Wang et al. BMC Geriatrics (2025) 25:8
https://doi.org/10.1186/s12877-024-05625-7

BMC Geriatrics

RESEARCH

Open Access

Effects of intermittent theta burst stimulation on cognitive and swallowing function in patients with MCI and dysphagia risk: a randomized controlled trial

Jie Wang[1,3], Mengqing Zhang[2], Xiaomei Wei[3], Cheng Yang[4], Meng Dai[3], Zulin Dou[3*] and Yonghui Wang[1*]

Abstract

Background Mild cognitive impairment (MCI) is a high-risk factor for dementia and dysphagia; therefore, early intervention is vital. The effectiveness of intermittent theta burst stimulation (iTBS) targeting the right dorsal lateral prefrontal cortex (rDLPFC) remains unclear.

Methods Thirty-six participants with MCI were randomly allocated to receive real ($n = 18$) or sham ($n = 18$) iTBS. Global cognitive function was assessed using the Montreal Cognitive Assessment (MoCA), and executive function was evaluated with the Trail Making Test (TMT), Digital span test (DST) and Stroop color word test (SCWT). Quantitative swallowing measurements were obtained using temporal and kinetic parameters based on the videofluoroscopic swallowing study (VFSS). Resting-state functional magnetic imaging (fMRI) was performed to observe brain plasticity, functional connectivity (FC) values were calculated. All assessments were completed at baseline and two weeks after treatment. Participants received 10 sessions of daily robotic navigated iTBS.

Results The MoCA score and the SCWT duration of the real group improved significantly compared with that of the sham group. Temporal parameters of VFSS included 5-ml oral transit time (OTT), 5-ml soft palate elevation time (SET) and 10-ml OTT showed a decreasing trend. However, there was significant improvement in 10-ml OTT when choosing patients with OTT exceeding 1000 ms. FC value between the left middle frontal gyrus and the rDLPFC increased significantly in real stimulation group ($p < 0.05$ with false discovery rate corrected). We found that baseline FC scores were negatively correlated with the SCWT task duration ($r = -0.554$, $p = 0.017$) and with the 10-ml OTT (rho = -0.442, $p = 0.027$) across all participants. Among those in the iTBS group with a pre-10-ml OTT greater than 1000 ms, we observed a positive correlation between changes in MoCA scores and changes in FC values ($r = 0.789$, $p = 0.035$). Furthermore, changes in MoCA scores were positively correlated with changes in 10-ml OTT ($r = 0.648$, $p = 0.031$), as determined by Pearson analysis.

Conclusions Navigated iTBS over the rDLPFC has the potential to improve global cognition, response inhibition ability, and certain aspects of swallowing function for patients with MCI at high risk for dysphagia. Changes in FC

*Correspondence:
Zulin Dou
douzul@163.com
Yonghui Wang
yonghuiwangphd@163.com
Full list of author information is available at the end of the article

between right and left DLPFC may underlie the neural mechanisms responsible for the effectiveness of iTBS targeting the right DLPFC.

Keywords Dorsal lateral prefrontal cortex, Mild cognitive impairment, Swallowing function, Intermittent theta burst stimulation

Background

Mild cognitive impairment (MCI) is defined as a state between the normal decline in cognitive function that occurs with aging and dementia. Early intervention from the time of MCI onset or before is necessary to prevent dementia as more than half of older people with MCI will go on to develop dementia [1]. We observed that swallowing function deterioration was associated with the cognitive impairment in older adults with MCI through videofluoroscopic swallowing study (VFSS) and functional magnetic resonance imaging (fMRI) in our previous work [2]. Moreover, the swallowing function tends to become worse with a decline of cognition [3]. Additionally, poor nutritional status, a common complication of swallowing disorders, was reported to be associated with the clinical progression of cognitive impairment [4]. Non-invasive brain stimulation (NIBS) may alleviate the progression of cognitive impairment and has emerged as a promising treatment for patients with MCI.

The NIBS technique repetitive transcranial magnetic stimulation (rTMS) is being increasingly utilized in a number of researches and clinical applications. Prior studies have shown that various paradigms of rTMS have increasingly been investigated in enhancing cognitive function [5]. Furthermore, theta burst stimulation (TBS) is a high-frequency neuromodulation technique typically delivered in bursts of three pulses at 50 Hz, repeated every 200 ms [6]. There are two main TBS protocols: intermittent TBS (iTBS) and continuous TBS (cTBS). The former consists of 2-s trains of stimuli delivered at 8-s intervals over 190 s, while cTBS involves 40-s continuous trains without intervals, with a total of 600 pulses in both protocols. These short and powerful protocols modulate cortical excitability, with iTBS enhancing excitability and cTBS leading to inhibition [7–9]. A review highlighted that iTBS might be the most effective intervention for enhancing cognitive function and activities of daily living (ADL) compared to both high-frequency and low-frequency rTMS [10]. This approach has gained popularity as a conditioning method for the brain [11]. The theta burst protocol's low stimulus intensity, short stimulation cycle, and proven long-term benefits have made it to become an optimized rTMS pattern [12]. The efficacy of iTBS on cognitive outcomes has been shown to depend on precise targeting of stimulation sites [5]. Using neuronavigation systems significantly improves the accuracy of iTBS application, ensuring better alignment with intended target locations.

It has been shown that iTBS can induce relatively robust and consistent improvements in the performance of cognition in domains such as memory and executive function [13]. Notably, executive function has a meaningful influence on swallowing function [14]. The right prefrontal lobe is known to play a crucial role in executive function [15, 16]. Moreover, the right dorsal lateral prefrontal cortex (DLPFC) is founded to be co-activated during swallowing and cognitive tasks using fMRI [17]. Given these connections, the aim of this study is to explore the effectiveness of iTBS on cognitive and swallowing functions in patients with MCI who are at high risk of dysphagia. The right DLPFC was chosen as the stimulation target. To ensure precise targeting, a robotic navigation system was used. We performed a single-center, randomized, pseudo-controlled trial, blinded to both participants and assessors, to explore the effects of iTBS over the right DLPFC in this patient population. And general cognitive function, executive function and quantitative swallowing measurements were used to evaluate the treatment efficiency. Additionally, we also aim to explore the brain plasticity mode related to the iTBS effectiveness with resting state fMRI, which is widely used in brain functional imaging for swallowing networks[18, 19].

Materials and methods

Study design

This prospective, single-center, randomized, double-blind, pseudo-controlled pilot trial adhered to the Code of Ethics of the World Medical Association (Declaration of Helsinki) and was approved by the Medical Ethics Committee of the Third Affiliated Hospital of Sun Yat-sen University ([2018] 02–374-01). Most participants were recruited from the Memorial Clinic, and written informed consent was obtained from participants or their families. This experiment is part of a broader study registered in the Chinese Clinical Trial registry (ChiCTR1900021795).

