Current Behavioral Neuroscience Reports
https://doi.org/10.1007/s40473-024-00281-y

Efficacy and Safety of Deep Transcranial Magnetic Stimulation Versus High-Frequency Repetitive Transcranial Magnetic Stimulation for Major Depressive Disorder: A Systematic Review

Nan Zhang[1] · Yu Mo[2] · Xian-Jun Lan[2] · Qi-Man Liu[3,4] · Wen-Xiu Li[1] · Xing-Bing Huang[3,4] · Hua-Wang Wu[1] · Shi-Chao Xu[3,4] · Shu-Yun Li[3,4] · Xin-Hu Yang[3,4] · Wei Zheng[3,4]

Accepted: 12 June 2024

Abstract

Objective Deep transcranial magnetic stimulation (dTMS), an alternative technique to repetitive transcranial magnetic stimulation (rTMS), can generate suprathreshold fields in the lateral frontal regions up to 5–6 cm in depth, with stimulator output power exceeding 120% of the hand movement threshold. This systematic review aimed to evaluate and compare the safety and effectiveness of dTMS with that of high-frequency rTMS (HF-rTMS; ≥10 Hz) in individuals diagnosed with major depressive disorder (MDD).

Methods Chinese and English databases were searched for randomized controlled trials (RCTs) comparing dTMS and HF-rTMS. The overall antidepressant response and remission rates were the co-primary outcomes.

Results Two RCTs ($n=203$) investigating the efficacy and safety of dTMS ($n=100$) versus HF-rTMS ($n=103$) in adult patients with MDD met the inclusion criteria. The two included studies were of high quality, with a Jadad score of ≥3. Among the two RCTs, the overall antidepressant response rate was significantly higher in the dTMS (60.0%) than in the HF-rTMS group (41.7%). Only one RCT reported the antidepressant remission rates, demonstrating no significant difference between the two TMS groups. Compared to HF-rTMS, dTMS elicited more muscle twitching/spasms or jaw pain incidences. Other adverse events and discontinuation rates (dTMS group: 12% versus HF-rTMS group: 5%) were similar across both RCTs.

Conclusion dTMS leads to a better antidepressant response than HF-rTMS, although both interventions have favorable safety profiles. However, more RCTs using rigorous methodologies are warranted.

Keywords Deep TMS · High-frequency rTMS · Major depressive disorder · Systematic review · Response

Introduction

Depression is a leading cause of the global burden of disease and a major contributor to disability worldwide [1]. Approximately 4.7% of the world's population experiences depression during a 12-month period [2]. Moreover, major depressive disorder (MDD) is one of the primary global causes of premature death [3]. Patients with MDD are more likely (approximately 20 times more) to die by suicide than those in the general population [4]. Although medication has demonstrated greater effectiveness in treating MDD than placebo [5], it is associated with side effects [6]. Further, only one-third of the patients with MDD achieve remission after initial antidepressant therapy [7]. Consequently, a key strategy to manage MDD is developing and

Nan Zhang and Yu Mo contributed equally to this work.

✉ Xin-Hu Yang
youngxinhu@foxmail.com

✉ Wei Zheng
zhengwei0702@163.com

1 Beijing Haidian Psychological Rehabilitation Hospital, Beijing, China

2 The Brain Hospital of Guangxi Zhuang Autonomous Region, LiuZhou, China

3 The Affiliated Brain Hospital of Guangzhou Medical University, Guangzhou, China

4 Key Laboratory of Neurogenetics and Channelopathies of Guangdong Province and the Ministry of Education of China, Guangzhou Medical University, Guangzhou, China

Published online: 05 August 2024

testing novel therapies, such as high-frequency repetitive transcranial magnetic stimulation (HF-rTMS) [8], deep TMS (dTMS) [9], transcranial direct current stimulation (tDCS) [10], and transcranial alternating current stimulation (tACS) [11].

Among these interventions, rTMS is a non-invasive neuromodulation technique producing brain activity changes in relation to the applied frequency. In principle, high-frequency stimulation (≥ 5 Hz) increases neuronal excitability and inhibits synaptic transmission [12]. Increasing randomized controlled trials (RCTs) and meta-analyses have shown that active rTMS is more effective than sham stimulation in treating adult MDD [13–15] or adolescent first-episode MDD [16, 17]. In 2008, the US Food and Drug Administration (FDA) approved the first rTMS device for MDD treatment, utilizing a figure-of-eight (F8)-coil [18]. However, several studies have reported low rates of rTMS treatment response and remission in MDD [13, 14]. For example, Berlim et al. found that approximately 13 rTMS sessions yielded response and remission rates of 30% and 20%, respectively [13]. Nevertheless, rTMS has been demonstrated to be therapeutically safe [19–21]. Therefore, clinically valuable strategies are warranted to enhance rTMS efficacy.

In the case of coil types, the Hesed coil (H1-coil) generates a wider electric field than the F8-coil, thereby addressing concerns over target localization in clinical practice [22]. Moreover, the deep magnetic field created by dTMS has been suggested to enhance white matter recruitment and facilitate propagation to the subcortical areas, potentially improving antidepressant response to TMS [22, 23]. In 2013, the FDA approved a second TMS device, a dTMS instrument employing the H-coil, for MDD treatment [18]. The benefits and good tolerance of dTMS have been indicated in numerous RCTs among patients with depression [9, 24, 25]. Furthermore, a meta-analysis of 10 studies suggested that high-frequency dTMS was effective and acceptable for managing unipolar and treatment-resistant depression [26]. However, studies comparing dTMS and HF-rTMS for depression treatment have found inconsistent results [27, 28]. For example, Filipčić et al. determined that dTMS resulted in superior response rates compared with rTMS [27]. However, another study [28] revealed no significant differences in the response rates between dTMS and HF-rTMS treatments.

