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ORIGINAL REPORT

NEURONAVIGATED HIGH-FREQUENCY REPETITIVE TRANSCRANIAL MAGNETIC STIMULATION FOR CHRONIC POST-STROKE DYSPHAGIA: A RANDOMIZED CONTROLLED STUDY

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Objective: **There are potential benefits of repetitive transcranial magnetic stimulation (rTMS) in improving swallowing functions after stroke; however, few studies have been performed in the chronic stroke population. This study aims to distil the key effects of rTMS on swallowing functions and swallowing-related quality of life.**
Methods: **Twenty-two participants with chronic post-stroke dysphagia were randomly assigned into active or sham rTMS groups. Seven participants withdrew from the study, thus data from 15 participants (mean age 64.6 years) were analysed. Participants received 3,000 pulses of 5 Hz rTMS (active: $n=11$; sham: $n=4$) on the tongue area of the motor cortex for 10 days over a period of 2 weeks. All participants were assessed 1 week before, and 2 months, 6 months and 12 months after stimulation. Outcomes were measured by a videofluoroscopic swallowing study, swallowing-related quality-of-life questionnaire and Iowa Oral Performance Instrument.**
Results: **No statistically significant effects were identified for any outcome measures.**
Conclusion: **This study indicates that 5 Hz rTMS applied over the tongue area of the motor cortex is not effective for improving swallowing function in individuals with chronic post-stroke dysphagia. Possible explanations for these non-significant results are dis cussed. Future studies should explore the potential of the current protocol in conjunction with conventional dysphagia therapy.**

Key words: neurorehabilitation; dysphagia; repetitive transcranial magnetic stimulation; stroke.

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Repetitive transcranial magnetic stimulation (rTMS) is a rapidly emerging neurorehabilitation technique. Studies have shown that rTMS can improve limb motor functions (1–3), language functions (4, 5), and swallowing functions (6–12) after stroke. In this study, the effects of rTMS on the swallowing functions of individuals with chronic post-stroke dysphagia were investigated. Dysphagia is a common complication after stroke, the prevalence of which ranges from 41% to 78% (13–17). The quality of life of individuals with dysphagia is often hampered by discomfort and anxiety during eating, and by the need for special mealtime arrangements, which may hinder social interaction during mealtimes (18). Treatments that aim to restore or improve swallowing functions after stroke; for example, exercises for the swallowing muscles (19), are commonly used in clinical settings. However, these treatments require the active participation of patients and, as such, the efficacy of treatment depends largely on patient compliance. Individuals with cognitive impairments may find it difficult to follow the instructions.

rTMS has been proposed as an alternative post-stroke dysphagia treatment. It is a non-invasive technique that modulates brain activity, and thereby induces physiological changes, using electromagnetic induction. An advantage of rTMS is that the patients do not need to be actively engaged during treatment, thus overcoming issues of patient compliance and the ability to understand instructions. Studies have shown that both high- (3 Hz and 5 Hz) and low- (1 Hz) frequency rTMS can improve swallowing functions of acute, subacute and chronic stroke patients (6–9, 11, 12). A previous study conducted by our team found preliminary evidence for using 10 sessions of 5 Hz rTMS applied to the tongue area of the motor cortex as a treatment for chronic post-stroke dysphagia (6). Although these studies showed therapeutic potential of rTMS in post-stroke dysphagia, stronger evidence is still needed to confirm its efficacy, especially for those with chronic (>1 year) dysphagia.

The current study aimed to investigate the short- (2 months) and long-term (6 and 12 months) effects of 5 Hz rTMS on chronic post-stroke dysphagia. The stimulation target was determined based on 2 factors. Firstly, the tongue is important in transportation of food boluses during the oral phase of swallowing, and studies have shown that swallowing functions of post-stroke dysphagic individuals can be improved by improving tongue functions (20–22). Moreover, the affected hemisphere was stimulated based on the evidence that high-frequency rTMS (>1 Hz) applied over the stroke hemisphere could increase cortical ex-

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citability and improve swallowing functions in stroke patients (7, 8). Therefore, the current study hypothesized that by stimulating the tongue area of the motor cortex of the affected hemisphere using 5 Hz rTMS, tongue motor functions could be improved, and hence swallowing functions and swallowing-related quality of life may also be improved.

