denmark) for our rTMS protocol. The stimulation procedure for each session targeted the motor area of the left and right cerebral hemispheres at the point where the maximum motor-evoked potentials (MEP) were measured for pharyngeal muscles. Pharyngeal MEP were recorded using a pair of noninvasive intraluminal platinum ring electrodes attached at 20 cm from the tip of a catheter (external diameter 3 mm; inter-electrode distance 1 cm; Unique Medical, Komaeshi, Japan) that was swallowed and positioned in the oropharynx. Pulses were applied twice daily at 3 Hz for 10 s with a 25-second interval, 20 times per session, alternating between left and right hemispheres (300 pulses for the left hemisphere and 300 pulses for the right hemisphere in one treatment session, 1,200 pulses per day; [fig. 2](#)). In addition, we set our stimulus strength at 130% of the resting state MEP threshold of the respective left/right abductor pollicis brevis muscles. In a recent study, rTMS safely improved poststroke dysphagia using a frequency of 3 Hz [9]. Accordingly, the same frequency was used in the present study. The intensity of stimulation was set to 130% of the resting motor threshold (rMT) for the first dorsal interosseous muscle of the unaffected hemisphere.

Swallowing Rehabilitation Program

Following rTMS, individualized indirect 20-min swallowing exercises were provided by a speech pathologist. These exercises included combining oral stretching, tongue push-up exercise, and isokinetic Shaker exercise [1]. Oral stretching exercises consisted of opening and closing the mouth, filling and collapsing the cheeks with air, protruding and withdrawing the tongue, and touching the left and right corners of the mouth with the tongue, 10–20 times each within a range where they could be done. The tongue push-up exercise consisted of pushing down on the tongue with a flat object, with simultaneous pushing up the tongue for 10 s, followed by a 30-second rest, repeated five times. The isokinetic Shaker exercise consisted of lifting the head only until the toes became visible, while the subject was in supine position and keeping the shoulders against the bed, 10 times followed by 30 s of rest, repeated three times. When elevating the head for 10 times was difficult, the number was reduced to 50% of the maximum times that the patient could perform. If pain or fatigue appeared the day after a training exercise, the intensity of the exercise was reduced on the second day to avoid their appearance again.

Evaluation of Swallowing Function

We evaluated swallowing function upon admission and discharge, using the Modified Barium Swallow (MBS) study with thickening agent three times, taking the worst scores of both the Penetration Aspiration Scale (PAS) [11] and laryngeal elevation delay time (LEDT) [12]. The PAS determines the severity of laryngeal penetration and tracheal aspiration, and is scored out of eight points with a high score corresponding to severe tracheal aspiration. LEDT was defined as the delay between the time when the bolus head reaches the basal part of the piriform recess and when the laryngeal elevation reaches its maximum. Patients were scored using the FOIS (where level 1 indicates inability to eat and level 7 indicates ability to eat a regular diet) [13], Modified Mann Assessment of Swallowing Ability (MMASA; where a lower score indicates severe dysphagia) [14], a 100-point clinical evaluation scale of swallowing function derived from 12 items of physical observations that identify the validity of stroke, and the Repetitive Saliva-Swallowing Test (RSST), a count of swallows over a 30-second period [15]. This test involves placing the patient in a resting position, and wetting the patient's mouth with cold water. The patient is instructed to repeatedly swallow air, and the number of swallows are monitored. Swallows are identified either visually or by palpation, as laryngeal elevation.

Results

Six days of combination therapy were completed without deterioration of neurological symptoms or adverse reactions such as convulsions or pneumonia. Swallowing-like motion occurred during rTMS when the pharynx was observed by endoscopy. With regard to the swallowing function, MMASA remained unchanged or improved after treatment (table 3). A trend towards improvement in swallowing reflex in terms of LEDT was also noted. PAS remained unchanged or improved after the intervention, and penetration and aspiration tended to diminish after the treatment. RSST and FOIS showed a trend toward slight improvement. None of the patients showed signs of worsening in those scores. Increases in oral intake function as well as decreases in choking were noted during actual meal settings.

Discussion

Our results confirmed the safety and feasibility of rTMS combined with swallowing rehabilitation for poststroke dysphagia, based on the completion of the treatment protocol by all patients with no obvious adverse effects. The usefulness of the combination of rTMS and intensive rehabilitation in functional recovery of motor function in patients with upper limb paralysis has been reported previously [3]. However, there was no study that used the combination of bilateral rTMS with swallowing rehabilitation for treatment of poststroke dysphagia during the chronic stage.