Participants enrolled in our study were randomly assigned to either the iTBS group or the sham control group. Each of them underwent cognitive function measurements, including the Montreal Cognitive Assessment (MoCA), Trail Making Test (TMT), Digital span test (DST) and Stroop color word test (SCWT). VFSS and subsequent quantitative analysis were performed for each participant. Additionally, resting-state fMRI was conducted to explore changes in brain Functional connectivity (FC) at baseline. Cognitive assessments and fMRI analysis were performed by the two authors who were unaware of the grouping before treatment began. To understand the lasting effect of iTBS, we reassessed cognitive and swallowing function measurements and fMRI 2 weeks after the end of the last session of iTBS. None of the subjects and the assessors were aware of the grouping, and the physiological effects of treatments were isolated from various psychological sources of bias.

Participants

The participants with MCI were screened by a specialist at the Memorial clinic. Each participant, along with their informants, underwent an individualized interview conducted by the specialist, lasting approximately 40–60 min. The interview provided a comprehensive assessment of the participants' ADL, the progression of cognitive impairment, and mood status, with particular attention to anxiety and depression. The inclusion criteria for participants in this study were as follows (1) memory complaints reported by the participant or their family members, (2) normal ADLs, as determined by physicians based on the Clinical Dementia Rating (CDR); a CDR score of < 0.5 (or a total score across 6 boxes below 3.5) was considered indicative of preserved ADLs, (3) overall normal cognitive performance, (4) no evidence of dementia, as defined by the Diagnostic and Statistical Manual of Mental Disorders [20]. High risk of dysphagia, diagnosed by meeting at least one of the following criteria: a score of ≥ 3 on the Eating Assessment Tool (EAT-10) or abnormalities detected on a VFSS [21], such as pharyngeal residue and/or delayed swallowing initiation [22, 23]. (5) age ≥ 60 years. (6) right-handedness, based on the Edinburgh handedness inventory [2].

Exclusion criteria included the following: (1) presence of conditions, such as cerebral ischemia, brain hemorrhage, brain-occupying lesions identified via CT or MRI, Parkinson's disease (PD), major depression or other psychological illnesses, a history of seizures, or alcohol or psychotropic substance addiction, which could cause cognitive impairment, (2) presence of disease that could cause swallowing disorders, such as stroke, head and neck cancer, amyotrophic lateral sclerosis (ALS), or myasthenia gravis, etc., (3) with serious medical conditions that rendered participants unsuitable for undergoing rTMS and/or fMRI testing, (4) with relevant contraindications to fMRI scanning and/or rTMS intervention, including the presence of ferromagnetic metals in their body (e.g., heart stents, hearing aids, pacemakers or cranial implants, or claustrophobia).

Sixty participants with MCI were recruited, twelve of whom did not meet the inclusion criteria, seven had fMRI contraindications, three did not complete all baseline evaluations, and two declined to participate. Finally, 36 patients met the inclusion criteria and were included in this study.

Randomization and allocation

This study was a randomized, double-blind, sham-controlled trial conducted in accordance with CONSORT guidelines. Participants diagnosed with MCI were randomly allocated to the real iTBS or sham control groups. Randomization was accomplished with the Microsoft excel function and was performed by an independent investigator who was not involved in iTBS administration, outcome assessment, or data analysis. Investigators performing iTBS were unaware of the randomization until immediately before the first session. A flow diagram describing this study is shown in Fig. 1.

Navigated iTBS procedures

We conducted iTBS with a figure of eight coil (mean 70 mm outer diameter) connected to a CCY-II stimulator (Yiruide Medical Equipment Co., Wuhan, China). An AIM robot (Yiruide Medical Equipment Co., Wuhan, China) was used as the navigation system.

The participants' anatomical 3D-T1 MR images were imported to rebuild a head model aimed to co-registration with their face. The participant was instructed to lie in the treatment bed, and five dots were used to distinguish the face located in bilateral inner corners of the eyes, nose tip, and bilateral margins of the lip. Then, the operator selected the F4 electrode in 10–20 EEG international system as the stimulation target of right DLPFC. This can position the target automatically with the help of the AIM robot and control the stimulation target to be the same for every subsequent treatment. The coil was able to adjust its position if the participant moved their head ≥ 2 cm. For more details, please refer to Fig. 2.

The iTBS protocol was applied as described in [7]. It consisted of 2-s trains of stimulation at a frequency of 5 Hz and repeated every 10 s, each train consisted of three pulses delivered at 50 Hz, for a total duration of 190 s (600 pulses per session). The stimulation intensity was set at 80% of the resting motor threshold (RMT) of the first dorsal interosseus (FDI) muscle. The treatment was immediately discontinued if participants reported any discomfort. Sham stimulation was administered by angling the coil by 60 degrees outward, with only the handle making contact with the head. This configuration ensured that no effective magnetic stimuli reached the

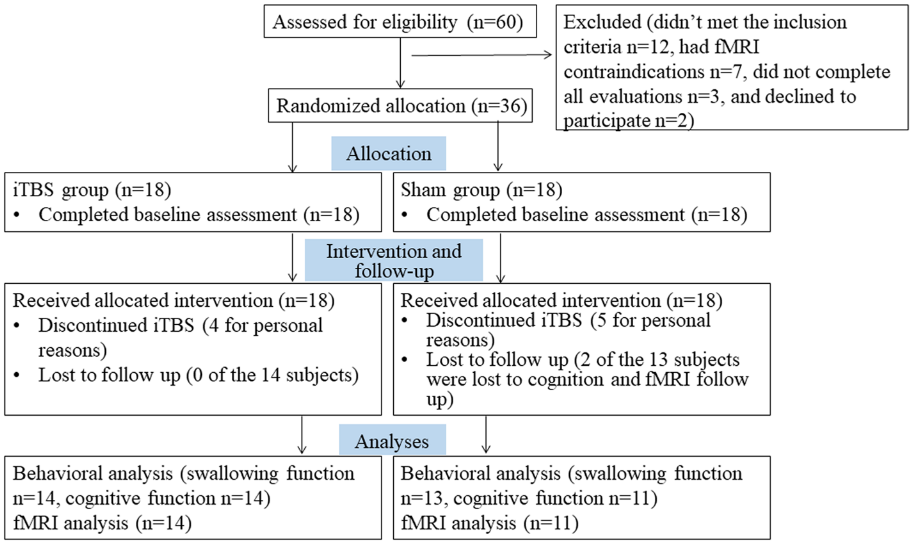

Fig. 1 Flow of recruitment, group allocation, intervention and follow-up, and analyses. iTBS: intermittent theta burst stimulation, fMRI: functional magnetic resonance imaging

Fig. 2 Diagram of navigated iTBS treatment. **A** Overview of the treatment. **B** The T1 MR images were imported to rebuild a head model aimed to co-registration with their face. The coil is located in the right DLPFC

target site, consistent with the methodology in a previous study [24].

