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Deep transcranial magnetic stimulation is superior to normal in motor-evoked potentials

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Abstract

Background: Deep transcranial magnetic stimulation (dTMS) using an H7 coil is widely applied in the treatment of several neurological diseases. However, whether dTMS with an H7 coil is superior to figure-of-eight coil transcranial magnetic stimulation (TMS) for neurophysiological assessment remains unclear. *Methods:* This study compared the latency and amplitude of motor-evoked potentials (MEPs) induced by dTMS with an H7 coil and figure-of-eight coil TMS in the lower-extremity region of the primary motor cortex (M1) in healthy individuals. *Results:* dTMS with the H7 coil demonstrated a significantly higher elicitation rate for resting MEPs than figure-of-eight coil TMS, whereas no significant difference was observed for facilitated MEPs. The latency and amplitude of both resting and facilitated MEPs differed significantly between the two stimulation methods. Significant differences in elicitation rate and amplitude were observed between resting and facilitated MEPs, but no latency difference was detected. No significant differences in elicitation rate, latency, or amplitude were observed between the left and right sides for MEPs induced by either stimulation technique. *Conclusions:* dTMS with an H7 coil is an effective method for eliciting resting MEPs in the lower extremity but does not outperform figure-of-eight coil TMS for facilitated MEPs. The responsiveness is influenced by facilitation status but not by handedness.

Keywords: Transcranial magnetic stimulation, deep transcranial magnetic stimulation, motor-evoked potential

INTRODUCTION

Transcranial magnetic stimulation (TMS) is a safe, noninvasive[1], and painless technique that has proven effective in the treatment of a range of neuropsychiatric disorders[2], including neuropathic pain, depression, and schizophrenia. TMS also serves as a valuable diagnostic tool for assessing the integrity of the fast-conducting corticomotorpathway in various neurological diseases by eliciting motor-evoked potentials (MEP).[3] Furthermore, analysis of MEP latency and amplitude provides important insights into cortical excitability and is useful for determining optimal TMS treatment parameters and evaluating therapeutic efficacy.[4]

The figure of-eight coil is one of the most commonly used TMS coils for MEP evaluation and treatment. However, it primarily stimulates superficial cortex of the brain[5]but its use requires patients to undergo an invasive procedure. Repetitive transcranial magnetic stimulation (rTMS, with an average stimulation depth of approximately 1.5 cm.[6] In contrast, the lower-extremity area of the primary motor cortex (M1) is located in a deeper cortical region. Consequently, figure-of-eight coil stimulation may provide suboptimal assessment of lower-extremity MEPs.

Recently, deep transcranial magnetic stimulation (dTMS) has emerged as a technique designed to stimulate deeper brain regions. The

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effective stimulation depth of H-coils can reach 5–6 cm, depending on the specific coil type. The H7 coil[6,7] primarily targets the prefrontal cortex (PFC) and has been used in conditions such as attention-deficit/hyperactivity disorder and obsessive-compulsive disorder.[7] Tendler *et al*. reported that the H7 coil can generate a magnetic field intensity exceeding the motor threshold for the foot representation, thereby expanding the potential applications of dTMS. Therefore, dTMS with the H7 coil.[7]

dTMS with H7 coil may overcome the limitations of figure-of-eight coil TMS in assessing lower-extremity MEPs due to its ability to deliver suprathreshold stimulation to deeper motor areas. However, to the best of our knowledge, no study has directly investigated whether dTMS with the H7 coil outperforms figure-of-eight coil TMS in neurophysiological assessment in healthy individuals. Accordingly, this study aimed to compare the two stimulation methods in inducing lower-extremity MEPs and to determine whether dTMS with the H7 coil could serve as a viable alternative assessment technique.

METHODS

Participants

This study was approved by the Institutional Ethics Committee of Xijing Hospital, Fourth Military Medical University (KY20172051), and was conducted in accordance with the ethical standards of the 1964 Declaration of Helsinki. All participants read and signed the informed consent before enrollment. Participants were recruited between October 1, 2020, and November 30, 2020.

All investigators had more than five years of professional experience in rehabilitation science. To ensure consistency and stability of the results, the same investigator performed both the stimulation and testing procedures.

Study design

This prospective crossover study enrolled healthy adult volunteers. Each participant underwent both stimulation protocols with a 3-week washout interval between sessions.