Although swallowing function is considered to be under the control of both cerebral hemispheres, there are also reports of hemispheric dominance [16]. However, clinical identification of the dominant hemisphere is frequently difficult. Our bilateral stimulation method has the advantage of high generalization because it can be implemented without regard to dominance, unlike most other rTMS methods (table 1).

In the present study, the combination of bilateral cerebral rTMS and intensive swallowing rehabilitation resulted in improvement of swallowing function. It is hypothesized that rTMS induces plasticity and neuromodulation of the motor cortex. In addition, our results

are compatible with those of Khedr and Abo-Elfetoh [9], who also applied bilateral high-frequency stimulation of the cerebral motor areas in patients with acute poststroke dysphagia and reported improvement in swallowing function.

Improvements of the swallowing reflex were seen in all patients in the present study. Verin and Leroi [6] also reported improvement in the swallowing reflex delay time after rTMS, although they used low-frequency stimulation of the unaffected hemisphere. We did not measure pharyngeal constrictor muscle activity or swallowing pressure in the present study.

Since our method does not require the direct use of food, the intervention is safe for patients who have difficulties with direct oral intake, compared with traditional rehabilitation. Although this study did not examine these outcomes adequately, the results suggest that the combination treatment seems to improve pharyngeal constrictor muscle function, prevent aspiration pneumonia by decreasing nocturnal saliva aspiration, improve tongue pressure and mastication coordination, and reduce gastroesophageal reflux.

The present study has certain limitations. First, it was a case series lacking a control group, highlighting the need for future comparative studies. Second, the subtype of stroke, the lesion size, and the degree of dysphagia in the subjects were heterogeneous. It is desirable to perform the analysis after statistical corrections for these clinical factors. Third, the period between the onset of stroke and treatment varied among the subjects. By clarifying what kind of pathophysiology our therapy is most effective against, we can begin to discuss more appropriate rehabilitation programs.

Conclusion

The combination therapy of bilateral cerebral rTMS and intensive swallowing rehabilitation was safely completed in 4 patients with chronic poststroke dysphagia. The therapeutic protocol resulted in improvement of swallowing function in all patients, suggesting that our method is feasible and safe for chronic stroke dysphagia.

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Disclosure Statement

The authors have no conflicts of interest to disclose.

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Table 1. Clinical studies utilizing rTMS for dysphagia

Author	Patients	Days from onset	Stimulation target	Stimulation modality
Khedr et al. [4]	Acute stroke 14 active, 12 sham	5~10 days	Affected hemisphere	3 Hz 120% rMT
Verin and Leroi [6]	7 chronic stroke	11~132 months	Healthy hemisphere	1 Hz 120% rMT
Khedr and Abo-Elfetoh [9]	22 medulla oblongata or brain stem infarction	~3 months	Bilateral hemisphere	3 Hz 130% rMT
Kim et al. [7]	2 brain injury 28 stroke	~3 months	Healthy or affected hemisphere	1 or 5 Hz 100% rMT
Park et al. [5]	18 stroke	~3 months	Healthy hemisphere	5 Hz 90% rMT

Table 2. Clinical characteristics of the subjects

	Patient 1	Patient 2	Patient 3	Patient 4
Age at treatment, years	80	68	61	56
Sex	female	male	male	female
Time between onset and treatment, months	24	25	31	37
Type of stroke and lesion	both cerebri	both cerebri	both cerebri	both cerebri
National Institute of Health Stroke Scale	5	5	4	5
FOIS	5	6	5	6
Functional independence measure	92	90	93	96

Table 3. Change in clinical measures of swallowing function

	Patient 1		Patient 2		Patient 3		Patient 4	
	before	after	before	after	before	after	before	after
MMASA	87	90	82	88	78	82	73	69
PAS	4	1	3	2	5	2	3	3
LED _T , s	0.12	0.08	0.24	0.2	0.32	0.16	0.36	0.12
RSST	1	2	2	2	2	3	0	0
FOIS	5	6	6	6	5	5	6	6

	1 st day	2 nd day	3 rd day	4 th day	5 th day	6 th day
AM	Admission	3Hz rTMS(10 min)				
		Swallowing Exercise (20 min)				
PM	3Hz rTMS(10 min)					Discharge
	Swallowing Exercise(20 min)					

Fig. 1. Treatment protocol. rTMS was performed twice daily, followed by swallowing exercise in the last 6 days.

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Fig. 2. rTMS protocol. A figure-of-eight coil was positioned over the cortical area where stimulation produced the maximum MEP in pharyngeal muscles. Both hemispheres were stimulated.