Currently, no systematic reviews have been published on the efficacy and safety of HF-rTMS and dTMS in adults with MDD. Therefore, this systematic review aimed to examine the safety and effectiveness of dTMS versus HF-rTMS in adults with MDD. Based on the findings of Filipčić et al. [27], we hypothesized that dTMS would yield a significantly higher response rate than HF-rTMS in adult patients with MDD.

Methods

Literature Review

Two independent investigators (NZ and YM) systematically searched six online databases (Chinese Journal Net, WanFang, PubMed, the Cochrane Library, PsycINFO, and EMBASE) up to July 6, 2023. The search terms used were as follows: ("repetitive transcranial magnetic stimulation" OR rTMS OR TMS OR "transcranial magnetic stimulation") AND ("deep transcranial magnetic stimulation" OR "deep repetitive transcranial magnetic stimulation" OR deep rTMS OR deep TMS OR dTMS OR H-coil) AND (depress* OR dysphor* OR dysthymi* OR melanchol* OR antidepress* OR bipolar OR MDD). Additionally, hand-searching of the references from the included studies [27, 28] and the relevant reviews [22, 29]was conducted independently by two investigators (NZ and YM) to identify any additional studies .

Selection Criteria

According to the Preferred Reporting Items for Systematic Reviews and Meta Analyzes guidelines [30], the following PICOS criteria were considered when selecting the relevant studies. ***P***articipants: based on the respective studies, adults (≥ 18 years) diagnosed with MDD. ***I***ntervention versus ***C***omparison: dTMS with the H-coil plus antidepressants versus HF-rTMS with the F8-coil plus antidepressants. ***O***utcomes: remission (e.g., the Montgomery–Asberg Depression Rating Scale [MADRS] [31] scores ≤ 10 or Hamilton Depression Scale [HAMD] [32] scores ≤ 7) and antidepressant response (e.g., 50% reduction from the baseline HAMD or MADRS scores) rates as measured by the corresponding depression scales were the primary outcomes of the analysis. Secondary outcomes comprised depressive symptom changes as evidenced by the depression scales (e.g., HAMD or MADRS), discontinuation rates, and adverse events. ***S***tudy: the inclusion of the studies was limited to published RCTs on the efficacy and safety of dTMS with the H-coil versus HF-rTMS with the F8-coil for patients with MDD. No review articles, retrospective studies, or case reports/series were included in this systematic review.

Data Extraction

Using a predetermined checklist, two investigators (NZ and YM) independently extracted the data. Specifically, data concerning the characteristics of each included study (e.g.,sex and age), stimulation parameters (e.g., intensity, duration, and train time per stimulation session), and treatment details (e.g., total pulses, total sessions, and total pulses per session) were collected. In the case of discrepancies, the two investigators attempted to reach a consensus,

along with the assistance of a senior researcher (WZ), when necessary. Further, the first and/or corresponding authors of the respective studies were contacted when clarification for unclear or missing information was required.

Assessment of Study Quality

The Cochrane risk of bias tool [33] and the Jadad scale [34] were independently applied by the two investigators (NZ and YM) to assess study quality. Studies scoring 3 points on the Jadad scale were considered high quality.

Results

Database Search Results

Using the earlier mentioned databases, we initially identified 1,025 articles (Fig. 1). Ultimately, two RCTs [27, 28] that met the inclusion criteria were included.

