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Comparing the efficacies of transcranial magnetic stimulation treatments using different targeting methods in major depressive disorder: protocol for a network meta-analysis

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ABSTRACT

Introduction Transcranial magnetic stimulation (TMS) over the left dorsolateral prefrontal cortex (lDLPFC) has been widely used as a treatment for major depressive disorder (MDD) in the past two decades. Different methods for localising the lDLPFC target include the '5 cm' method, the F3 method and the neuro-navigational method. However, whether TMS efficacies differ between the three targeting methods remains unclear. We present a protocol for a systematic review and network meta-analysis (NMA) to compare the efficacies of TMS treatments using these three targeting methods in MDD.

Methods and analysis Relevant studies reported in English or Chinese and published up to May 2023 will be identified from searches of the following databases: PubMed, Cochrane Central Register of Controlled Trials, Embase, PsycINFO, China National Knowledge Infrastructure, Wan Fang Database, Chinese BioMedical Literature Database, and China Science and Technology Journal Database. We will include all randomised controlled trials assessing the efficacy of an active TMS treatment using any one of the three targeting methods compared with sham TMS treatment or comparing efficacies between active TMS treatments using different targeting methods. Interventions must include a minimum of 10 sessions of high-frequency TMS over the lDLPFC. The primary outcome is the reduction score of the 17-item Hamilton Depression Rating Scale, 24-item Hamilton Depression Rating Scale or Montgomery-Asberg Depression Rating Scale. The dropout rate is a secondary outcome representing the TMS treatment's acceptability. Pairwise meta-analyses and a random-effects NMA will be conducted using Stata. We will use the surface under the cumulative ranking curve to rank the different targeting methods in terms of efficacy and acceptability.

Ethics and dissemination This systematic review and NMA does not require ethics approval. The results will be submitted for publication in a peer-reviewed journal.

PROSPERO registration number CRD42023410273.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ The network meta-analysis (NMA) will provide both direct and indirect comparisons with respect to the efficacy and acceptability of different targeting methods.
⇒ We will only search Chinese and English databases, and some trials may be unpublished and thus not identified from our searches.
⇒ Transitivity in indirect comparisons may be another potential limitation, which can impact the validity of our NMA results.
⇒ Potentially high heterogeneity among different studies may influence the NMA result.

INTRODUCTION

Major depressive disorder (MDD) is a common disabling and chronic psychiatric disorder. Globally, approximately 3.8% of the population experiences depression.[1] There is a range of established treatments for MDD, including first-generation and second-generation antidepressants, psychotherapy, and electroconvulsive therapy. However, about 30% of patients with MDD failed in response to the sequenced treatment in a large-scale trial, the Sequenced Treatment Alternatives to Relieve Depression (STAR*D) study.[2] Transcranial magnetic stimulation (TMS) is a newly developed, non-invasive treatment for MDD.[3] Daily TMS administered over the left dorsolateral prefrontal cortex (lDLPFC) for 4–6 weeks has been used for treating adult patients with MDD who failed in response to prior antidepressant medications.[4–6] Multiple studies reveal that the response rate ranges from 29% to 46%, and the remission rate ranges from 18% to 31%.[7 8] Thus, there are increasing attempts to improve the efficacies of TMS treatment in MDD.

One important step is the choice of targeting methods for lDLPFC. The '5 cm' method is a conventional method in clinical practice. The lDLPFC was determined as the area 5 cm anterior to the optimum scalp position to

activate the first dorsal interosseous.[9] According to individual variations of head sizes, the targets localised by the '5 cm' method may go outside of lDLPFC in more than a third of the cases, as observed in a multicentre clinical trial.[10] Modified '5.5 cm' or '6 cm' methods could not fully address the above issue.[11 12] Considering the variation of head size, the F3 method is used, which relies on the international 10–20 system. In some studies, the F3 electrode is selected as an approximation of the scalp site for lDLPFC.[13–15] One study compared the localisations of lDLPFC targets by the '5 cm' method with those by the F3 method, showing that targets were more anterior for the F3 method.[16] A new approach, the Beam F3 method, was a modified and more efficient way to find the F3 position using only three skull measurements.[17] Some researchers found that the Beam F3 method might not locate the exact position of F3.[18 19] This method was cost-effective and easy to implement, but whether it improves efficacy was uncertain. Trapp *et al* compared the reliability of the '5.5 cm' method and the Beam F3 method and found that the latter had greater target precision.[20] In their recent article, two methods achieved similar antidepressant outcomes for treating MDD.[21]