The inclusion criteria were as follows: adults aged 18–60 years who were right-handed according to the Chinese version of the Edinburgh Handedness Inventory[8], had no history of neurological or psychiatric illness, showed normal neurological examination findings, had intact scalp and lower extremities without injury, passed the TMS Adult Safety Screen[9], and provided informed consent.

The exclusion criteria were as follows: Participants were excluded if they had a personal or family history of epileptic seizure, neurological or psychiatric disorders (e.g., stroke, traumatic brain injury, depression, or anxiety, implanted stimulators or metallic implants such as cardiac pacemakers, alcohol or substance abuse, long-term psychotropic drugs or use of medications interfering with TMS, and pregnant or nursing women.

dTMS procedure

dTMS was delivered using an M-100 Ultimate magnetic stimulator (Shenzhen Yingchi Technology Co., Ltd.) equipped with an H7 coil (BrainsWay Inc., Jerusalem, Israel). Participants sat upright comfortably on the inspection chair in a quiet room, and the H7-coil helmet was positioned according to the manufacturer's instructions. MEPs were recorded from the tibialis anterior muscle contralateral to the stimulated hemisphere. After the skin was cleaned with alcohol wipes, two Ag-AgCl disposable self-adhesive surface electromyography (EMG) electrodes 1 cm^2 were placed over the muscle belly. Participants remained relaxed during resting MEP recordings and performed brief voluntary foot dorsiflexion for facilitated MEP recordings. Stimulation intensity was set at 100% of the device output (approximately 1.2 T). Stimuli were delivered at 5–10 s intervals. Each condition was repeated five times. EMG signals were filtered, amplified, displayed, and stored digitally.

TMS procedure

Conventional TMS was performed using a CCY-2 stimulator (YIRUIDE Medical Equipment Company, China) with a figure-of-eight coil. Stimulation intensity was set at 100% device output (approximately 1.55 T) with a 45° coil orientation.[10] The lower-extremity area of the left and right M1 was localized using a neuronavigation system (Visor2, Enschede, the Netherlands).[11] All other procedures, including posture, stimulus interval, and recording methods, were identical to those used in the dTMS protocol.

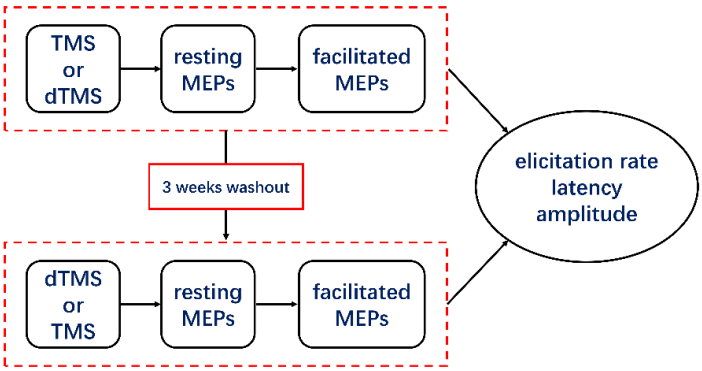

Figure 1. Diagram of motor-evoked potentials using two types of transcranial magnetic stimulation.

MEP measurements

Neurophysiological parameters were evaluated at two time points corresponding to dTMS with the H7 coil and figure-of-eight coil TMS. Both resting and facilitated MEPs were analyzed for amplitude and latency on the right and left sides. Each value was calculated as the average of five responses to ensure repeatability. MEP amplitude was defined as the peak-to-peak EMG response of the contralateral first dorsal interosseous muscle. The MEP latency was defined as the interval between stimulus onset and the onset of the EMG response in the contralateral target muscle. An MEP was considered present if more than two of five stimuli produced a detectable response.[5,7]

Statistical analysis

Elicitation rates (percentages) were compared using McNemar's chi-square test. Differences in latency and amplitude were analyzed using paired t-tests for normally distributed data (based on the Shapiro–Wilk test) or the Mann–Whitney U test otherwise. Comparisons were performed between stimulation methods, sides, and resting versus facilitated conditions. $P < 0.05$ was considered statistically significant. All analyses were conducted using R software (version 4.0.3).