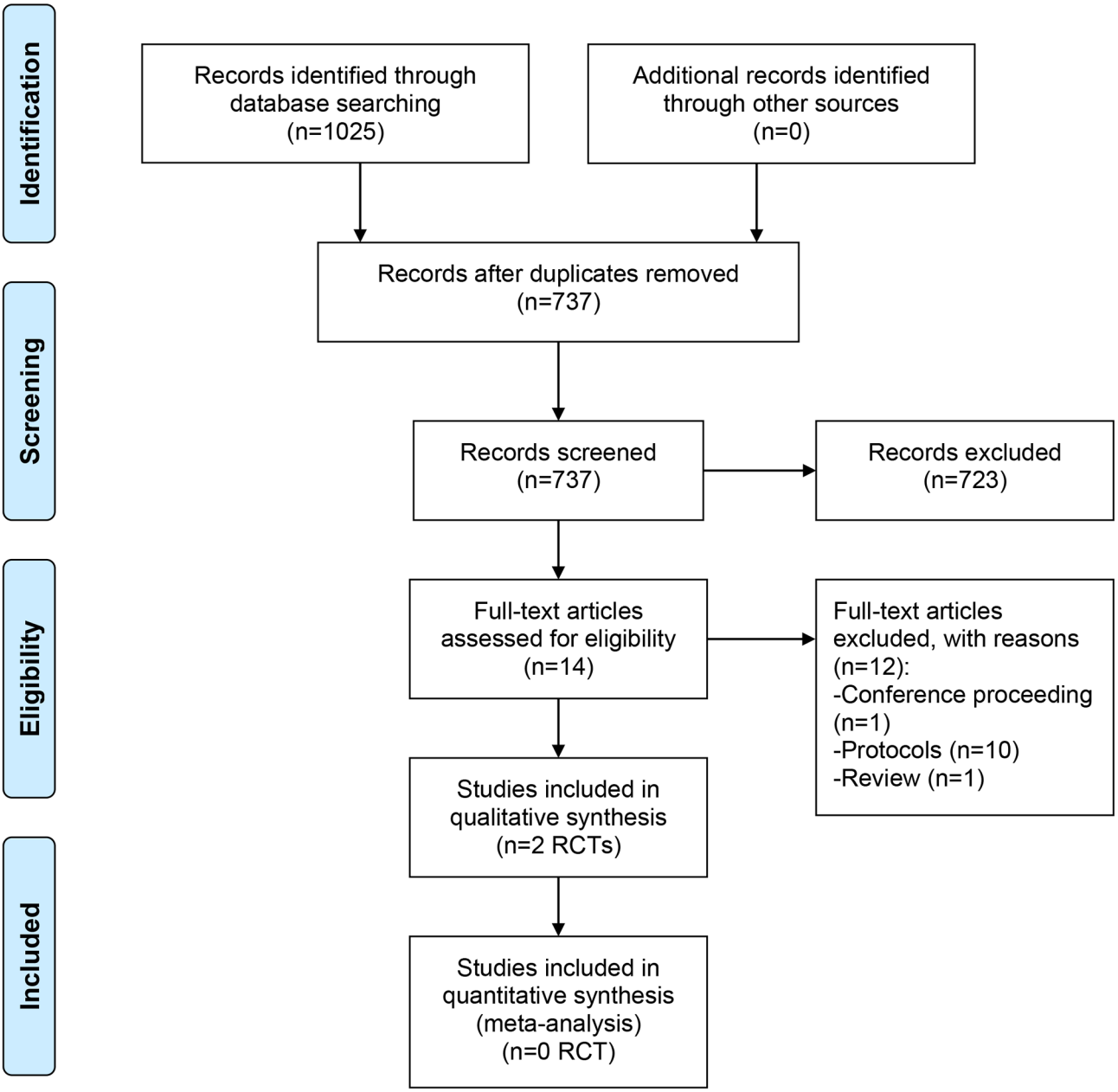

Fig. 1 Cochrane risk of bias tool items
Abbreviations: PRISMA=Preferred Reporting Items for Systematic reviews and Meta-Analyses; RCT=randomized clinical trial.

Characteristics of Study Samples

The patient characteristics and dTMS/HF-rTMS parameters of each included RCT are summarized in Table 1. A total of 203 patients with MDD were enrolled in the two RCTs that compared dTMS ($n = 100$) with HF-rTMS ($n = 103$). Among them, 43.3% of the patients were male, with a median age of 23–51 years. All patients received treatment at the left dorsolateral prefrontal cortex (L-DLPFC) for 2 or 4 weeks. In the included RCTs, dTMS (18 Hz) was administered at an average dose of 1,980 pulses per session, whereas HF-rTMS (10 Hz) was provided at 1,400–3,000 pulses per session. Furthermore, the total dose of dTMS varied from 19,800 to 39,600 pulses, while that of HF-rTMS was 14,000–60,000 pulses.

Quality Assessment

As shown in Fig. 2, the two included RCTs [27, 28] were judged to be "low risk" in terms of random sequence generation, blinding of outcome assessment, incomplete outcome data addressed, and selective reporting according to the Cochrane risk of bias tool. Additionally, the two RCTs had Jadad scores of 3 [27] and 4 [28], indicating their high quality.

Study-Defined Response and Remission

The antidepressant response and remission rates of dTMS versus HF-rTMS as adjunctive therapy for MDD are listed in Table 2. In the two RCTs [27, 28] the overall antidepressant response rate was significantly higher in the dTMS (60.0%) than in the HF-rTMS group (41.7%). However, only one RCT [27] reported the antidepressant remission rates, in which no significant difference was observed between the two TMS groups (dTMS group: 59.7% versus HF-rTMS group: 42.7%; $P > 0.05$).

Improvement in Depressive Symptoms

The two RCTs [27, 28] revealed alleviation of depressive symptoms as measured by HAMD-17, although these findings were inconsistent (Table 2). Moreover, dTMS was found to be significantly superior to HF-rTMS in ameliorating depressive symptoms in the study by Filipčić et al. [27]; however, this observation was not corroborated by Yang et al. [28].

Adverse Events and Discontinuation Rates

Filipčić et al. [27] showed that compared to HF-rTMS (0%), dTMS (12%) caused more muscle twitching/spasms or jaw

Table 1 Patient characteristics and dTMS/HF-rTMS parameters in the included studies

Study	Sample size (n)[a]	•Diagnostic criteria •Setting (%) •Diagnosis (%)	•Illness duration (years)[c] •Male[a] (%)	Age (years), median	Medication status	•Treatment duration (wk) •Treatment site	•Intensity (%MT) •Frequency (Hz) •Coil type		•Stimulus time per session (min) •Train duration (s) •Intertrain interval (s)		•Pulses per session •Number of sessions •Total pulses		Jadad score
							dTMS	HF-rTMS	dTMS	HF-rTMS	dTMS	HF-rTMS	
Filipčić et al., 2019	Total: 147 dTMS: 72 rTMS: 75	•DSM-5 •Outpatients (100) •MDD (100)	•7–10 •49.0	dTMS: 50.0; rTMS:51.0	Psychotropics allowed	•4 •L-DLPFC	•120 •18 •H1-coil	•120 •10 •F8-coil	•20 •2 •20	•40 •4 •26	•1980 •20 •39,600	•3000 •20 •60,000	3
Yang et al., 2023	Total: 56 dTMS: 28 rTMS: 28	•ICD-10[b] •NR •MDD (100)	•NR •28.6	dTMS: 23.0; rTMS:25.0	Psychotropics allowed	•2 •L-DLPFC	•120 •18 •H1-coil	•100 •10 •F8-coil	•20.2 •2 •20	•21.3 •4 •28	•1980 •10 •19,800	•1400 •10 •14,000	4

[a]Overall number of patients.

[b]Diagnosis verified using the MINI.

[c]Available data were median (IQR).

Abbreviations: DSM-5 = Diagnostic and Statistical Manual of Mental Disorders 5th edition; dTMS = deep transcranial magnetic stimulation; F8 = figure-of-eight; HF-rTMS = high-frequency repetitive transcranial magnetic stimulation; ICD-10 = International Classification of Diseases 10th edition; IQR = interquartile range; L-DLPFC = left dorsolateral prefrontal cortex; MDD = major depressive disorder; MINI = Mini International Neuropsychiatric Interview; min = minutes; MT = motor threshold; NR = not reported; s = seconds; wk = weeks.