The '5 cm' method and the F3 method localise the TMS target on the scalp's surface as indirect ways to identify the cortical lDLPFC targets. Recently, neuro-navigational TMS guided by MRI data has made it possible to directly localise the cortical lDLPFC targets.[22 23] There have been attempts to explore the optimal localisation for the lDLPFC target in different ways, including guided by structural MRI,[16] functional connectivity between lDLPFC and subgenual anterior cingulate cortex,[24 25] and positron emission tomography.[26] Neuro-navigational TMS over lDLPFC leads to more accurate localisation[27 28] and may have better therapeutic efficacy in patients with MDD.[29]

However, few studies have directly compared the efficacies of TMS treatments in MDD using different targeting methods. Fitzgerald *et al* first explored the neuro-navigational targeting method compared with the '5 cm' method and found a better outcome in the neuro-navigational group.[30] Hebel *et al* directly compared the neuro-navigational targeting method with the F3 method. But they found no significant between-group differences in absolute change of depressive symptoms or the number of responses or remission in an interim analysis.[31] There is other evidence from two retrospective studies. They examined the therapeutic potential of the neuro-navigational targeting method in an alternative way by calculating the Euclidean distances between the optimal neuro-navigational targets and the conventional targets by the '5 cm' method or the F3 method. They found a significant correlation between a closer distance and a better antidepressant outcome.[32 33] Another retrospective study further proposed symptom-specific targets. The TMS targets are localised within two distinct circuits and are effective for two symptomatic clusters: dysphoric and anxiety and somatic symptoms.[34 35] The discrepancies between the Beam F3 method and neuro-navigational TMS were <1.36 cm in 95% of subjects,[36] but no direct comparison of efficacy between the two methods has been reported.

Therefore, whether and how the targeting methods for TMS treatments influence the antidepressant efficacy in MDD is important but remains uncertain. The best way is to run randomised controlled trials (RCTs) which can directly compare the TMS efficacies between different targeting methods but will cost much time and resources. In the present study, this systematic review and network meta-analysis (NMA) aims to compare the efficacy and acceptability of different TMS targeting methods for patients with MDD and to provide valuable clues for clinical practices.

METHODS AND ANALYSIS

Criteria for considering studies for this review

Types of studies

We will include all relevant RCTs with sample sizes of at least five. We will not include quasi-randomised studies, cluster trials, cross-over trials, cohort trials, and case-control and case report studies.

Types of participants

All persons with MDD are diagnosed by standard operationalised diagnostic criteria (Feighner criteria, Research Diagnostic Criteria, Diagnostic and Statistical Manual, Third Edition (DSM-III), DSM-III-R, DSM-4, DSM-5, the 10th revision of International Statistical Classification of Diseases (ICD-10) or ICD-11). Differences in diagnostic schema will be considered while evaluating the certainty of the evidence. All persons are irrespective of gender, age or nationality. Participants with a concurrent primary diagnosis of another mental disorder will be excluded.

Types of interventions

We will include trials that compare the efficacies between active TMS using one or more of the following targeting methods and sham TMS, or that compare efficacies of active TMS between any two or three targeting methods: the '5 cm' method, including similar methods, such as '5.5 cm', '6 cm' or '7 cm' methods; the F3 method or the Beam F3 method; neuro-navigational methods combined with individual imaging data, including structural MRI, functional MRI or diffusion MRI.