At the end of iTBS treatment, participants were asked whether they believed they had received real or sham iTBS. Since none of the participants had prior experience with rTMS, all reported being unsure whether they had received real or sham stimulation.

Evaluation of cognition function

One of the authors completed the MoCA with the subjects and the subsequent executive function examinations. MoCA score was the primary outcome, and the Trail Making Test (TMT), digital span test (DST) and Stroop color word test (SCWT) were the secondary outcomes.

1) MoCA

We assessed global cognitive function using the Chinese Beijing Version of MoCA. This tool evaluates eight cognitive domains: visuospatial and executive function, naming, verbal memory, attention, language, abstraction, 5-min delayed verbal recall, and orientation [25]. To minimize the potential for learning effects, the Chinese Changsha Version of MoCA was applied during the post-treatment retest.

2) TMT

The TMT was employed to evaluate processing speed, complex attention, and visual scanning, adapted from the original version in the Army Individual Test Battery [26]. TMT involved of two parts: Part A and Part B. In Part A, participants were asked to connect 25 numbered circles in ascending order using a continuous line. In Part B, participant performed a similar task but alternated between numbers (1–13) and letters (A-L) in ascending order (e.g., $1 \rightarrow A \rightarrow 2 \rightarrow B$). Participants were instructed to complete both tasks as quickly and accurately as possible. If an error occurred, the assessor stopped the participants, instructed them to return to the last correct response, and provided corrections. Participants were not permitted to preview the test materials before starting the tasks. Each trial was timed independently, and the completion times for Part A and Part B were included in the final statistical analysis.

3) DST

The DST required participants to accurately repeat sequences of digits read aloud by the experimenter at a rate of one digit per second. The test began with sequences of three digits, increasing by one digit at each level. If a participant made an error, they were given a second attempt with a sequence of the same length. The test was stopped when the participants failed to correctly recall both examples of a given sequence length. The core for each participant was the length of the longest sequence they successfully recalled.

4) SCWT

Response inhibition was measured using a computerized version of the SCWT. Participants were presented with four different Chinese words—red, green, blue, and yellow—displayed in either red or blue ink, one word at a time. They were instructed to press the left button when a word appeared in red ink and the right button when it appeared in blue ink, responding as quickly and accurately as possible. The test comprised a total of 24 words. The duration to complete the task in the incongruent color-word condition was recorded and used for statistical analysis.

Swallowing evaluation

Both the temporal parameters and kinetic parameters were secondary outcome.

1) VFSS

The VFSS was performed using a digital radiography (DR) system (Toshiba DBA-300, Tokyo, Japan). Participants were seated on a chair mounted on an electrically adjustable tilt table, and real time lateral VFSS images were captured using a digital image acquisition system (LGT-4000, Guangzhou Longest Science & Technology Co., Ltd., Guangzhou, China). Images were recorded at a frame rate of 30 frames per second with a resolution of 1920×1080 pixels. Participants were instructed to swallow two different bolus volumes (5-mL and 10-mL) three times each. To minimize radiation exposure, the DR system was activated only during the swallowing actions and turned off during bolus preparation. The operator conducting the VFSS was blinded to the participants' group assignments.

2) Quantitative analysis of VFSS data

Quantitative analysis of the VFSS data was performed following the methodology outlined in reference [2]. The analysis process is summarized as follows: Two experienced investigators, each with 2 to 5 years of analytical expertise, conducted the analysis using ImageJ software (National Institutes of Health, Bethesda, MD, USA, https://imagej.nih.gov/ij/). Temporal parameters included oral transit time (OTT) and soft palate elevation time (SET). Kinetic hyoid parameters assessed were hyoid anterior movement (HAM) and hyoid superior movement (HSM). To account for variations in participant height, HAM and HSM were normalized by dividing them by the distance between the second and fourth cervical vertebra before further analysis. Throughout the analysis, the assessors were blinded to the participants' group assignments to ensure unbiased results.

Resting-state fMRI test and analysis

1) fMRI test

FMRI was performed using a Siemens Verio 3.0 T scanner (Siemens, Erlangen, Germany) equipped with an eight-channel coil. Form padding was utilized to minimize head movement, and earplugs were provided to reduce the noise from the scanner. The fMRI data were acquired using an echo-planar imaging (EPI) sequence with the following parameters: repetition time (TR) = 2000 ms, echo time (TE) = 28 ms, flip angle (FA) = 90°, field of view (FOV) = 224 mm × 224 mm, matrix size = 64×64, slice thickness = 3.5 mm, voxel size = 3.5 mm × 3.5 mm × 3.5 mm, and an interleaved scanning pattern with no gap between slices. Thirty-two axial slices were acquired during each TR, resulting in a total of 240 volumes. For anatomical imaging, a MPRAGE T1-weighted sequence was employed with the following parameters: TR = 2300 ms, TE = 3.24 ms, FOV = 256 mm × 256 mm, matrix = 256×256, FA = 70°, slice thickness = 1.0 mm, voxel size = 1 mm × 1 mm × 1 mm. And 176 slices covered the entire brain with continuous sections were obtained.

2) FC calculation

Resting FC is a powerful tool to assess neuropsychiatric disorders in the absence of task conditions, which is assessed based on spontaneous fluctuations in blood-oxygen level dependent signals measured using fMRI [27, 28]. Before FC analysis, preprocess procedure included discarding first 10 scans, slice timing, spatial correction, realignment, normalization to the Montreal Neurological Institute (MNI) template, smoothing with 6 mm full-width at half maximum, and a band filter of 0.01–0.08 Hz. Imaging signals from white matter, cerebrospinal fluid, and head movement were regressed as nuisance covariates. We excluded participants with head displacement ≥ 3 mm in the x-, y-, and z-transactional directions, or ≥ 3° of deflection in pitch, roll, and yaw. We placed a 10-mm spherical region of interest (ROI) centered over the stimulation coordinates in the right DLPFC, Montreal Neurological Institute (MNI) coordinate is (42, 44, 30). The F4 location can be included in the ROI area based on an investigation related to TMS coil locating [29]. The obtained correlation coefficients were transformed to z-values using Fisher's r-to-z transformation to enhance normality.

Statistical analyses

To compare the demographic parameters of the participants, an independent two-sample t-test was used to compare body mass index (BMI), age and years of education when they are in normal distribution, otherwise, the nonparametric Wilcoxon test was used, a chi-square test was used for sex comparisons.

Statistical analyses of the behavioral measurements were conducted using SPSS version 26.0 (IBM Corp., Armonk, NY, USA). Shapiro–Wilk was applied in the normality of distribution tests of all continuous variables; Levene statistics were used for homogeneity of variance tests. A two-sample t-test was applied for normally distributed variables with homogeneous variances. Otherwise, a Wilcoxon test was used. A p value of < 0.05 were considered statistically significant. To assess the changes in cognitive performance over time, we first compared cognitive measurements at baseline. A two-sample t-test was used to compare the pre- and post-treatment changes between groups in these parameters if no significant differences between groups at baseline.