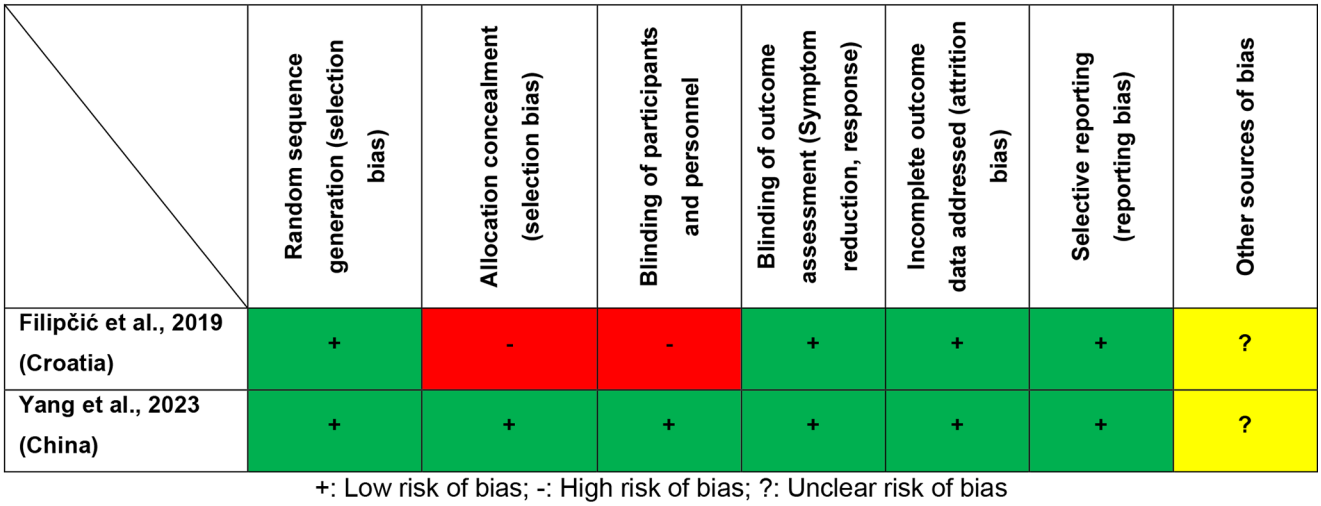

Fig. 2 Cochrane risk of bias tool items. +: Low risk of bias; -: High risk of bias; ?: Unclear risk of bias.

Table 2 dTMS versus HF-rTMS for patients with MDD: study-defined response and change in depressive symptoms

Study	Primary outcomes	dTMS group (% [*n*])	HF-rTMS group (% [*n*])	Significance[b]
Filipčić et al., 2019	Study-defined response[a]	66.7 (48/72)	44.0 (33/75)	$P < 0.05$
Yang et al., 2023	Study-defined response[a]	42.9 (12/28)	35.7 (10/28)	NS
Total	Study-defined response	60.0 (60/100)	41.7 (43/103)	$P < 0.05$
Filipčić et al., 2019	Study-defined remission[c]	59.7 (43/72)	42.7 (32/75)	NS
Yang et al., 2023	Study-defined remission	NR	NR	-
Total	Study-defined remission	-	-	-
Study	Secondary outcomes	dTMS group (mean [± SD])	HF-rTMS group (mean [± SD])	Significance[b]
Filipčić et al., 2019	Improvement in depressive symptoms[d] (at endpoint)	7 (5.6)	10 (6.9)	$P < 0.05$
Yang et al., 2023	Improvement in depressive symptoms[d] (at endpoint)	11.9 (4.4)	14.7 (8.4)	NS

[a]Defined as ≥ 50% reduction from the HAMD-17 total score at baseline.

[b]Reflects the differences between the rTMS and rTMS groups at the treatment endpoints.

[c]Defined as HAMD-17 score ≤ 7.

[d]Measured by HAMD-17.

Abbreviations: dTMS = deep transcranial magnetic stimulation; HAMD-17 = a 17-item Hamilton Depression Rating Scale; HF-rTMS = high-frequency repetitive transcranial magnetic stimulation; MDD = major depressive disorder; NS = not significant; NR = not reported.

pain incidences (Table 3). Other adverse events (e.g., headaches and dizziness) and discontinuation rates were not significantly different between the two TMS groups (dTMS group: 12% versus HF-rTMS group: 5%) in both RCTs (Table 3).

Discussion

Our systematic review, encompassing two RCTs [27, 28] involving 203 adults with MDD, is the first to examine the efficacy and safety of dTMS versus HF-rTMS for treating MDD. The main findings of this systematic review are as follows: (1) dTMS provides a more pronounced overall antidepressant response than HF-rTMS; (2) dTMS causes more muscle twitching/spasms or jaw pain incidences than HF-rTMS; and (3) both RCTs have similar rates of other adverse events and discontinuation. Moreover, the two RCTs were published within the last 5 years, implying growing clinical interest in applying HF-rTMS and dTMS for patients with MDD.

In our systematic review, the dTMS group exhibited a significantly higher overall antidepressant response rate than the HF-rTMS group. However, these results were inconsistent between the two included RCTs, possibly due to the differences in the treatment courses. According to previous meta-analyses [35, 36], depression severity demonstrated greater reduction after 20 sessions than after 10 sessions

Table 3 dTMS versus HF-rTMS for patients with MDD: rates of discontinuation and adverse effects

Study	Adverse effects	dTMS group (*n* [%])	HF-rTMS group (*n* [%])	Significance[a]
Filipčić et al., 2019	Anxiety	0 (0)	1 (1)	NS
	Application site pain	5 (7)	0 (0)	NS
	Application site discomfort	3 (4)	1 (1)	NS
	Dizziness	4 (6)	2 (3)	NS
	Headache	20 (29)	15 (20)	NS
	Insomnia	5 (7)	5 (7)	NS
	Muscle twitching/spasms or jaw pain	8 (12)	0 (0)	$P < 0.05$
Yang et al., 2023	Dizziness	1 (4)	0 (0)	NS
	Facial numbness	1 (4)	0 (0)	NS
	Headache	1 (4)	2 (7)	NS
	Neck and dental discomfort	1 (4)	0 (0)	NS
Study	Discontinuation rate (*n* [%])	dTMS group (*n* [%])	HF-rTMS group (*n* [%])	Significance[a]
Filipčić et al., 2019	10 (7)	7 (10)	3 (4)	NS
Yang et al., 2023	7 (13)	5 (18)	2 (7)	NS
Total	17 (8)	12 (12)	5 (5)	NS

[a]Reflects the differences between the dTMS and rTMS groups at the treatment endpoints.