Other TMS parameters in the trials we choose should meet the following requirements:

1. TMS frequency ≥5 Hz or intermittent theta-burst stimulation (iTBS). There is evidence suggesting that the high-frequencies (5 Hz or more) TMS or iTBS may increase cortical excitability.[5 37] Thus, we will include TMS trials delivering high-frequency (≥5 Hz) or iTBS over the lDLPFC.
2. TMS intensity ranges from 80% to 120% resting motor threshold.
3. The target was over the lDLPFC.

4. Patients with MDD received at least 10-session TMS treatments. There is evidence that the rate of responders increased when the number of sessions was more than 10.[5]

We will include trials using TMS as an augmentation therapy or a monotherapy because TMS is often used as an augmentation therapy in clinical practice for patients who have not responded adequately to traditional antidepressant medication. Including studies that use TMS as augmentation therapy can provide valuable information about the treatment's potential benefits and limitations. We will analyse the primary and secondary outcomes for TMS treatments used as augmentation therapy and used as monotherapy, separately. The pairwise meta-analyses and NMA will be performed if enough trials are included.

Types of outcomes

Primary outcomes

The reduction score is the primary outcome, which will be assessed for each TMS targeting method through specific standardised scales. The reduction score is defined as absolute change in the 17-item Hamilton Depression Rating Scale (HDRS-17), the 24-item Hamilton Depression Rating Scale (HDRS-24) or the Montgomery-Asberg Depression Rating Scale Score compared with the baseline.

Secondary outcomes

Acceptability of TMS treatment: we will use the dropout rate to represent the acceptability of TMS treatment. We will assess the number of patients with MDD who initially enrolled, dropped out and completed the study to estimate the dropout rate. The dropped-out subject is defined as a participant who enables to finish the entire experimental process for any reason.

Incidence of significant improvement in the Clinical Global Impression: we will assess the number of patients with MDD who scored 1 or 2 in global improvement (1 = 'very much' improved or 2 = 'much' improved).

Incidence of adverse effects (side effects and complications): we will assess the number of patients with MDD who suffer from adverse effects, including lightheadedness, hearing problems, mild headaches, tingling sensation in the face, jaw or scalp, facial twitching, and scalp sensations.

We will explore changes in other aspects, including anxiety symptoms, insomnia and cognitive function. However, the trials containing evaluations on these aspects may be unable to reach the required number for meta-analysis. We will evaluate the changes by the following variables:

Improvement of anxiety symptoms: we will use the response rate and remission rate of anxiety symptoms to evaluate the improvements of anxiety symptoms. The response is defined as a 50% or greater reduction in the absolute Hamilton Anxiety Rating Scale (HAM-A) Score compared with the baseline. Remission is defined as HAM-A Scores ≤8 after TMS treatments. We will also analyse the reduction rate of the anxiety factor score (items 10, 11) of HDRS if the results are provided in detail. The factor scores of HDRS include mood, guilt, suicide, insomnia, agitation, anxiety, weight loss and somatic symptoms. The reduction rate is the difference between the baseline and post-treatment scores divided by the baseline score and multiplied by 100%.

Improvement of insomnia: we will use the reduction rate of any sleep scales, including but not limited to the Athens Insomnia Scale, Pittsburgh Sleep Quality Index and the Insomnia Severity Index to evaluate the improvement of insomnia. We will also analyse the reduction rate of the insomnia factor score (items 4, 5, 6) of HDRS if the results are provided in detail.

Incidence of change of cognitive function: we will assess the number of patients who have a change of cognitive functioning as defined by individual studies. The prefrontal cortex is a critical brain region involved in executive function, decision-making and emotional processing. Patients suffering from MDD have deficits in multiple domains of cognitive function, such as attention, executive function, processing speed and episodic memory.[38 39] We will mainly focus on these cognitive functions.

Search strategy and study selection

Electronic searching resources

We will search the following databases: PubMed, Cochrane Central Register of Controlled Trials, Embase, PsycINFO, China National Knowledge Infrastructure, Wan Fang Database, Chinese BioMedical Literature Database (SinoMed), China Science and Technology Journal Database. We will search the articles published before 1 May 2023. Articles selected should be published in English or Chinese. We will not restrict on publication status. A draft search strategy is included in Appendix 1, revised by one of the experts with systematic review experience from our team (HL). After the PubMed strategy is finalised, it will be adapted to the syntax and subject headings of the other databases.