Statistical analysis of the brain image was as follows. A flexible factorial design was used to compare the group × time interactive areas, and the mean value of FC in each area was calculated with Data Processing & Analysis of Brain Imaging (DPABI) (http://rfmri.org/dpabi). The results were validated with a significance threshold of $p < 0.05$, and extracted as mask. Next, we performed two-sample post hoc t-tests within this mask to further detect significant differences between the groups, age, sex, and educated years were controlling for covariates (corrected $p < 0.05$, as determined by false discovery rate (FDR) correction).

Correlation analyses

We extracted the cluster showing significant FC differences between the real and sham stimulation groups and calculated the average FC value to explore the correlation between FC scores and behavioral measurements using the canonical correlation analysis, respectively ($p < 0.05$ were considered statistically significant).

Results

Demographic parameters' comparison

There were 4 (one male and three females) and 5 (2 males and 3 females) participants in the real iTBS group and sham group didn't complete all the treatment due to personal reasons. At a result, 14 in real group and 13 in sham group completed the iTBS treatment. Among these participants, two of them didn't complete the cognitive measurements and fMRI after the treatment for personal reasons in the sham group. Finally, 14 in the real group and 13 in the sham group were enrolled in the VFSS analysis, and 14 in the real group and 11 in the sham group were enrolled in the cognition and fMRI analysis.

There were no significant differences in terms of age, gender, educated years, and BMI at baseline between the two groups (Table 1).

Cognitive results

The MoCA scores at baseline of the real group had no significant difference compared with the sham group (Table 2). We compared the changes in scores across time for each variable between the two groups, and the results indicated that there were significant differences in MoCA scores, iTBS group showed greater improvement compared with the sham group ($p = 0.039$, confidence interval (CI) = (0.08 2.84), effect size of Hedges' g = 0.89). The change of duration in incongruent task of SCWT in the real group decreased higher than that in the sham group

Table 1 Comparison of demographic information of participants between groups

	Real	Sham	Statistical value	*p*
Age	69.63 ± 6.38	69.86 ± 6.80	t = −0.114	0.909
Education(years)	12.95 ± 3.01	11.59 ± 3.98	t = 1.251	0.218
Gender (M: F)	5:9	4:9	$\chi^2 = 1.0$	0.555
BMI	23.69 ± 2.08	23.14 ± 2.65	t = 0.45	0.331

BMI body mass index; Data were expressed as $\overline{x}$±SD when they met normal distribution

Table 2 Examination of cognitive and swallowing function Pre- and 2 weeks post-iTBS in both groups

		iTBS	sham	statistical value	p
Cognition					
MoCA	pre	22.08 ± 2.60	22.92 ± 2.57	t = −0.836	0.411
	post	25.08 ± 2.96	24.69 ± 3.52		
TMT_A(s)	pre	52.61 ± 19.74	45.23 ± 13.20	t = 1.089	0.29
	post	62.21 ± 62.37	43.27 ± 17.14		
TMT_B(s)	pre	120.54 ± 61.86	124.40 ± 53.50	t = −0.166	0.869
	post	110.44 ± 37.95	111.76 ± 32.82		
DST_forward(s)	pre	6.5(2)	7(3)	z = −0.223	0.823
	post	7.5(1)	7(3)		
DST_backward(s)	pre	4(2)	4(1)	z = −0.276	0.783
	post	4.5(3)	4(1)		
SCWT(s)	pre	40.56(37.33)	33.26(9.38)	z = −1.311	0.19
	post	36.80(19.63)	33.75(8)		
Swallowing					
5 ml OTT(ms)	pre	1142.78 ± 189.273	964.19 ± 247.82	t = −0.053	0.958
	post	760.35 ± 64.80	598.45 ± 84.85		
10 ml OTT(ms)	pre	1094.29 ± 397.87	927.13 ± 497.24	t = 1.889	0.075
	post	705.88 ± 323.24	779.73 ± 304.45		
5 ml SET(ms)	pre	1512.57 ± 131.15	1404.5 ± 171.72	t = −0.777	0.448
	post	1305.92 ± 93.13	1379.02 ± 121.94		
10 ml SET(ms)	pre	1315.25 ± 80.96	1296.62 ± 106.00	t = −0.126	0.901
	post	1444.53 ± 101.84	1444.33 ± 133.34		
5 ml HAMr	pre	0.28 ± 0.03	0.28 ± 0.03	t = 0.463	0.649
	post	0.27 ± 0.04	0.16 ± 0.04		
10 ml HAMr	pre	0.27 ± 0.02	0.29 ± 0.02	t = 0.754	0.461
	post	0.27 ± 0.04	0.15 ± 0.04		
5 ml HSMr	pre	0.32 ± 0.03	0.25 ± 0.03	t = −0.032	0.975
	post	0.32 ± 0.05	0.18 ± 0.05		
10 ml HSMr	pre	0.38 ± 0.04	0.31 ± 0.04	t = −0.45	0.658
	post	0.36 ± 0.06	0.19 ± 0.06		

All the cognitive and swallowing function measures showed no difference between real and sham groups pre iTBS. The statistical value represents the comparison results of changes of assessments across time, t value for data with normal distribution, z value for data with non- normal distribution

MoCA Montreal cognitive assessment; *TMT* Trail Making Test; *DST* digital span test; *SCWT* Stroop Color Word Test; *OTT* oral transit time; *SET* soft palate elevation time; *HAMr* rate of hyoid anterior movement to the distance between second and fourth cervical vertebrae; *HSMr* rate of hyoid superior movement to the distance between second and fourth cervical vertebrae

significantly ($p = 0.016$, CI = (0.01 0.02), effect size of Hedges' g = 0.77). However, we found no significant difference in DST and TMT test between the real and sham groups. Please refer to Table 3 for more details. These results indicate iTBS applied to the right DLPFC have the potential to improve global cognitive function and response inhibition ability.