RESULTS

A total of 106 healthy volunteers were screened for eligibility. Three were excluded: two declined to participate, and one withdrew because of scheduling conflicts. Ultimately, 103 participants (mean height 168.1 ± 7.9 cm; 52.4% women) were enrolled in the study. The median age was 29 years (interquartile range, 22–36). The demographic characteristics of the participants are presented in Table 1. No serious adverse effects occurred during the study. In the figure-of-eight coil TMS group, one participant briefly experienced a headache, and another reported numbness. In the dTMS with H7-coil group, one participant briefly experienced a headache, and another reported dizziness during the examination period. Because the elicitation rates for MEP latency and amplitude were identical under the same stimulation parameters,

Table 1: Demographics of study participants (N = 103)

Demographics	n	Percent
Gender		
Female	54	52.4%
Male	49	47.6%
Age (years)		
18-21	20	19.4%
22-29	36	35.0%
30-39	25	24.3%
40-49	16	15.5%
50+	6	5.8%
Height (cm)		
150-159	12	11.7%
160-169	46	44.7%
170-179	37	35.9%
180+	8	7.8%

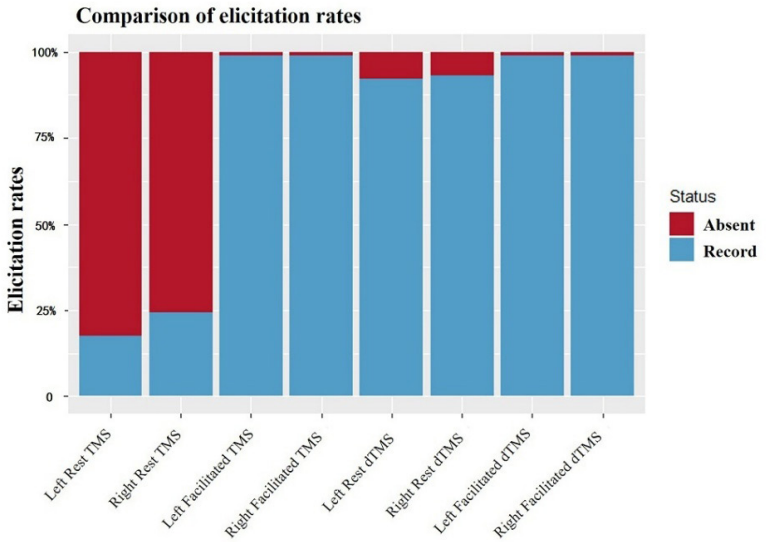

Figure 2. Elicitation rates of the two types of stimulation (transcranial magnetic stimulation [TMS] indicated Figure of eight coil TMS, deep transcranial magnetic stimulation [dTMS] indicated dTMS with H7 coil).

only a single proportion is presented for each stimulation type.

Differences between the dTMS with H7-coil and figure of eight coil TMS groups

The elicitation rates of resting MEPs were markedly higher in the dTMS group than in the TMS group (Figure 2 and Table 2; dTMS vs. TMS; left, 92.2% vs. 17.5%, $p < 0.001$; right, 93.2% vs. 24.3%, $p < 0.001$). However, no significant difference in facilitated MEP elicitation rate was observed between the two groups ($p = 1$).

The latency of both resting and facilitated MEPs on both sides was significantly longer

Table 2: Comparison of motor-evoked potentials between deep transcranial magnetic stimulation with H7-coil and figure of eight coil TMS group

			dTMS	TMS	CI	*t/χ2*	*p*
Elicitation rate (n, %)	Rest	Left	95(92.2%)	18(17.5%)		73.11§	<0.001*
		Right	96(93.2%)	25(24.3%)		69.01§	<0.001*
	Facilitation	Left	102(99.0%)	102(99.0%)		0§	1
		Right	102(99.0%)	102(99.0%)		0§	1
Latency (ms)	Rest	Left (n=17)	27.3±1.61	25.9±1.95	0.65~2.13	3.97†	0.001*
		Right (n=25)	27.6±1.54	26.6±2.12	0.42~1.71	3.42†	0.002*
	Facilitation	Left (n=102)	27(25.3~28)	26(24.2~27.6)			0.016*
		Right (n=102)	27(25.4~28.3)	26.2(24.2~27.6)			0.004*
Amplitude (μv)	Rest	Left (n=17)	1808±1375	846±1082	325~1598	3.20†	0.001*
		Right (n=25)	1302(650~2900)	863(140~960)			0.006*
	Facilitation	Left (n=102)	2550(1275~4300)	1100(512~1878)			<0.001*
		Right (n=102)	3000(2000~4000)	1100(682~2700)			<0.001*

†: t value; §: χ^2 value.