Abbreviations: dTMS = deep transcranial magnetic stimulation; HF-rTMS = high-frequency repetitive transcranial magnetic stimulation; MDD = major depressive disorder; NR = not reported; NS = not significant.

of dTMS or HF-rTMS. In the included RCT by Filipčić et al., dTMS resulted in a significantly greater response rate than HF-rTMS after 20 sessions [27]. In contrast, Yang et al. found that the response rates were not statistically different after 10 sessions of dTMS versus HF-rTMS [28]. Therefore, at least 20 sessions may be required to obtain clinically meaningful effects in patients with acute MDD, regardless of rTMS or dTMS techniques [37]. Apart from the antidepressant effects of dTMS, dTMS using different H-coils has also been applied for treating obsessive-compulsive disorder (OCD) [38], smoking addiction [39], and schizophrenia [40]. For example, the Yale–Brown Obsessive-Compulsive Scale scores of patients with OCD who were treated with active dTMS were shown to be significantly lower than those of sham-treated patients [38].

The precise mechanism underlying the alleviation of depressive symptoms by dTMS in patients with MDD remains uncertain. Nevertheless, accumulating studies have suggested that individuals with MDD exhibit diminished activity in the L-DLPFC when experiencing negative emotions [41, 42]. Thus, the DLPFC, a component of the cognitive control network (CCN), represents a critical target for TMS therapy [43, 44]. In this strategy, dTMS can be used to stimulate the left DLPFC to directly affect the cognitive processes regulated by the CCN, subsequently modulating the cognitive and affective functions [44, 45]. Consequently, applying dTMS to specifically target the left DLPFC may serve as an effective intervention for MDD. Additionally, the H1-coil provides a greater penetration depth in specific brain structures than the F8-coil [46], suggesting a potential link between dTMS efficacy and the ability of the H1-coil to directly stimulate wider and deeper PFC structures [46]. However, the effect of distinct stimulation parameter settings and pulse counts on treatment efficacy remains unclear in both TMS modalities. Hence, further investigation on the varied treatment parameters of dTMS and HF-rTMS is essential.

Although the incidence of muscle twitches/spasms or jaw pain was greater in dTMS than in HF-rTMS, the rates of discontinuation and adverse events were similar across both techniques. Moreover, dTMS has been proven safe among patients with OCD [38], severe and enduring anorexia nervosa (SE-AN) [47], bipolar depression (BD) [48], Parkinson's disease (PD) [49], and obesity [50]. For example, Knyahnytska et al. demonstrated that dTMS was low-risk and well-accepted in patients with SE-AN [47]. Similarly, dTMS was shown to be a well-received add-on therapy for patients with BD undergoing appropriate pharmacotherapy [48]. All these findings imply that using dTMS or HF-rTMS in clinical practice may be a generally safe and well-tolerated treatment strategy [51].

This systematic review has several limitations that should be considered. First, we were only able to extract data from two existing RCTs. Consequently, the study should be expanded with more RCTs in the future. Second, a meta-analysis could not be conducted due to significant heterogeneity among the included RCTs. Third, other unpublished studies with smaller (non-significant) effect sizes may be present because we did not incorporate unpublished data in this systematic review, leading to the possibility of publication bias. Finally, our systematic review was unregistered.

Conclusion

dTMS is associated with a better antidepressant response than HF-rTMS in adult patients with MDD, although both treatment modalities have favorable safety profiles. However, additional RCTs employing rigorous methodologies are warranted.

Acknowledgements None.

Author Contributions Study design and conceptualization: Wei Zheng and Xin-Hu Yang; conducting of the literature search: Zhang Nan, Yu Mo and Xian-Jun Lan; Data analysis: Yu Mo, Qi-Man Liu, Hua-Wang Wu, Shi-Chao Xu and Shu-Yun Li; Drafting of the manuscript: Nan Zhang and Yu Mo. Critical revision of the manuscript: Wei Zheng, Xin-Hu Yang, Wen-Xiu Li and Xing-Bing Huang; Approval of the final version for publication: All the authors.

Funding This study was funded by the National Natural Science Foundation of China (82101609), Scientific Research Project of Guangzhou Bureau of Education (202032762), Guangzhou Health Science and Technology Project (20211A011045), Guangzhou Science and Technology Project of traditional Chinese Medicine and integrated traditional Chinese and Western medicine (20212A011018), China International Medical Exchange Foundation (Z-2018-35-2002), Science and Technology Program Project of Guangzhou (202102020658), the Science and Technology Program of Guangzhou (2023A03J0839 and 2023A03J0436), Science and Technology Planning Project of Liwan District of Guangzhou (202201012), The Natural Science Foundation Program of Guangdong (2023A1515011383), Guangzhou Municipal Key Discipline in Medicine (2021–2023), Guangzhou High-level Clinical Key Specialty, Department of Emergency Medicine of National clinical key specialty, and Guangzhou Research-oriented Hospital. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Data Availability No datasets were generated or analysed during the current study.

Declarations

Research Involving Human Participants and/or Animals Not applicable.

Conflicts of Interest The authors declare no conflicts of interest in conducting this study or preparing the manuscript.