METHODS

This was a double-blinded, randomized controlled study. The participants and assessors were not aware of group assignment. Data were collected from September 2013 to September 2015. The study was approved by the ethics committee of the Institutional Review Board of the University of Hong Kong/ Hospital Authority Hong Kong West Cluster (reference number: UW 14-193). Signed informed consent was obtained from all participants prior to data collection.

Trial registration

The study was registered with the HKU Clinical Registry (Identifier: HKUCTR-1868).

Participants

Inclusion criteria were: presence of post-stroke dysphagia for at least 12 months; adequate cognitive ability to follow simple instructions; aged below 80 years; and able to sit upright for at least 30 min. Exclusion criteria included: previous history and/or family history of epilepsy; history of head injury or neurological disease other than stroke; neurosurgery; oral and maxillofacial surgery; dysphagia prior to stroke; presence of magnetic implants inside the body; and medically unstable and on medications that lower the neural threshold (23). All participants were randomly assigned to the active rTMS group or the sham rTMS group using a randomly-generated sequence. Each participant underwent magnetic resonance imaging (MRI) of the brain before stimulation. The site of brain lesions was confirmed by a radiologist (author WCS) (Table I).

Obtaining resting motor threshold

Before the first rTMS session, the resting motor threshold (RMT) of each participant was obtained to determine the stimulation intensity. The motor evoked potentials (MEPs) of the tongue were recorded using 2 silver/silver chloride electrodes mounted on a mouthpiece, which were connected to the built-in of the Brainsight^{TM} neuronavigation system (Rogue Research Inc., Montreal, Canada). The electrodes were placed on the surface of the tongue contralateral to the stimulation side. Single TMS pulses were delivered onto the tongue area of motor cortex to elicit MEPs from the tongue. The RMT was defined as the minimum stimulus intensity required to elicit 5 responses of 50 µV or above in 10 consecutive trials (50% successful MEPs) (23). Once the stimulation site was identified, the site was marked onto the participant's MRI scan using the neuronavigation system.

Repetitive transcranial magnetic stimulation (rTMS)

The experimental group received 30 100-pulse trains of 5 Hz rTMS, with inter-train interval of 15 s, per day for 10 days over 2 weeks.

Biphasic rTMS pulses were delivered through a 70-mm Double Air Film coil (Magstim®, Whitland, UK) attached to a Magstim Rapid^2 (Magstim®). rTMS was applied at 90% RMT over the tongue area of the motor cortex of the affected hemisphere, as identified and retrieved from the previous MEP session using the neuronavigation system (Table I). For participants with bilateral lesion, the left hemisphere was stimulated due to left hemispheric dominance for swallowing (24). The sham group received sham rTMS via a 70-mm Double Air Film sham coil (Magstim®), which had an identical appearance and noise as the real coil, but does not deliver active stimulation of deep nerves. The stimulation schedules were identical for both groups.

Outcome measurements

All participants were assessed at 4 time-points: 1 week before stimulation, 2, 6 and 12 months after stimulation. The evaluation of outcomes was performed using: (*i*) videofluroscopic swallowing study (VFSS); (*ii*) a swallowing-related quality of life

Table I. Participants' demographics and repetitive transcranial magnetic stimulation (rTMS) intensity