VFSS results

Eight swallowing measurements were included in the statistical analysis and no significant difference were observed in the baseline data between groups (Table 2). We found no significant differences in the pre and post changes of swallowing measurements between groups. However, temporal parameters included 5-ml OTT, 5-ml SET and 10-ml OTT showed a decreasing trend, indicating that the oral phase of swallowing becoming more efficient in some degree without significance. Please refer to Table 3 for more details. When we selected patients with a 10-ml OTT > 1000 ms (seven in the real group included two males and five females and five in the sham group included two males and three females), the change in 10-ml OTT showed significant difference (10-ml OTT in iTBS group during pretreatment was 1361.64 ± 128.42, post treatment was 643.28 ± 185.00, sham group during pretreatment was 1388.97 ± 515.25, posttreatment

Table 3 Pre- and 2 weeks post-treatment differences of cognitive and swallowing function assessments in each group

	iTBS	Sham	Statistical value	*p*	Effect size	CI
Cognition						
MoCA	3.23 ± 1.30	1.77 ± 2.01	t = 2.204	**0.039**	0.89[a]	(0.08 2.84)
TMT_A(s)	−3.06 ± 23.59	−1.96 ± 11.92	t = −0.139	0.891	0.06[c]	(−17.89 15.70)
TMT_B(s)	−21.06 ± 33.93	−12.64 ± 52.39	t = −0.473	0.641	0.20[c]	(−45.40 28.57)
DST_forward(s)	1(2)	0(1)	z = −0.583	0.56	0.56[b]	(0.56 0.58)
DST_backward(s)	0(1.25)	0(1)	z = −0.274	0.784	0.47[c]	(0.81 0.82)
SCWT	−4.16(7.29)	−0.5(4.13)	z = −2.404	**0.016**	0.77[b]	(0.01 0.02)
Swallow						
5ml OTT(ms)	−382.43 ± 664.14	−365.70 ± 643.09	t = −0.054	0.958	0.03[c]	(−685.30,651.92)
10ml OTT(ms)	−427.53 ± 685.67	−219.48 ± 429.44	t = −0.813	0.428	0.35[c]	(−748.55,332.45)
5ml SET(ms)	−206.65 ± 565.74	−25.4 ± 306.50	t = −0.905	0.378	0.38[c]	(−603.67,241.32)
10ml SET(ms)	129.28 ± 311.94	147.71 ± 300.58	t = −0.127	0.901	0.06[c]	(−331.40,294.53)
5ml HAMr	0.05 ± 0.10	0.03 ± 0.09	t = 0.48	0.638	0.21[c]	(−0.07,0.11)
10ml HAMr	0.04 ± 0.08	0.01 ± 0.09	t = 0.73	0.48	0.36[c]	(−0.06,0.12)
5ml HSMr	0.05 ± 0.13	0.05 ± 0.11	t = −0.034	0.973	0[c]	(−0.12,0.12)
10ml HSMr	0.02 ± 0.16	0.05 ± 0.10	t = −0.518	0.611	0.22[c]	(−0.15,0.09)

The changes of MoCA and changes of SCWT showed significant differences pre-and 2 weeks post-iTBS between real and sham groups

CI confidence interval; *MoCA* Montreal cognitive assessment; *TMT* Trail Making Test; *DST* digital span test; *SCWT* Stroop color word test; *OTT* oral transit time; *SET* soft palate elevation time; *HAMr* rate of hyoid anterior movement to the distance between second and fourth cervical vertebrae; *HSMr* rate of hyoid superior movement to the distance between second and fourth cervical vertebrae

The statistical value represents the comparison results of changes of assessments across time, t value for data with normal distribution, z value for data with non-normal distribution

P value in bold indicates significant statistically. Hedges' g of 0.2, 0.5. 0.8 represents small, medium, and large effect size

[a] : large effect size, [b]: medium effect size, [c]: small effect size. For the normal data, the CI was estimated with mean and SD. For the non-normal data, the CI was estimated with bootstrapping method which is a non-parametric method percentile of 2.5 and percentile 97.5

was 1140.84 ± 412.82, t = 2.941, $p = 0.015$, effect size of Hedges' g = 0.520).

FC analysis of fMRI results

We calculated the FC between the seed ROI and the whole brain. We found that there was a time × group interaction effect on the FC in several regions, such as the bilateral precuneus, right cingulate gyrus, and left middle frontal gyrus (MFG). Among them, the FC of left MFG which is included in the left DLPFC exhibited a significant increase in the real iTBS group compared with that in sham group after application of a post hoc t test ($p < 0.05$ with FDR corrected). Please refer to Fig. 3. Therefore, the FC score between right and left DLPFC was involved in the subsequent analysis.

Correlation analysis

We conducted a correlation analysis to examine the relationship between the behavioral assessments and the FC scores obtained via fMRI. At baseline among all the participants, SCWT task duration showed a negative correlation with the FC score (r = −0.554, $p = 0.017$) indicating a positive correlation between the response inhibition ability and FC scores, and the 10-ml OTT demonstrated a negative correlation with the FC score (rho = −0.442, $p = 0.027$), suggesting a positive correlation between oral transport efficiency during swallowing and FC scores.

In the iTBS group, the changes in MoCA scores were positive correlated with the changes in 10-ml OTT ($r = 0.648$, $p = 0.031$). The changes in MoCA scores and the changes in FC values were positively correlated ($r = 0.789$, $p = 0.035$) among patients with pre10-ml OTT greater than 1000 ms in the iTBS group using Pearson correlation analysis. However, we found no significant correlation between the changes in FC value and changes in MoCA or OTT in the sham group.

Statistical power

We determined the sample size based on a previous experiment [30]. A total of 36 participants in this study can achieve 81% power to detect a difference between groups, with a significance level (alpha) of 0.05 using a two-sided two-sample t-test.

Side effects

Epileptic seizures or other serious adverse events didn't occur during or after iTBS treatment in any participants. Reported minor adverse effects included: a slight headache felt once by one female participant, post iTBS

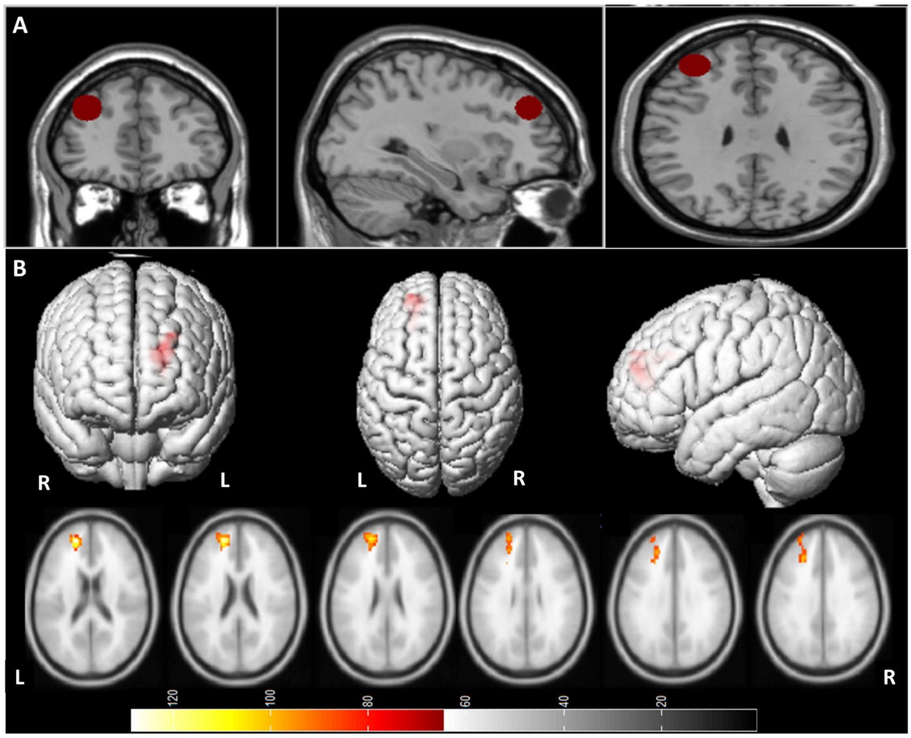

Fig. 3 The FC between left MFG and right DLPFC significantly increased in iTBS group after treatment. **A** The right DLPFC was selected as region of interest located in Montreal Neurological Institute (MNI) coordinate commonly used in previous articles (42, 44, 30). **B** The FC in left MFG significantly increased in iTBS group after treatment compared with that in sham group. Different view of the left MFG. R means right, L means left, MFG means middle frontal gyrus