Competing Interests The authors declare no competing interests.

References

1. GBD 2019 Diseases and Injuries Collaborators. Global burden of 369 diseases and injuries in 204 countries and territories, 1990–2019: a systematic analysis for the global burden of disease study 2019. Lancet (London England). 2020;396:1204–22. https://doi.org/10.1016/s0140-6736(20)30925-9
2. Ferrari AJ, Somerville AJ, Baxter AJ, Norman R, Patten SB, Vos T, Whiteford HA. Global variation in the prevalence and incidence of major depressive disorder: a systematic review of the epidemiological literature. Psychol Med. 2013;43:471–81. https://doi.org/10.1017/s0033291712001511
3. Herrman H, Patel V, Kieling C, Berk M, Buchweitz C, Cuijpers P, Furukawa TA, Kessler RC, Kohrt BA, Maj M, et al. Time for united action on depression: a lancet-world psychiatric association commission. Lancet (London England). 2022;399:957–1022. https://doi.org/10.1016/s0140-6736(21)02141-3
4. Chesney E, Goodwin GM, Fazel S. Risks of all-cause and suicide mortality in mental disorders: a meta-review. World Psychiatry: Official J World Psychiatric Association (WPA). 2014;13:153–60. https://doi.org/10.1002/wps.20128
5. Chen C, Shan W. Pharmacological and non-pharmacological treatments for major depressive disorder in adults: a systematic review and network meta-analysis. Psychiatry Res. 2019;281:112595. https://doi.org/10.1016/j.psychres.2019.112595
6. Croatto G, Vancampfort D, Miola A, Olivola M, Fiedorowicz JG, Firth J, Alexinschi O, Gaina MA, Makkai V, Soares FC, et al. The impact of pharmacological and non-pharmacological interventions on physical health outcomes in people with mood disorders across the lifespan: an umbrella review of the evidence from randomised controlled trials. Mol Psychiatry. 2023;28:369–90. https://doi.org/10.1038/s41380-022-01770-w
7. Trivedi MH, Rush AJ, Wisniewski SR, Nierenberg AA, Warden D, Ritz L, Norquist G, Howland RH, Lebowitz B, McGrath PJ, et al. Evaluation of outcomes with citalopram for depression using measurement-based care in STAR*D: implications for clinical practice. Am J Psychiatry. 2006;163:28–40. https://doi.org/10.1176/appi.ajp.163.1.28
8. Lan XJ, Yang XH, Qin ZJ, Cai DB, Liu QM, Mai JX, Deng CJ, Huang XB, Zheng W. Efficacy and safety of intermittent theta burst stimulation versus high-frequency repetitive transcranial magnetic stimulation for patients with treatment-resistant depression: a systematic review. Front Psychiatry. 2023;14. https://doi.org/10.3389/fpsyt.2023.1244289
9. Levkovitz Y, Isserles M, Padberg F, Lisanby SH, Bystritsky A, Xia G, Tendler A, Daskalakis ZJ, Winston JL, Dannon P, et al. Efficacy and safety of deep transcranial magnetic stimulation for major depression: a prospective multicenter randomized controlled trial. World Psychiatry: Official J World Psychiatric Association (WPA). 2015;14:64–73. https://doi.org/10.1002/wps.20199
10. Palm U, Hasan A, Strube W, Padberg F. tDCS for the treatment of depression: a comprehensive review. Eur Arch Psychiatry Clin NeuroSci. 2016;266:681–94. https://doi.org/10.1007/s00406-016-0674-9
11. Zheng W, Cai DB, Nie S, Chen JH, Huang XB, Goerigk S, Brunoni AR, Zheng W. Adjunctive transcranial alternating current stimulation for patients with major depressive disorder: a systematic review and meta-analysis. Front Psychiatry. 2023;14. https://doi.org/10.3389/fpsyt.2023.1154354
12. Milev RV, Giacobbe P, Kennedy SH, Blumberger DM, Daskalakis ZJ, Downar J, Modirrousta M, Patry S, Vila-Rodriguez F, Lam RW, et al. Canadian network for mood and anxiety treatments (CANMAT) 2016 clinical guidelines for the management of adults with major depressive disorder: Sect. 4. Neurostimulation treatments. Can J Psychiatry. 2016;61:561–75. https://doi.org/10.1177/0706743716660033
13. Berlim MT, van den Eynde F, Tovar-Perdomo S, Daskalakis ZJ. Response, remission and drop-out rates following high-frequency repetitive transcranial magnetic stimulation (rTMS) for treating major depression: a systematic review and meta-analysis of randomized, double-blind and sham-controlled trials. Psychol Med. 2014;44:225–39. https://doi.org/10.1017/s0033291713000512
14. George MS, Lisanby SH, Avery D, McDonald WM, Durkalski V, Pavlicova M, Anderson B, Nahas Z, Bulow P, Zarkowski P, et al. Daily left prefrontal transcranial magnetic stimulation therapy for