Group assignment	Participant ID	Sex	Site of lesion	Age (years)	Time post-stroke (months)	Stimulation intensity (% of maximum stimulator output)
Active	1	M	Left temporal	66	69	66
	2	M	Right pons	74	75	59
	3	F	Bilateral periventricular white matter	66	20	54
	4	F	Left corona radiata	56	56	41
	5	M	Bilateral periventricular white matter	65	42	63
	6	F	Right basal ganglia	75	22	50
	7	M	Left parietal	53	41	54
	8	F	Right thalamus	69	19	57
	9	M	Left pons	51	24	75
	10	M	Bilateral periventricular white matter	69	42	45
	11	M	Brainstem and left cerebellar	72	56	72
			Mean (SD)	65.1 (8.3)	42.4 (19.9)	
Sham	12	M	Bilateral basal ganglia	70	77	68
	13	M	Bilateral subcortical white matter	65	35	59
	14	M	Right occipital	66	25	63
	15	M	Right parietal	52	22	60
			Mean (SD)	63.3 (7.8)	39.8 25.4)	

SD: standard deviation; M: male; F: female.

questionnaire; and (*iii*) maximum tongue strength measurement at each assessment time.

Videofluroscopic swallowing study (VFSS). Participants were asked to swallow 3 trials of 5 ml of each of the following: thin, mildly-thick and extremely-thick fluid. The barium sulphate (8.7% w/v, E-Z-Paque®, E-Z-EM, New York, USA) liquid was first prepared and then thickened to different consistencies using thickener (ThickenUp®, Nestle, Lutry, Switzerland). The swallowing process was recorded and then quantitatively analysed in terms of: (*i*) oral transit time; (*ii*) stage transit time; (*iii*) pharyngeal transit time; (*iv*) amount of post-swallow residue in valleculae (normalized residue ratio scale; NRRSv); and (*v*) in piriform sinus (NRRSps); and (*vi*) pharyngeal constriction ratio. The VFSS was digitally recorded at a frame-rate of 30 frames/s.

The software program ImageJ (National Institute of Health) was used to perform frame-by-frame analysis and spatial measurements on VFSS videos. All measures were obtained from lateral views. Appendix I shows the definitions of the VFSS measures.

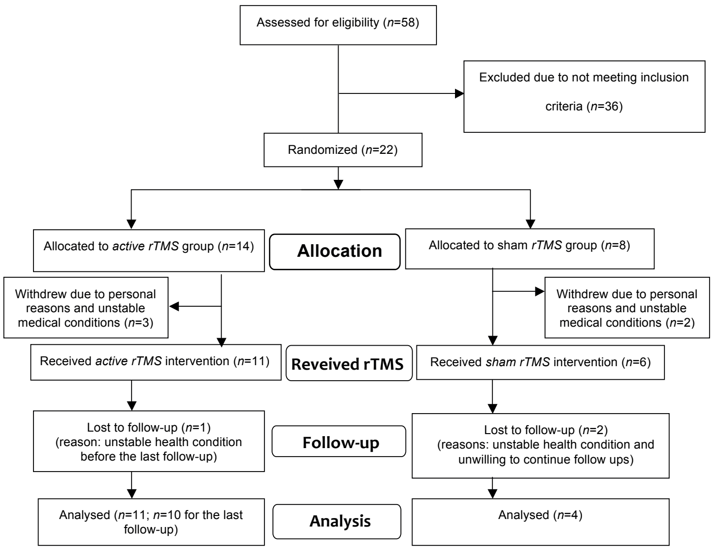

Fig. 1. Flow of participants in the study according to the Consolidated Standards of Reporting Trials (CONSORT) statement. rTMS; repetitive transcranial magnetic stimulation.

Swallowing-related quality of life questionnaire. The Swallowing Activity and Participation Profile (SAPP) was used to evaluate the swallowing-related quality of life of the participants. The SAPP was developed under the International Classification of Functioning, Disability and Health (ICF; World Health Organization) framework (25), consisting of 38 items grouped into swallowing impairment, personal, social and emotional subscales. The higher the SAPP total scores, the poorer the swallowing-related quality of life.

Maximum tongue strength. The maximum tongue strength of each participant was measured using the Iowa Oral Performance Instrument (IOPI; IOPI Medical LLC, Washington, USA). Participants were asked to use the tongue to press the air-filled IOPI tongue bulb against the hard palate 3 times using maximal strength. The maximum tongue pressure among the 3 trials was recorded as the maximum tongue strength.