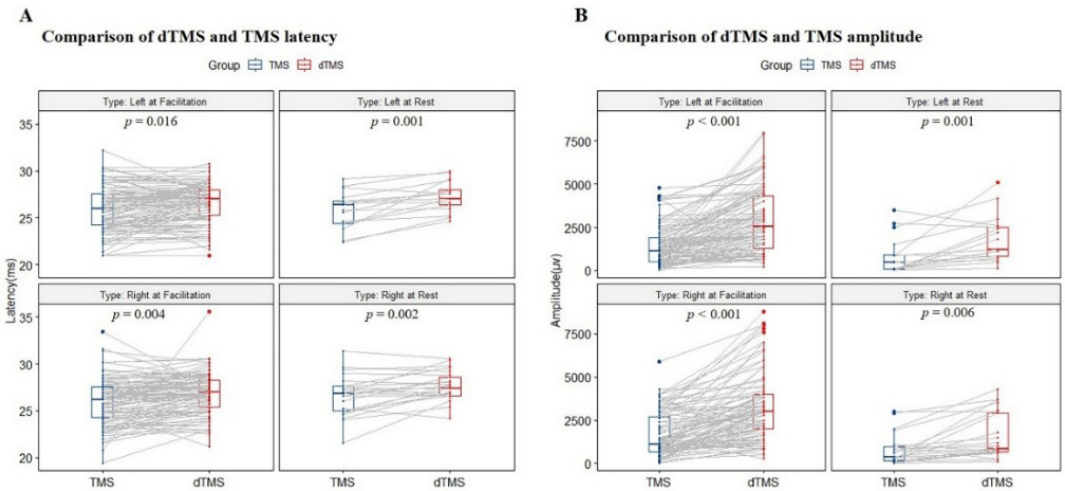

Figure 3. (A) Motor-evoked potentials (MEP) latency in the deep transcranial magnetic stimulation (dTMS) with H7 coil and Figure of eight coil TMS groups. (B) MEP amplitude in the dTMS and Figure of eight TMS groups.

in the dTMS group than in the TMS group (Table 2 and Figure 3A; resting MEP left, p = 0.001; resting MEP right, p = 0.002; facilitated MEP left, p = 0.016; facilitated MEP right, p = 0.004). In addition, the amplitudes of both resting and facilitated MEPs on both sides were significantly higher in the dTMS group than in the TMS group (Table 2 and Figure 3B; resting MEP left, p = 0.001; resting MEP right, p = 0.006; facilitated MEP left, p < 0.001; facilitated MEP right, p < 0.001).

Differences between the resting and facilitated MEPs

When resting and facilitated MEPs were compared (Table 3), elicitation rates were significantly higher for facilitated MEPs on both sides in both the dTMS and TMS groups (Figure 2; dTMS left, p = 0.023; dTMS right, p = 0.041; TMS left, p < 0.001; TMS right, p < 0.001).

Table 3: Comparison between rest and facilitated motor-evoked potentials

			Rest	Facilitation	CI	t/χ^2	*p*
Elicitation rate (n, %)	dTMS	Left	95(92.2%)	102(99.0%)		5.14§	0.023*
		Right	96(93.2%)	102(99.0%)		4.17§	0.041*
	TMS	Left	18(17.5%)	102(99.0%)		82.01§	<0.001*
		Right	25(24.3%)	102(99.0%)		75.01§	<0.001*
Latency (ms)	dTMS	Left (n=95)	27.4(26.1~28.6)	27(25.5~28)			0.091
		Right (n=96)	27.6(26.4~28.6)	27(25.5~28.2)			0.149
	TMS	Left (n=18)	25.9±1.89	25.9±1.99	-0.89~0.94	0.05†	0.960
		Right (n=25)	26.8(25.0~27.6)	25.8(25.0~27.4)			0.485
Amplitude (μv)	dTMS	Left (n=95)	740(335~1550)	3000(1550~4400)			<0.001*
		Right (n=96)	810(312~1825)	3000(2000~4125)			<0.001*
	TMS	Left (n=18)	836±1050	2028±1143	372~2012	3.06†	0.006*
		Right (n=25)	723±863	2194±1402	843~2099	4.84†	<0.001*

†: t value; §: χ^2 value. TMS indicated Figure of eight coil TMS, dTMS indicated dTMS with H-7 coil.