major depressive disorder: a sham-controlled randomized trial. Arch Gen Psychiatry. 2010;67:507–16. https://doi.org/10.1001/archgenpsychiatry.2010.46
15. Vida RG, Sághy E, Bella R, Kovács S, Erdősi D, Józwiak-Hagymásy J, Zemplényi A, Tényi T, Osváth P, Voros V. Efficacy of repetitive transcranial magnetic stimulation (rTMS) adjunctive therapy for major depressive disorder (MDD) after two antidepressant treatment failures: meta-analysis of randomized sham-controlled trials. BMC Psychiatry. 2023;23. https://doi.org/10.1186/s12888-023-05033-y
16. Sun CH, Mai JX, Shi ZM, Zheng W, Jiang WL, Li ZZ, Huang XB, Yang XH, Zheng W. Adjunctive repetitive transcranial magnetic stimulation for adolescents with first-episode major depressive disorder: a meta-analysis. Front Psychiatry. 2023;14. https://doi.org/10.3389/fpsyt.2023.1200738
17. Zheng W, Lan XJ, Qin ZJ, Yang XH, Shi ZM. Low-frequency repetitive transcranial magnetic stimulation for children and adolescents with first-episode and drug-naïve major depressive disorder: a systematic review. Front Psychiatry. 2023;14. https://doi.org/10.3389/fpsyt.2023.1111754
18. Perera T, George MS, Grammer G, Janicak PG, Pascual-Leone A, Wirecki TS. The clinical TMS society consensus review and treatment recommendations for TMS therapy for major depressive disorder. Brain Stimul. 2016;9:336–46. https://doi.org/10.1016/j.brs.2016.03.010
19. Rossi S, Hallett M, Rossini PM, Pascual-Leone A. Safety, ethical considerations, and application guidelines for the use of transcranial magnetic stimulation in clinical practice and research. Clin Neurophysiology: Official J Int Federation Clin Neurophysiol. 2009;120:2008–39. https://doi.org/10.1016/j.clinph.2009.08.016
20. Majumder P, Balan S, Gupta V, Wadhwa R, Perera TD. The safety and efficacy of repetitive transcranial magnetic stimulation in the treatment of major depression among children and adolescents: a systematic review. Cureus. 2021;13:e14564. https://doi.org/10.7759/cureus.14564
21. Overvliet GM, Jansen RAC, van Balkom A, van Campen DC, Oudega ML, van der Werf YD, van Exel E, van den Heuvel OA, Dols A. Adverse events of repetitive transcranial magnetic stimulation in older adults with depression, a systematic review of the literature. Int J Geriatr Psychiatry. 2021;36:383–92. https://doi.org/10.1002/gps.5440
22. Zibman S, Pell GS, Barnea-Ygael N, Roth Y, Zangen A. Application of transcranial magnetic stimulation for major depression: coil design and neuroanatomical variability considerations. Eur Neuropsychopharmacology: J Eur Coll Neuropsychopharmacol. 2021;45:73–88. https://doi.org/10.1016/j.euroneuro.2019.06.009
23. Roth Y, Amir A, Levkovitz Y, Zangen A. Three-dimensional distribution of the electric field induced in the brain by transcranial magnetic stimulation using figure-8 and deep H-coils. J Clin Neurophysiology: Official Publication Am Electroencephalographic Soc. 2007;24:31–8. https://doi.org/10.1097/WNP.0b013e31802fa393
24. Kaster TS, Daskalakis ZJ, Noda Y, Knyahnytska Y, Downar J, Rajji TK, Levkovitz Y, Zangen A, Butters MA, Mulsant BH, et al. Efficacy, tolerability, and cognitive effects of deep transcranial magnetic stimulation for late-life depression: a prospective randomized controlled trial. Neuropsychopharmacology: Official Publication Am Coll Neuropsychopharmacol. 2018;43:2231–8. https://doi.org/10.1038/s41386-018-0121-x
25. Matsuda Y, Kito S, Igarashi Y, Shigeta M. Efficacy and safety of deep transcranial magnetic stimulation in office workers with treatment-resistant depression: a randomized, double-blind, sham-controlled trial. Neuropsychobiology. 2020;79:208–13. https://doi.org/10.1159/000505405
26. Kedzior KK, Gellersen HM, Brachetti AK, Berlim MT. Deep transcranial magnetic stimulation (DTMS) in the treatment of major depression: an exploratory systematic review and meta-analysis. J Affect Disord. 2015;187:73–83. https://doi.org/10.1016/j.jad.2015.08.033
27. Filipčić I, Šimunović Filipčić I, Milovac; Sučić S, Gajšak T, Ivezić E, Bašić S, Bajić; Heilig M. Efficacy of repetitive transcranial magnetic stimulation using a figure-8-coil or an H1-Coil in treatment of major depressive disorder; a randomized clinical trial. J Psychiatr Res. 2019;114:113–9. https://doi.org/10.1016/j.jpsychires.2019.04.020
28. Yang L, Ren RJ, Lu WT, Zhao TY, Guo SJ, Liu BF, Huang FF, Chen H, Jin N, Lin Q, et al. An exploratory randomised controlled study on the efficacy and safety of deep transcranial magnetic stimulation in the treatment of depression (in Chinese). Chin J Psychiatry. 2023;56:161–6. https://doi.org/10.3760/cma.j.cn113661-20220920-00266
29. Brunoni AR, Chaimani A, Moffa AH, Razza LB, Gattaz WF, Daskalakis ZJ, Carvalho AF. Repetitive transcranial magnetic stimulation for the acute treatment of major depressive episodes: a systematic review with network meta-analysis. JAMA Psychiatry. 2017;74:143–52. https://doi.org/10.1001/jamapsychiatry.2016.3644
30. Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gøtzsche PC, Ioannidis JP, Clarke M, Devereaux PJ, Kleijnen J, Moher D. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. PLoS Med. 2009;6:e1000100. https://doi.org/10.1371/journal.pmed.1000100
31. Montgomery SA, Asberg M. A new depression scale designed to be sensitive to change. Br J Psychiatry: J Mental Sci. 1979;134:382–9. https://doi.org/10.1192/bjp.134.4.382
32. Hamilton M. A rating scale for depression. J Neurol Neurosurg Psychiatry. 1960;23:56–62. https://doi.org/10.1136/jnnp.23.1.56
33. Higgins JP, Altman DG, Gøtzsche PC, Jüni P, Moher D, Oxman AD, Savovic J, Schulz KF, Weeks L, Sterne JA. The cochrane collaboration's tool for assessing risk of bias in randomised trials. BMJ. 2011;343:d5928. https://doi.org/10.1136/bmj.d5928
34. Jadad AR, Moore RA, Carroll D, Jenkinson C, Reynolds DJ, Gavaghan DJ, McQuay HJ. Assessing the quality of reports of randomized clinical trials: is blinding necessary? Control Clin Trials. 1996;17:1–12. https://doi.org/10.1016/0197-2456(95)00134-4
35. Kedzior KK, Gellersen HM. Two vs. four weeks of high-frequency deep repetitive transcranial magnetic stimulation (HF-DTMS) for major depression: a systematic review and meta-analysis. In Proceedings of the The Magstim 2015 Neuroscience Conference (May 9–10, 2015), Oxford, UK, 2015.
36. Teng S, Guo Z, Peng H, Xing G, Chen H, He B, McClure MA, Mu Q. High-frequency repetitive transcranial magnetic stimulation over the left DLPFC for major depression: session-dependent efficacy: a meta-analysis. Eur Psychiatry: J Association Eur Psychiatrists. 2017;41:75–84. https://doi.org/10.1016/j.eurpsy.2016.11.002
37. Gellersen HM, Kedzior KK. Antidepressant outcomes of high-frequency repetitive transcranial magnetic stimulation (rTMS) with F8-coil and deep transcranial magnetic stimulation (dTMS) with H1-coil in major depression: a systematic review and meta-analysis. BMC Psychiatry. 2019;19:139. https://doi.org/10.1186/s12888-019-2106-7
38. Carmi L, Tendler A, Bystritsky A, Hollander E, Blumberger DM, Daskalakis J, Ward H, Lapidus K, Goodman W, Casuto L, et al. Efficacy and safety of deep transcranial magnetic stimulation for obsessive-compulsive disorder: a prospective multicenter randomized double-blind placebo-controlled trial. Focus (American Psychiatric Publishing). 2022;20:152–9. https://doi.org/10.1176/appi.focus.20103