Statistical analysis

The oral transit time, stage transit time, pharyngeal transit time and pharyngeal constriction ratio for all consistencies, and NRRSv and NRRSps for extremely-thick fluid, the total SAPP scores and maximum tongue strength were analysed using general linear mixed model (GLMM) to compare the between-group and across-time differences. The GLMM was used because it was designed to account for a wide variability of data, which is common in experimental, longitudinal studies and can accommodate for missing and unbalanced data (26).

RESULTS

Fig. 1 shows the flow diagram for participant recruitment. Participants were openly recruited from the public and through a rehabilitation hospital. Fifty-eight individuals were screened face-to-face and/or via phone interview for eligibility for the study. Twenty-two subjects met the inclusion and exclusion criteria and joined the study. They were randomly allocated into active or sham groups. Five of participants in the sham group withdrew before rTMS sessions for personal reasons and unstable medical conditions. Upon completion of the 10 rTMS sessions, 2 participants in the sham group did not return after the first follow-up. One participant in the active group did not return for the 12 months post-rTMS follow-up assessment. A final total of 14 participants completed all follow-ups. In the current study, the data from15 participants (11 males, 4 females; mean age 64.5 years), including the one who did not return for the final follow-up, were analysed. Table I shows the demographic information for the participants.

All participants received 10 sessions of rTMS (active or sham) with no reports of discomfort. There was no significant difference between the groups in age ($p=0.706$) or post-stroke duration ($p=0.861$).

Videofluoroscopic swallowing study (VFSS)

The VFSS videos were analysed by a speech therapist (author CKYI) blinded to the group assignment. Since 53% of the participants in the current study showed pharyngeal residue after swallowing extremely-thick fluid, but not the other consistencies, the analysis of such residue focused only on extremely-thick fluid consistency. Lower NRRSv and NRRSps values indicated less pharyngeal residue. A lower pharyngeal constriction ratio indicated a larger maximum pharyngeal constriction.

Tables II–VII present the results of VFSS measures. Significant main effects for time were found in: (*i*) oral transit time for mildly-thick and extremely-thick fluid; (*ii*) stage transit time; (*iii*) pharyngeal transit time for all consistencies; and (*iv*) NRRSps for extremely-thick

Table II. Descriptive statistics for videofluroscopic swallowing study (VFSS) measures for thin liquid

VFSS measures	Group	Baseline Mean (SD)	2 months follow-up Mean (SD)	6 months follow-up Mean (SD)	12 months follow-up Mean (SD)
Oral transit time, s	Active	0.97 (0.33)	0.98 (0.16)	1.37 (0.26)	1.37 (0.34)
	Sham	0.54 (0.29)	1.46 (0.68)	0.59 (0.17)	0.90 (0.19)
Stage transit time, s	Active	0.65 (0.12)	0.99 (0.16)	1.05 (0.27)	1.48 (0.32)
	Sham	0.43 (0.11)	1.09 (0.38)	1.18 (0.45)	1.02 (0.17)
Pharyngeal transit time, s	Active	1.04 (0.19)	1.32 (0.18)	1.39 (0.32)	1.90 (0.36)
	Sham	0.63 (0.14)	1.38 (0.38)	1.57 (0.51)	1.35 (0.23)
Pharyngeal constriction ratio	Active	0.04 (0.01)	0.03 (0.01)	0.02 (0.00)	0.03 (0.01)
	Sham	0.02 (0.01)	0.02 (0.00)	0.01 (0.00)	0.01 (0.00)

SD: standard deviation.

fluid. All of the above-mentioned timing measures increased after rTMS, whereas NRRSps decreased after rTMS. However, no significant main effects for group or interaction effects between group and time were found for all measures.