Facilitated MEP latency in the dTMS group tended to be shorter than resting MEP latency but did not reach statistical significance, and no difference was observed in the TMS group (Figure 4A: dTMS left, p = 0.091; dTMS right, p = 0.149; TMS left, p = 0.960; TMS right, p = 0.485). In contrast, facilitated MEP amplitude was significantly higher than resting MEP amplitude for both stimulation types (Figure 4B; dTMS left, p < 0.001; dTMS right, p < 0.001; TMS left, p = 0.006; TMS right, p < 0.001).

Differences between left- and right-sides

To assess the effect of handedness, outcomes were compared between the left and right sides (Table 4). The elicitation rate of resting MEP in the TMS group was slightly higher on the right than on the left, but the difference was not statistically significant (Figure 2; right vs. left, 24.3% vs. 17.5%, p = 0.070).

The elicitation rate of facilitated MEP did not differ significantly between the left and right sides in the TMS group (p = 1). Similarly, both resting and facilitated MEP elicitation rates were comparable between the left and right sides in the dTMS group (p = 1). No significant differences in latency or amplitude of either resting or facilitated MEPs were observed between sides, regardless of stimulation type (Figure 5; p > 0.05).

DISCUSSION

This study is the first prospective crossover trial to compare conventional TMS using a figure-of-eight coil with dTMS using an H7 coil for examination of lower-limb motor cortex MEPs in healthy adult volunteers. We found that dTMS with the H7 coil produced a higher elicitation rate than figure-of-eight coil TMS, although the H7 coil was originally designed for PFC stimulation. MEPs induced by dTMS with the H7 coil showed greater amplitudes and longer latencies than those induced by conventional TMS. For both stimulation methods, facilitated MEPs demonstrated higher elicitation rates and amplitudes than resting MEPs, whereas latency did not differ significantly between facilitated and resting conditions. In addition, elicitation rate, latency, and amplitude did not differ significantly between the left and right sides.

dTMS is a recently developed noninvasive magnetic stimulation technique first introduced by Roth *et al*. in 2002.[12] Compared with conventional TMS, dTMS produces a deeper and more widely distributed magnetic field. The electric field generated by an H-coil arises from multiple coil elements with currents flowing in the same direction.[12] Multiple windings arranged in different planes within the H-coil helmet allow deeper stimulation without requiring a proportional increase in electric field intensity. In contrast, a figure-of-eight coil generates a concentrated electric field centered beneath the coil[13] and is positioned more tangentially to the skull surface than the H-coil.[13] Consequently, dTMS with the H7 coil can stimulate the motor cortex at depths of up to approximately 5.5 cm with a stimulation volume of about 75 cm^3.[14] In

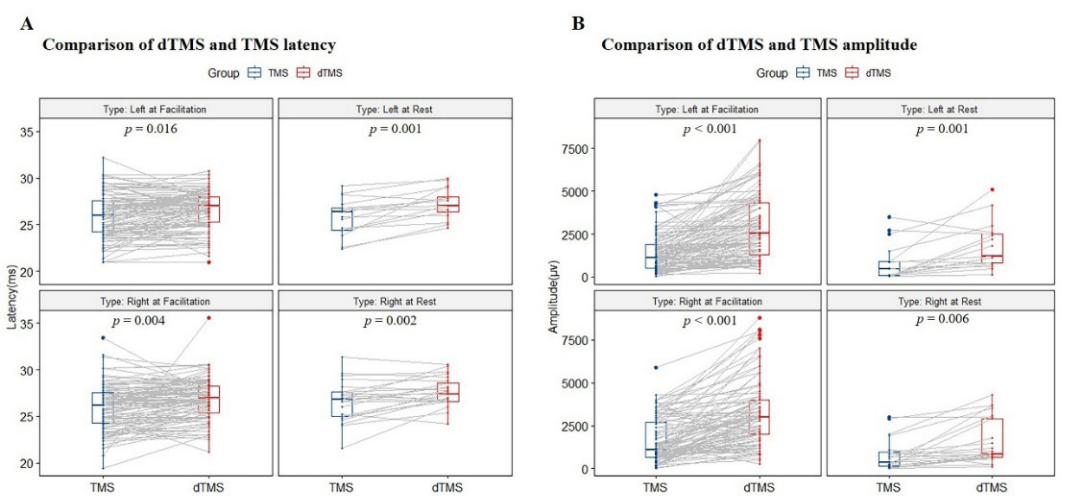

Figure 4. Comparison of resting motor-evoked potentials (MEP) and facilitated MEP for latency (A) and amplitude (B). transcranial magnetic stimulation (TMS) indicated Figure of eight coil TMS, deep transcranial magnetic stimulation (dTMS) indicated dTMS with H7 coil.