dizziness felt once by a female participant, and minor discomfort and face twitching during iTBS felt by a male participant. All the patients recovered quickly. These participants didn't discontinue the subsequent treatment, because the side effect is minor and can be effectively alleviated with relaxation and education. They all completed the 10 sessions' treatment. As a result, they were included in the final analysis.

Discussion

In this study, we observed that iTBS applied to the right DLPFC has the potential to improve both global cognitive function and executive function, as well as certain aspects of swallowing function. Notably, the FC between the right and left DLPFC increased significantly in the real iTBS group after iTBS compared with the sham group. Correlation analyses revealed that baseline FC scores were negatively correlated with the SCWT task duration and with the 10-ml OTT across all participants. Among those in the iTBS group with a pre-10-OTT greater than 1000 ms, we observed a positive correlation between changes in MoCA scores and changes in FC values ($r=0.789$, $p=0.035$). Furthermore, changes of MoCA scores were positively correlated with changes of 10-OTT ($r=0.648$, $p=0.031$), as determined by Pearson analysis.

We found that right DLPFC iTBS may be able to improve global cognitive function, as evidenced by a large effect size. In an interview, the iTBS seems to be the most effective to enhance the scores in MoCA, MMSE, and modified Barthel Index (MBI) for post-stroke patients, especially when compared to high and low frequency rTMS [10]. However, the lack of specificity in stimulation target is a critical factor influencing the efficacy of rTMS interventions. By focusing on the right DLPFC, iTBS represents a promising approach to enhance overall cognitive function in patients with MCI. Moreover, we observed a positive correlation between changes in MoCA scores and changes in FC values, suggesting that enhanced connectivity between the right and left DLPFC may play an important role in improving cognitive outcomes. This finding aligns with the notion that iTBS, by closely mimicking natural neuronal firing patterns, can lead to robust changes in cortical excitability [31].

The response inhibition ability, as measured by the SCWT, a task known to engage bilateral prefrontal lobes and serve as a key component of executive function [32], was improved after iTBS with a medium effect size. As highlighted in a meta-analysis, high-frequency rTMS targeting the right DLPFC has been shown to significantly enhance executive function, with effects lasting up to 4–12 weeks [33]. Notably, we found a negative correlation between the FC score and SCWT task duration at baseline; however, no significant correlation emerged between these variables two weeks after the last session of iTBS in either group. This lack of significant correlation may suggest that the enhancement in response inhibition was not sufficiently robust, warranting further investigation.

In this study, there was no significant difference of changes in swallowing function between groups. The lack of significant difference across groups may partly stem from the high variability of VFSS parameters. Another plausible explanation is that iTBS targeting the right DLPFC may have a differential impact on individuals with poorer swallowing function, leaving limited room for improvement among those with mild dysphagia. Notably, patients with 10-ml OTT exceeding 1000 ms showed significant improvement in iTBS group, accompanied by a medium effect size. Additionally, temporal parameters such as 5-ml OTT, 5-ml SET and 10-ml OTT demonstrated a decreasing trend, suggesting possible enhancement of efficiency in the oral phase of swallowing. Furthermore, within the iTBS group, changes in 10-ml OTT were positively correlated with the changes in MoCA scores, indicating an indirect relationship between cognitive performance and oral swallowing function. While the changes in FC scores were positively correlated with changes in 10-ml OTT, the small sample size limits the generalizability of these conclusions. Further studies with larger sample are warranted to better understand the efficacy of right DLPFC iTBS on swallowing disorders associated with MCI and the possible underlying neural mechanisms.

Prior researches have predominantly favored targeting the left DLPFC with NIBS in patients with cognitive impairment. For instance, Wu et al. demonstrated improved executive function with iTBS over the left DLPFC compared to sham stimulation [34], similarly, Yuan et al. noted enhanced cognition in patients with MCI following 10 Hz rTMS over the left DLPFC [35]. Meinzer et al. also reported that anodal tDCS (exciting model) targeting on the left inferior prefrontal lobe led to cognitive improvements in subjects with MCI [36]. Moreover, improvements in post-stroke cognitive impairment have been documented with iTBS applied to the left DLPFC [37].

In contrast, the effectiveness of stimulating the right DLPFC has been less emphasized in clinical practice. Smith, Jonides, and Koeppe [38] observed lateralized DLPFC activations during verbal and visual working memory tasks in the adults, with the left DLPFC primarily engaged in verbal working memory tasks and the right DLPFC activated during visual working memory tasks. However, other studies have indicated an absence of lateralization of DLPFC activation during executive function-related tasks in older adults and patients with MCI [39, 40]. It has been proposed that this reduction in lateralization may result from the recruitment of neurons from the opposite hemisphere to compensate for neuronal decline associated with aging and cognitive impairment.

In summary, right DLPFC iTBS may represent a valuable approach for treating MCI, particularly in patients at high risk for dysphagia. While right DLPFC iTBS appears to enhance global cognitive function and response inhibition ability, further investigation, including comparisons between left and right DLPFC as stimulation targets, is warranted to fully elucidate its potential benefits.

In this study, we employed a navigation system to ensure that stimulation was consistently applied to the same targeted area during each treatment session. The integration of robotic rTMS with neuro-navigation and automation offers a precise method for brain stimulation, resulting in repeatable outcomes and improved treatment efficiency. In contrast, non-navigated TMS may inaccurately target the DLPFC area, leading to target variability across treatment sessions, therefore results are often inconsistent across sessions [41]. Recent advancements in neuronavigational techniques have facilitated the integration of MRI data, which can enhance the efficacy of rTMS. For example, Ayache et al. [42] demonstrated the added value of using neuro-navigation in guiding rTMS therapy in patients with pain in terms of analgesic efficacy. We assert that the use of iTBS combined with robotic navigation system effectively improved the treatment efficiency in our study. However, the current robotic navigation relies solely on the 10–20 EEG international system based on the individual structural MRI scans, which limits its precision in functional location. To improve individualization and accuracy, the incorporation of fMRI data may prove benefit.