Swallowing Activity and Participation Profile (SAPP)

The total SAPP scores of both groups were calculated (Table VIII). No significant main effects or interaction effects for groups and time were found for the total SAPP scores.

Maximum tongue strength

No significant main effects or interaction effects for groups and time were found for the maximum tongue pressure (Table IX).

Table III. General Linear Mixed Model results of the videofluroscopic swallowing study (VFSS) measures for thin liquid

VFSS measures	Significance level for time	Significance level for groups
Oral transit time, s	$F(3, 11.7)=1.610$ $p=0.240$	$F(1, 13.0)=0.253$ $p=0.532$
Stage transit time, s	$F(3, 8.8)=8.134$ $^*p=0.007$	$F(1, 12.0)=0.539$ $p=0.477$
Pharyngeal transit time, s	$F(3, 8.4)=6.425$ $^*p=0.014$	$F(1, 12.2)=0.756$ $p=0.401$
Pharyngeal constriction ratio	$F(3, 12.7)=0.666$ $p=0.588$	$F(1, 12.5)=3.813$ $p=0.074$

$^*p<0.05$.

Table IV. Descriptive statistics for videofluoroscopic swallowing study (VFSS) measures for mildly-thick fluid

VFSS measures	Group	Baseline Mean (SD)	2 months follow-up Mean (SD)	6 months follow-up Mean (SD)	12 months follow-up Mean (SD)
Oral transit time, s	Active	0.77(0.17)	1.14 (0.13)	1.82 (0.40)	1.89 (0.41)
	Sham	0.69 (0.19)	1.64 (0.57)	1.20 (0.42)	0.99 (0.30)
Stage transit time, s	Active	1.07 (0.29)	1.28 (0.24)	1.78 (0.55)	1.84 (0.58)
	Sham	1.07 (0.50)	2.09 (0.83)	1.81 (0.80)	1.51 (0.71)
Pharyngeal transit time, s	Active	1.38 (0.30)	1.65 (0.27)	2.15 (0.57)	2.31 (0.60)
	Sham	1.33 (0.52)	2.59 (0.90)	2.14 (0.89)	1.90 (0.72)
Pharyngeal constriction ratio	Active	0.05 (0.01)	0.08 (0.03)	0.04 (0.00)	0.04 (0.01)
	Sham	0.04 (0.02)	0.05 (0.01)	0.02 (0.00)	0.02 (0.00)

SD: standard deviation.

Table V. Generalized Linear Mixed Model results of the videofluoroscopic swallowing study (VFSS) measures for mildly-thick fluid

VFSS measures	Significance level for time	Significance level for groups
Oral transit time, s	$F(3, 12.7)=7.710$ $^*p=0.003$	$F(1,13.0)=0.720$ $p=0.411$
Stage transit time, s	$F(3, 12.8)=3.720$ $^*p=0.040$	$F(1, 13.0)=0.007$ $p=0.933$
Pharyngeal transit time, s	$F(3, 12.8)=5.009$ $^*p=0.016$	$F(1, 13.0)=0.002$ $p=0.890$
Pharyngeal constriction ratio	$F(3, 12.4)=1.562$ $p=0.248$	$F(1, 12.9)=1.279$ $p=0.279$

$^*p<0.05$.

DISCUSSION

This study found no significant treatment effects of 5 Hz rTMS on swallowing function, tongue strength or swallowing-related quality of life in patients with chronic post-stroke dysphagia. All participants completed the entire rTMS protocol with no reports of discomfort or adverse reactions, suggesting that 10 days of 5 Hz rTMS applied over 2 weeks is safe and tolerable.