Other searching resources

We will search ClinicalTrials.gov (www.clinicaltrials.gov), the WHO International Clinical Trials Registry Platform (apps.who.int/trialsearch/) and the China National Medical Research Platform (https://www.medicalresearch.org.cn/) for unpublished and ongoing trials. We will search bioRXiv and medRxiv for relative preprints. We will search unpublished data and grey literature through personal communications with researchers and others interested in the field. We will screen the related systematic reviews and meta-analyses for eligible articles. We will also involve articles from references of related reviews and information provided by experts in relevant fields.

Data collection and analysis

Study selection

Duplicate publications will be sorted using Endnote V.20 while the author, publication year and title match. Two

review authors (SW and GK) will independently assess all citations identified by the search strategy and sort out citations thought to be relevant based on information included in the abstract and/or method section of the trial report. Authors should be blind from authors, institutions, journals or results of the identified articles. Next, we will order the full-text study reports of potentially eligible studies. Two review authors (SW and GK) will independently screen the full texts and assess these for inclusion/exclusion criteria. Any disagreements will be resolved by discussing or involving the third review author (YT).

Data extraction and management

Data extraction

Two review authors (SW and GK) will independently extract data from included studies. Any disagreements will be resolved through discussion, and if necessary, we will contact the studies' authors for clarification. Again, any disagreement will be by discussion or involving the third review author (YT).

Data management

We will extract data into standard, simple forms. We will extract the following information:

1. Study design: leading author, publication year, journal, duration, trial design, the number of treatment arms, missing data methods and randomisation approaches.
2. Participant characteristics: the overall number, the number in each arm, withdrawal, gender, age, diagnostic method, type and the number of participants.
3. Intervention: type of TMS targeting method, frequency, position, intensity, the number of sessions and overall pulses.
4. Outcomes: measurements, baseline data, the number of patients who remitted, responded, or had adverse events, the number of dropout results from each follow-up, and the mean and SD of continuous variables.
5. Adverse events and withdrawal situation: the number of patients who had adverse events, severity, the number of patients who withdrew due to adverse events, the number of patients who withdrew due to lack of efficacy and the number of severe adverse reactions.

Assessment of risk of bias in included studies

Two review authors (SW and GK) will independently assess the risk of bias for each study using version 2 of the Cochrane 'Risk of bias' tool, mentioned in the Cochrane Handbook for Systematic Reviews of Interventions. In case a disagreement arises as to which category a trial has to be allocated, resolutions will be made by discussion or involving the third review author. We will assess the following risk of bias domains: randomisation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective outcome reporting, overall risk of bias. We will rate them as 'high risk' or 'low risk', and 'unclear' will be rated if there is insufficient detail reported in the study. A judgement of high risk of bias in one or more domains will be considered as a 'high risk' study. We will exclude the 'high risk' studies in sensitivity analysis if necessary.

Data synthesis

Data will be quantitatively synthesised if we can select at least three trials for each outcome. Otherwise, we will just narratively describe the outcomes. If the targeting method is not included in selected trials, it will not be included in the meta-analysis. Instead, we will briefly describe the result. We will use summary ORs with 95% CIs for dichotomous data and standardised mean differences (SMDs) with 95% CIs for continuous variables. To rank the best targeting method for treatment, we will use the surface under the cumulative ranking curve (SUCRA), which was used to rank the effectiveness of each treatment and identify the best treatment. This method simplifies the information about the effect of each treatment into a single number, making interpreting results easier for clinicians.

First, we will demonstrate a network diagram showing the available direct comparisons between pairs of interventions by using Stata.[40] The size of the nodes will reflect the total number of patients receiving certain targeting methods, and the breadth of each edge will represent the number of trials included in this NMA.

Second, we will initially perform standard pairwise meta-analyses to evaluate the direct relative effect using Stata's random-effects model. We will use SMDs with 95% CIs for continuous data and summary ORs with 95% CIs for binary data.