Table 4: Comparison of motor-evoked potentials between the left- and right-side groups

			Left	Right	CI	X^2	*p*
Elicitation rate (n, %)	dTMS	Rest	95(92.2%)	96(93.2%)		0[§]	1
		Facilitation	102(99.0%)	102(99.0%)		0[§]	1
	TMS	Rest	18(17.5%)	25(24.3%)		3.27[§]	0.070
		Facilitation	102(99.0%)	102(99.0%)		0[§]	1
Latency (ms)	dTMS	Rest (n=94)	27.5（26.0~28.6）	27.6(26.4~28.6)			0.731
		Facilitation (n=102)	27(25.3~28)	27(25.4~28.3)			0.593
	TMS	Rest (n=16)	25.8±2.0	25.7±1.84	-4.7~0.67	0.38[†]	0.711
		Facilitation (n=102)	26.0±2.41	26.0±2.44	-0.28~0.24	0.16[†]	0.871
Amplitude (μv)	dTMS	Rest (n=94)	745(340~1575)	810(322~1800)			0.579
		Facilitation (n=102)	2550(1275~4300)	3000(2000~4000)			0.235
	TMS	Rest (n=16)	931±1.78	958±987	-560~506	0.11[†]	0.916
		Facilitation (n=102)	1404±1125	1633±1275	-472~13	1.88[†]	0.064

[†]: t value; [§]: χ^2 value. TMS indicated Figure of eight coil TMS, dTMS indicated dTMS with H-7 coil.

contrast, figure-of-eight coil TMS reaches only about 3 cm.[13] Therefore, a single H7-coil dTMS pulse can activate a larger neuronal population than a figure-of-eight coil pulse, increasing the likelihood of recording an MEP and explaining the higher elicitation rate. MEP amplitude reflects a compound signal generated by descending corticospinal volleys originating from different neural generators. Amplitude depends on the summation and temporal dispersion of these volleys as well as spinal mechanisms.[15] Broader stimulation recruits a larger number of

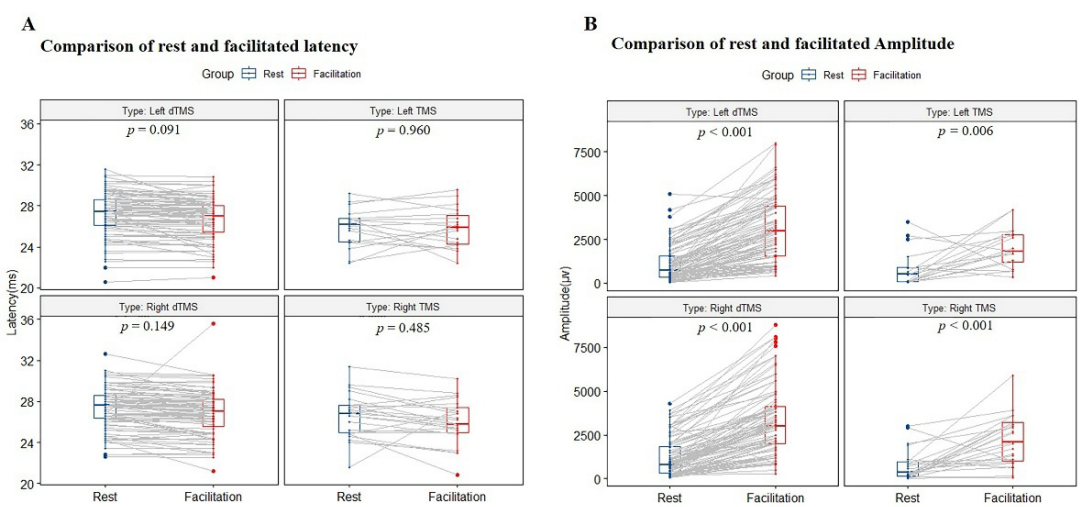

Figure 5. Comparison of the motor-evoked potentials latency (A) and amplitude (B) between the left and right sides (transcranial magnetic stimulation [TMS] indicated Figure of eight coil TMS, deep transcranial magnetic stimulation [dTMS] indicated dTMS with H7 coil).