Table VI. Descriptive statistics for videofluoroscopic swallowing study (VFSS) measures for extremely-thick fluid

VFSS measures	Group	Baseline Mean (SD)	2 months follow-up Mean (SD)	6 months follow-up Mean (SD)	12 months follow-up Mean (SD)
Oral transit time, s	Active	1.01 (0.45)	1.49 (0.79)	1.95 (1.37)	2.18 (1.49)
	Sham	0.85 (0.29)	2.08 (1.02)	2.77 (2.29)	1.64 (0.83)
Stage transit time, s	Active	1.21 (1.29)	3.11 (2.99)	2.71 (3.61)	2.35 (1.39)
	Sham	1.27 (1.13)	3.12 (2.97)	1.92 (1.59)	2.34 (1.28)
Pharyngeal transit time, s	Active	1.58 (1.38)	2.88 (2.54)	3.13 (3.73)	2.84 (1.52)
	Sham	1.64 (1.14)	3.62 (3.16)	2.31 (1.70)	2.71 (1.29)
+NRRSv	Active	0.19 (0.42)	0.15 (0.27)	0.03 (0.09)	0.13 (0.27)
	Sham	0.08 (0.11)	0.16 (0.17)	0.08 (0.12)	0.08 (0.14)
+NRRSps	Active	0.21 (0.46)	0.07 (0.12)	0.04 (0.09)	0.11 (0.25)
	Sham	0.01 (0.01)	0.03 (0.02)	0.01 (0.01)	0.01 (0.02)
Pharyngeal constriction ratio	Active	0.06 (0.05)	0.05 (0.04)	0.04 (0.02)	0.05 (0.04)
	Sham	0.03 (0.02)	0.04 (0.01)	0.02 (0.01)	0.03 (0.01)

+NRRSv: normalized residue ratio scale for valleculae residue; NRRSps: normalized residue ratio scale for piriform sinus residue; SD: standard deviation.

Table VII. Generalized Linear Mixed Model results of the videofluoroscopic swallowing study (VFSS) measures for extremely-thick fluid

VFSS measures	Significance level for time	Significance level for groups
Oral transit time, s	$F(3, 12.6)=6.01$ $^*p=0.009$	$F(1, 13.1)=1.149$ $p=0.706$
Stage transit time, s	$F(3, 12.9)=7.261$ $^*p=0.004$	$F(1, 13.0)=0.025$ $p=0.877$
Pharyngeal transit time, s	$F(3, 12.8)=8.758$ $^*p=0.002$	$F(1, 13.0)=0.000$ $p=0.984$
+NRRSv	$F(3, 13.0)=1.226$ $p=0.340$	$F(1, 13.0)=0.034$ $p=0.856$
+NRRSps	$F(3, 13.0)=3.427$ $p=0.049$	$F(1, 13.0)=0.900$ $p=0.360$
Pharyngeal constriction ratio	$F(3, 12.9)=1.333$ $p=0.307$	$F(1, 13.0)=0.804$ $p=0.386$

$^*p<0.05$.
+NRRSv: normalized residue ratio scale for valleculae residue; NRRSps: normalized residue ratio scale for piriform sinus residue; SD: standard deviation.

Table VIII. Descriptive statistics and Generalized Linear Mixed Model results in total Swallowing Activity and Participation Profile scores

	Baseline Mean (SD)	2 months follow-up Mean (SD)	6 months follow-up Mean (SD)	12 months follow-up Mean (SD)	Significance level for time	Significance level for groups
Active	111.1 (61.9)	83.1 (52.4)	80.2 (51.1)	74.1 (47.3)	F(3, 13) = 0.813	F(1, 13) = 1.397
Sham	57.8 (24.2)	51.0 (32.6)	56.3 (44.2)	65.3 (39.6)	*p = 0.509	p = 0.258

SD: standard deviation.

Table IX. Descriptive statistics and Generalized Linear Mixed Model results of maximum tongue pressure (kPa)

	Baseline Mean (SD)	2 months follow-up Mean (SD)	6 months follow-up Mean (SD)	12 months follow-up Mean (SD)	Significance level for time	Significance level for groups
Active	32.0 (17.4)	32.1 (14.9)	28.9 (15.2)	34.1 (14.6)	F(3, 9.3) = 0.419	F(1, 13) = 0.595
Sham	34.0 (19.3)	41.3 (27.3)	42.0 (24.6)	37.5 (19.9)	p = 0.744	p = 0.455

SD: standard deviation.