Conclusions

Administering navigated iTBS over the right DLPFC has the potential to improve global cognitive, executive function, and certain aspects of swallowing function, devoid of any serious adverse events. The observed enhancements in FC between the right and left DLPFC suggest that iTBS may facilitate neuroplastic changes that underlie these cognitive improvements. Furthermore, the changes of FC values between right and left DLPFC were positive correlated with the changes of

MoCA scores, and with 10-ml OTT among participants with 10-ml OTT longer than 1000 ms. However, our study had several limitations. Firstly, the limited sample size may restrict the generalizability of our findings. Future studies with larger sample sizes are needed to more accurately assess the efficacy of the treatment. Additionally, classifying participants into different MCI phenotypes could provide deeper insights into the treatment's effectiveness. Secondly, while we employed coil-tilting for the sham stimulation, using a dedicated sham coil for the control condition would improve the experimental design. Thirdly, there is a lack of comparison of the left DLPFC as a target location. Further research is needed to explore the differential effects of iTBS targeting the left and right prefrontal lobes on cognitive and swallowing function, as well as to better understand the long-term effects of this therapeutic approach. Lastly, the F4 in electrode in 10–20 EEG international system, which targets the right DLPFC, lacks individualization in iTBS targeting, functional location engaged in brain activity through fMRI or EEG may be useful in the future.

Acknowledgements
We thank the subjects who donated their time and effort to participate in this study. We thank the colleagues in our department for their comments on this experiment.

Authors' contributions
Jie Wang: first author, designed the experiments, conducted data collection, formal analysis, made figures and wrote manuscript; Mengqing Zhang: conducted data collection and performed iTBS; Xiaomei Wei: cognitive function assessments and collection and assembly of data; Cheng Yang: help to data analysis and made figures; Meng Dai: participants recruitment and fMRI analysis; Zulin Dou: resources, provided funding, funding acquisition, supervision, and reviewed manuscript; Yonghui Wang: supervision of the experiment and revision of the manuscript, funding acquisition. All authors read and approved the final manuscript.

Funding
This work was supported by the National Natural Science Foundation of China [Grant Numbers 82402961, 81972159, and 81972154], TaiShan Scholars Project (NO. tstp20230652).

Data availability
The data that support the findings of this study are not publicly available. However, the data are available from the authors upon reasonable reasons and with permission of the the Third Affiliated Hospital of Sun Yat-sen University.

Declarations

Ethics approval and consent to participant
This study was approved by the ethics committee of the Third Affiliated Hospital of Sun Yat-sen University (approval number [2018] 02–374-01). The participants or their caregivers provided written informed consent. This study was registered in the Chinese Clinical Trial registry (registration number ChiCTR1900021795) on 10/March/2019.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

Author details
[1]Department of Rehabilitation Medicine (Rehabilitation Center), Qilu Hospital of Shandong University, No. 107, Wenhuaxi Road, Jinan, Shandong 250012, China. [2]Department of Rehabilitation Medicine, Guangzhou Women and Children's Medical Center, Guangzhou Medical University, No. 318, Middle Renmin Road, Guangzhou, Guangdong 510120, China. [3]Department of Rehabilitation Medicine, The Third Affiliated Hospital, Sun Yat-Sen University, No. 600, Tianhe Road, Guangzhou, Guangdong 510630, China. [4]Department of Rehabilitation Medicine, Shenzhen Hospital of Southern Medical University, No. 1333, Xinhu Road, Shenzhen, Guangdong 518101, China.

Received: 28 March 2024 Accepted: 11 December 2024
Published online: 04 January 2025

References

1. Chertkow H, Cummings L, Leon MD, Feldman H, Ganguli M, Hampel H, Scheltens P, Tierney MC. Mild cognitive impairment. 2006.
2. Wang J, Yang C, Wei X, Zhang M, Dai M, Huang G, Huang W, Wen H, Dou Z. Videofluoroscopic Swallowing Study Features and Resting-State Functional MRI Brain Activity for Assessing Swallowing Differences in Patients with Mild Cognitive Impairment and Risk of Dysphagia. Dysphagia. 2023;38(1):236–46. https://doi.org/10.1007/s00455-022-10460-2.
3. Yang EJ, Kim KW, Lim JY, Paik NJ. Relationship between dysphagia and mild cognitive impairment in a community-based elderly cohort: The korean longitudinal study on health and aging. J Am Geriatr Soc. 2014;62(1):40–6.
4. Doorduijn AS, de van der Schueren MAE, van de Rest O, de Leeuw FA, Hendriksen HMA, Teunissen CE, Scheltens P, van der Flier WM, Visser M. Nutritional status is associated with clinical progression in Alzheimer's disease: the NUDAD project. J Am Med Dir Assoc. 2023;24(5):638-644 e631.
5. Pabst A, Proksch S, Médé B, Comstock DC, Ross JM, Balasubramaniam R. A systematic review and meta-analysis of the efficacy of intermittent theta burst stimulation (iTBS) on cognitive enhancement. Neurosci Biobehav-ioReviews. 2022;135:104587.
6. Mistry S, Michou E, Rothwell J, Hamdy S. Remote effects of intermittent theta burst stimulation of the human pharyngeal motor system. Eur J Neurosci. 2012;36(4):2493–9.
7. Huang YZ, Edwards MJ, Rounis E, Bhatia KP, Rothwell JC. Theta burst stimulation of the human motor cortex. Neuron. 2005;45(2):201–6.
8. Huang YZ, Rothwell JC, Lu CS, Wang JJ, Weng YH, Lai SC, Chuang WL, Hung J, Chen RS. The effect of continuous theta burst stimulation over premotor cortex on circuits in primary motor cortex and spinal cord. Clin Neurophysiol. 2009;120(4):796–801.
9. Di Lazzaro V, Pilato F, Dileone M, Profice P, Oliviero A, Mazzone P, Insola A, Ranieri F, Meglio M, Tonali PA, et al. The physiological basis of the effects of intermittent theta burst stimulation of the human motor cortex. J Physiol. 2008;586(16):3871–9.
10. Liu X, Li H, Yang S, Xiao Z, Li Q, Zhang F, Ma J. Efficacy of repetitive transcranial magnetic stimulation on post-stroke cognitive impairment: a systematic and a network meta-analysis. Int J Geriatr Psychiatry. 2024;39(7): e6117.
11. Oberman L, Edwards D, Eldaief M, Pascual-Leone A. Safety of theta burst transcranial magnetic stimulation: a systematic review of the literature. J Clin Neurophysiol. 2011;28(1):67–74.
12. Nowak DA, Bosl K, Podubecka J, Carey JR. Noninvasive brain stimulation and motor recovery after stroke. Restor Neurol Neurosci. 2010;28(4):531–44.
13. Lowe CJ, Manocchio F, Safati AB, Hall PA. The effects of theta burst stimulation (TBS) targeting the prefrontal cortex on executive functioning: a systematic review and meta-analysis. Neuropsychologia. 2018;111:344–59.
14. Jo SY, Hwang JW, Pyun SB. Relationship between cognitive function and dysphagia after stroke. Ann Rehabil Med. 2017;41(4):564–72.
15. Cox SR, Bastin ME, Ferguson KJ, Allerhand M, Royle NA, Maniega SM, Starr JM, MacLullich AM, Wardlaw JM, Deary IJ, et al. Compensation or