simultaneously activated neurons, influencing temporal dispersion and producing a stronger signal and therefore a larger amplitude. This interpretation is consistent with studies reporting lower resting and active motor thresholds with H-coil TMS than with figure-of-eight coil TMS.[16]

We also observed that dTMS with the H7 coil produced longer MEP latency than figure-of-eight coil TMS. At least four cortical motor regions are involved in movement generation: the primary motor cortex (M1), premotor cortex (PMC), supplementary motor area, and cingulate motor area.[17]54.23% [152] were located in the primary motor cortex (PMC MEPs can also be elicited from the PMC[17]54.23% [152] were located in the primary motor cortex (PMC, and dTMS with the H7 coil activates additional anterior cortical regions.[7] Therefore, dTMS-evoked MEPs may represent combined contributions from both M1 and PMC. In primates, the PFC influences movement not only through short association (U) fibers connecting to M1 but also via direct corticospinal projections[18], mediated by layer V pyramidal neurons in the PMC.[19] In humans, PMC–M1 connectivity has been demonstrated using a three-pulse ipsilateral TMS technique[20], and direct corticospinal connections have been suggested by fiber-tracking imaging, although evidence is limited.[21] Previous studies have reported longer MEP latency when stimulation involves the PMC rather than M1[19,22], consistent with our findings. Although the H-coil produces a broader electric field distribution than the figure-of-eight coil, the latter can generate locally stronger peak fields, and the mean electric field intensity above 100 V/m may exceed that of the H-coil.[16]

Motor imagery or voluntary facilitation markedly increases MEP responsiveness. The MEP response rate during movement imagery has been reported to be higher than at rest[23], consistent with our findings. Facilitation enhances corticospinal excitability. Voluntary contraction has been reported to produce higher MEP amplitude and shorter latency than resting MEPs.[24] Although we confirmed a higher amplitude in facilitated MEPs, we did not observe latency shortening, which differs from some previous reports. The increased amplitude and elicitation rate of facilitated MEPs may result from increased excitability of the spinal motoneuron pool and changes in descending corticospinal volleys.[25] Differences in latency findings may be attributable to population differences, as prior studies included patients with Parkinson's disease[24], whereas our participants were healthy volunteers.

We also evaluated the effect of handedness and found no significant influence on MEP responses for either stimulation type. In the resting condition with figure-of-eight coil TMS, the elicitation rate and amplitude approached but did not reach statistical significance. Previous studies have likewise reported that MEP responses are not significantly affected by handedness.[26] Although the left hemisphere may exhibit a slightly higher motor threshold than the right, the difference is not statistically significant.[26] A functional near-infrared spectroscopy study also found no significant difference in oxyhemoglobin peak values between hemispheres after M1 stimulation[27], supporting the absence of a handedness effect on MEP responses.

Beyond improved MEP elicitation, dTMS with the H7 coil has demonstrated therapeutic efficacy in several conditions, including treatment-resistant depression[28], substance-use disorders[29], and Alzheimer's disease.[30] In patients with severe stroke, dTMS with the H7 coil may offer advantages over figure-of-eight coil TMS, particularly in extensive M1 or PMC lesions. Future studies should further evaluate the therapeutic potential of H7-coil dTMS in these populations.

Despite the rigorous study design and implementation, several limitations should be acknowledged. First, MEPs influenced by age, height, and sex[31]; therefore, subgroup analyses are needed to determine the effects of these variables and their potential confounding influence. Second, the lower elicitation rate with figure-of-eight coil TMS resulted in a small sample size for comparisons of latency and amplitude in resting MEPs; studies with a larger simple size are required for confirmation. Third, round-coil TMS is generally considered more suitable for accurate hotspot localization, and thus, the present study provides limited insight specifically for figure-of-eight coil stimulation.

In conclusion, compared with figure-of-eight coil TMS, dTMS with the H7 coil more effectively elicits lower-extremity resting MEPs in healthy individuals but does not provide superior facilitated MEPs. MEP responses are influenced by facilitation state but not by handedness. Establishing normative reference values specifically for H7-coil dTMS is recommended, as currently available reference data were obtained using round coils.

DISCLOSURE

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Conflict of interest: None

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