39. Harmelech T, Roth Y, Tendler A, Deep. TMS H7 coil: features, applications & future. Expert Rev Med Dev. 2021;18:1133–44. https://doi.org/10.1080/17434440.2021.2013803
40. Levkovitz Y, Rabany L, Harel EV, Zangen A. Deep transcranial magnetic stimulation add-on for treatment of negative symptoms and cognitive deficits of schizophrenia: a feasibility study. Int J Neuropsychopharmacol. 2011;14:991–6. https://doi.org/10.1017/s1461145711000642
41. Groenewold NA, Opmeer EM, De Jonge P, Aleman A, Costafreda SGJN, Reviews B. Emotional valence modulates brain functional abnormalities in depression: evidence from a meta-analysis of fMRI studies. 2013, *37*, 152–63.
42. Zhong M, Wang X, Xiao J, Yi J, Zhu X, Liao J, Wang W, Yao S. Amygdala hyperactivation and prefrontal hypoactivation in subjects with cognitive vulnerability to depression. Biol Psychol. 2011;88:233–42. https://doi.org/10.1016/j.biopsycho.2011.08.007
43. Rayner G, Jackson G, Wilson S. Cognition-related brain networks underpin the symptoms of unipolar depression: evidence from a systematic review. Neurosci Biobehav Rev. 2016;61:53–65. https://doi.org/10.1016/j.neubiorev.2015.09.022
44. Li WY, Deng YY, Zhang B. Mechanism of transcranial magnetic stimulation in the treatment of different symptoms of depression. J Neurosci Mental Health(in Chinese). 2020;20:486–9.
45. Niendam TA, Laird AR, Ray KL, Dean YM, Glahn DC, Carter CS. Meta-analytic evidence for a superordinate cognitive control network subserving diverse executive functions. Cogn Affect Behav Neurosci. 2012;12:241–68. https://doi.org/10.3758/s13415-011-0083-5
46. Parazzini M, Fiocchi S, Chiaramello E, Roth Y, Zangen A, Ravazzani P. Electric field estimation of deep transcranial magnetic stimulation clinically used for the treatment of neuropsychiatric disorders in anatomical head models. Med Eng Phys. 2017;43:30–8. https://doi.org/10.1016/j.medengphy.2017.02.003
47. Knyahnytska YO, Blumberger DM, Daskalakis ZJ, Zomorrodi R, Kaplan AS. Insula H-coil deep transcranial magnetic stimulation in severe and enduring anorexia nervosa (SE-AN): a pilot study. Neuropsychiatr Dis Treat. 2019;15:2247–56. https://doi.org/10.2147/ndt.S207630
48. Tavares DF, Myczkowski ML, Alberto RL, Valiengo L, Rios RM, Gordon P, de Sampaio-Junior B, Klein I, Mansur CG, Marcolin MA, et al. Treatment of bipolar depression with deep TMS: results from a double-blind, randomized, parallel group, sham-controlled clinical trial. Neuropsychopharmacology: Official Publication Am Coll Neuropsychopharmacol. 2017;42:2593–601. https://doi.org/10.1038/npp.2017.26
49. Torres F, Villalon E, Poblete P, Moraga-Amaro R, Linsambarth S, Riquelme R, Zangen A, Stehberg J. Retrospective evaluation of deep transcranial magnetic stimulation as add-on treatment for Parkinson's disease. Front Neurol. 2015;6. https://doi.org/10.3389/fneur.2015.00210
50. Ferrulli A, Macrì C, Terruzzi I, Massarini S, Ambrogi F, Adamo M, Milani V, Luzi L. Weight loss induced by deep transcranial magnetic stimulation in obesity: a randomized, double-blind, sham-controlled study. Diabetes Obes Metab. 2019;21:1849–60. https://doi.org/10.1111/dom.13741
51. Tikka SK, Godi SM, Siddiqui MA, Garg S. Evidence from Indian studies on safety and efficacy of therapeutic transcranial magnetic stimulation across neuropsychiatric disorders- a systematic review and meta-analysis. Indian J Psychiatry. 2023;65:18–35. https://doi.org/10.4103/indianjpsychiatry.indianjpsychiatry_572_22