There are several possible explanations for these negative results. First, the stimulation protocol may not be optimized for increasing cortical excitability and inducing improvement in swallowing function of the participants. A recent systematic review by Pisegna et al. (27) suggested that non-invasive stimulation of the unaffected hemisphere may be more effective in improving swallowing functions after stroke. Further investigations on the changes in cortical excitability of tongue motor cortex after rTMS may provide insights into the optimization of stimulation protocol.

Secondly, the VFSS protocol, which used a bolus volume of 5 ml for all swallowing trials, may not be sensitive enough to detect the breakdown level of the patients. Dantas et al. found that larger bolus volume requires adaptation of swallowing structure movements, which might be more difficult for some patients (28).

The third explanation relates to patient selection. Since most of the participants have mild to moderate dysphagia, the room for extensive improvements may be small. The effects of the current rTMS protocol on individuals with more severe dysphagia are unknown.

Finally, the current protocol failed to increase tongue strength, suggesting that cortical stimulation alone may not be sufficient. Pairing rTMS with tongue or swallowing exercises may bring about more significant improvements. A study by Koganemaru et al. (29) suggested that improvement in grip strength may be best achieved with a combination of rTMS and use-dependent exercises in the chronic stroke population. Moreover, Dejaeger et al. (30) suggested that the degree of tongue-driving force affects clearance of pharyngeal residue. Through improving tongue strength, the clearance of pharyngeal residue after swallow may be more efficient.

The current study is limited by a small sample and unbalanced group sizes. Individual variations in swallowing functions may have masked any changes subsequent to rTMS. Future studies may adopt a block randomization process in order to balance group sizes. The recruitment of participants was of great challenge because most patients with chronic post-stroke dysphagia have other comorbidities; for example, dementia, history of epilepsy, bed-bound or unstable health condition, which may be counter-indicators for rTMS studies.

In conclusion, the current study indicated that 5 Hz rTMS applied over the tongue area of the motor cortex for 10 days was not effective in improving swallowing function in patients with chronic post-stroke dysphagia. However, given the limitations of the small and unbalanced group sizes in this study, the therapeutic effects of the current protocol remain uncertain. Future studies are needed that include patients with more severe dysphagia and balanced group sizes to study the effects of the current protocol in conjunction with swallowing exercises.

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Appendix I. Definitions of videofluoroscopic swallowing study measures

Duration measures

The definitions of the duration measures used in the current study were adapted from the Oropharyngeal Swallow Efficiency (31, 32):

1. Oral transit time is defined as the duration (in s) between the onset of bolus movement in the oral cavity and the arrival of the bolus head at the junction of the lower rim of the mandible and the tongue base.
2. Stage transit time is defined as the duration (in s) between the arrival of the bolus head at the junction of the lower rim of the mandible and the tongue base and the first laryngeal elevation.
3. Pharyngeal transit time is defined as the duration (in s) between the first laryngeal elevation and the restoration of upper oesophageal sphincter constriction after passage of bolus through the cricopharyngeal area.

Pharyngeal constriction ratio

The pharyngeal area at the hold position (PA_{hold}), where the bolus was held in the oral cavity before backward propulsion, and the pharyngeal area at maximum constriction position (PA_{max}) were measured as described in the study by Leonard and colleagues (33, 34) and recorded in cm^2. The pharyngeal constriction ratio is defined as PA_{max}/PA_{hold}.

Amount of post-swallow residue in valleculae and piriform sinus

The areas of the valleculae and piriform sinus and the residue in these 2 areas after the first swallow were measured. The normalized residue ratio scale (NRRS) (35) was calculated for vallecular (NRRSv) and piriform sinus (NRRSps) residue to estimate the amount of post-swallow residue. The NRRS is a recently developed pixel-based measurement that aims to provide a more objective and quantifiable judgment on the amount of pharyngeal residue (35, 36).