inhibitory failure? Testing hypotheses of age-related right frontal lobe involvement in verbal memory ability using structural and diffusion MRI. Cortex. 2015;63:4–15.
16. Stuss DT. Functions of the frontal lobes: relation to executive functions. J Int Neuropsychol Soc. 2011;17(05):759–65.
17. Wang J, Zhang M, Wen H, Yang C, Wei X, Wang Y, Dou Z. Correlation Between Swallowing and Cognitive Brain Networks in Older Adults via Functional MRI. J Oral Rehabil. 2024;51(12):2588–99. https://doi.org/10.1111/joor.13855.
18. Huang YZ. The modulation of cortical motor circuits and spinal reflexes using theta burst stimulation in healthy and dystonic subjects. Restor Neurol Neurosci. 2010;28(4):449–57.
19. Li S, Ma Z, Tu S, Zhou M, Chen S, Guo Z, Gong Q, He L, Huang X, Yao D, et al. Altered resting-state functional and white matter tract connectivity in stroke patients with dysphagia. Neurorehabil Neural Repair. 2014;28(3):260–72.
20. Verwoerd JH, Mattace-Raso FUS. Mild cognitive impairment. Huisarts en Wetenschap. 2012;55(10):464–7.
21. Marik PE, Kaplan D. Aspiration pneumonia and dysphagia in the elderly. Chest. 2003;124(1):328–36.
22. Stephen JR, Taves DH, Smith RC, Martin RE. Bolus location at the initiation of the pharyngeal stage of swallowing in healthy older adults. Dysphagia. 2005;20(4):266–72.
23. Leonard R. Predicting aspiration risk in patients with dysphagia: evidence from fluoroscopy. Laryngoscope Investig Otolaryngol. 2019;4(1):83–8.
24. Turriziani P, Smirni D, Zappala G, Mangano GR, Oliveri M, Cipolotti L. Enhancing memory performance with rTMS in healthy subjects and individuals with mild cognitive impairment: the role of the right dorsolateral prefrontal cortex. Front Hum Neurosci. 2012;6:62.
25. O'Driscoll C, Shaikh M. Cross-cultural applicability of the montreal cognitive assessment (MoCA): a systematic review. J Alzheimers Dis. 2017;58(3):789–801.
26. Reitan RM, Wolfson D. The trail making test as an initial screening procedure for neuropsychological impairment in older children. Archives of clinical neuropsychology : the official journal of the National Academy of Neuropsychologists. 2004;19(2):281–8.
27. Biswal B, Yetkin FZ, Haughton VM, Hyde JS. Functional connectivity in the motor cortex of resting human brain using echo-planar MRI. Magn Reson Med. 1995;34(4):537–41.
28. Greicius MD, Srivastava G, Reiss AL, Menon V. Default-mode network activity distinguishes Alzheimer's disease from healthy aging: evidence from functional MRI. Proc Natl Acad Sci USA. 2004;101(13):4637–42.
29. Jiang Y, Du B, Chen Y, Wei L, Zhang Z, Cao Z, Xie C, Li Q, Cai Z, Li Z, et al. A scalp-measurement based parameter space: towards locating TMS coils in a clinically-friendly way. Brain Stimul. 2022;15(4):924–6.
30. He W, Wang JC, Tsai PY. Theta burst magnetic stimulation improves parkinson's-related cognitive impairment: a randomised controlled study. Neurorehabil Neural Repair. 2021;35(11):986–95.
31. Benali A, Trippe J, Weiler E, Mix A, Petrasch-Parwez E, Girzalsky W, Eysel UT, Erdmann R, Funke K. Theta-burst transcranial magnetic stimulation alters cortical inhibition. J Neurosci. 2011;31(4):1193–203.
32. Song Y, Hakoda Y. An fMRI study of the functional mechanisms of stroop/reverse-stroop effects. Behav Brain Res. 2015;290:187–96.
33. Chou YH, Ton That V, Sundman M. A systematic review and meta-analysis of rTMS effects on cognitive enhancement in mild cognitive impairment and Alzheimer's disease. Neurobiol Aging. 2020;86:1–10.
34. Wu X, Wang L, Geng Z, Wei L, Yan Y, Xie C, Chen X, Ji GJ, Tian Y, Wang K. Improved cognitive promotion through accelerated magnetic stimulation. eNeuro. 2021;8(1):ENEURO.0392-20.2020.
35. Yuan LQ, Zeng Q, Wang D, Wen XY, Shi Y, Zhu F, Chen SJ, Huang GZ. Neuroimaging mechanisms of high-frequency repetitive transcranial magnetic stimulation for treatment of amnestic mild cognitive impairment: a double-blind randomized sham-controlled trial. Neural Regen Res. 2021;16(4):707–13.
36. Meinzer M, Lindenberg R, Phan MT, Ulm L, Volk C, Floel A. Transcranial direct current stimulation in mild cognitive impairment: behavioral effects and neural mechanisms. Alzheimer's Dementia. 2015;11(9):1032–40.
37. Li W, Wen Q, Xie YH, Hu AL, Wu Q, Wang YX. Improvement of poststroke cognitive impairment by intermittent theta bursts: a double-blind randomized controlled trial. Brain Behav. 2022;12(6): e2569.
38. Smith EE, Jonides J, Koeppe RA. Dissociating verbal and spatial working memory using PET. Cerebral cortex. 1996;6(1):11–20.
39. Reuter-Lorenz PA, Jonides J, Smith EE, Hartley A, Miller A, Marshuetz C, Koeppe RA. Age differences in the frontal lateralization of verbal and spatial working memory revealed by PET. J Cogn Neurosci. 2000;12(1):174–87.
40. Yeung MK, Sze SL, Woo J, Kwok T, Shum DH, Yu R, Chan AS. Altered frontal lateralization underlies the category fluency deficits in older adults with mild cognitive impairment: a near-infrared spectroscopy study. Front Aging Neurosci. 2016;8:59.
41. Ahdab R, Ayache SS, Brugieres P, Goujon C, Lefaucheur JP. Comparison of "standard" and "navigated" procedures of TMS coil positioning over motor, premotor and prefrontal targets in patients with chronic pain and depression. Neurophysiol Clin. 2010;40(1):27–36.
42. Ayache SS, Ahdab R, Chalah MA, Farhat WH, Mylius V, Goujon C, Sorel M, Lefaucheur JP. Analgesic effects of navigated motor cortex rTMS in patients with chronic neuropathic pain. European journal of pain (London, England). 2016;20(9):1413–22.

Publisher's Note