Third, we will present separate NMA for each outcome. The results from each trial will be synthesised using a frequentist analysis approach based on a multivariate meta-analysis. We will use a multivariate meta-regression model[41] in the Network package from Stata[42] to evaluate how variables such as TMS frequency, dose, intensity or other confounding factors influence the outcomes observed in NMA. These variables will be calculated as covariates in the multivariate meta-regression model.

Fourth, a contribution matrix will be drawn to present the percentage information that direct evidence contributes to each relative effect estimated in our NMA. In this matrix, direct comparisons in the network will be presented in the columns, and their contributions to the combined treatment effect will be presented in the rows.

Lastly, to rank the methods for each outcome by the probability of the best targeting method, we will use SUCRA.[43] The SUCRA Score ranged from 0% to 100%, a higher SUCRA Score indicating a high possibility of becoming the most suitable targeting method for TMS. SUCRA would be '1' when a treatment is certain to be the best and '0' when a treatment is certain to be the worst.

We will not differentiate between TMS used as augmentation therapy or monotherapy. Then, we will analyse the primary and secondary outcomes of TMS treatments used as augmentation therapy and monotherapy separately if enough trials are included.

Assessment of heterogeneity, transitivity and inconsistency

Assessment of heterogeneity

For pairwise analysis, we will assess heterogeneity using the I^2 statistic, calculated for each pairwise comparison on each outcome. We will use the global Wald test to evaluate heterogeneity for NMA. A value of $p<0.05$ in the global Wald test indicates global heterogeneity.

Assessment of transitivity

We will carefully investigate the distribution of clinical and methodological variables, which could act as effect modifiers across treatment comparisons.[44] To ensure good transitivity, we will only include studies with patients diagnosed with MDD based on ICD or DSM and high-frequency TMS treatment on lDLPFC. We will look into the following effect modifiers that could potentially influence outcomes, including age, severity of depression at baseline, treatment duration and treatment intensity. We will perform sensitivity analysis on these modifiers. We will verify the modification effect of these aspects by subgroup analysis or meta-regression if the amount of data is sufficient.

Assessment of inconsistency

We will use both global and local methods to assess the inconsistency between direct and indirect comparison. For the global method, we will use the design-by-treatment model, which can carefully examine all parts of the network. For the local method, the loop-specific method will be adopted to assess regions of the network separately.[41 45 46]

Dealing with missing data

We will first contact the study's authors for all missing data relevant to our analysis. If we cannot get the authors' data, we will follow the guidance from the Cochrane Handbook. If the attrition for a binary outcome is between 0% and 40% and the outcomes of these participants are described, we will include these data as reported. Where these data aren't clearly described, we will assume the worst case for all dropouts.[47] We will then discuss the implications of missing data on the review and NMA in the discussion section of the review.

Assessment of reporting biases

According to the Cochrane Handbook for Intervention, for the pairwise meta-analyses, if we can pool more than 10 trials, we will create a funnel plot to explore possible small-study and publication biases. For the NMA, if we can pool more than 10 trials, we will use comparison-adjusted funnel plots to assess small-study effects.[40]

Subgroup analysis and investigation of heterogeneity

We will perform subgroup analyses for all primary and secondary outcomes in the following three aspects:

1. Between the F3 method and the Beam F3 method.
2. Different neuro-navigational methods: localising the lDLPFC position with different imaging techniques, including structural MRI, functional MRI and diffusion MRI.
3. Between standard TMS protocol and iTBS protocol.

Where possible, we will perform the subgroup analyses by building separate models.

Sensitivity analysis

We will conduct the following sensitivity analyses to test whether critical methodological factors or decisions have affected the main result. We will remove studies for which we have judged the overall risk of bias as some concerns or high risk. We will remove the unpublished studies if we have any. We will remove one of the groups if it has significantly more subjects than the other groups. We will remove the trials with ambiguous descriptions of their targeting methods.

Summary of findings and assessment of the certainty of evidence

Two review authors (SW and GK) will independently judge the evidence's certainty. We will employ GRADEpro GDT with guidance from the Cochrane Handbook for Systematic Reviews of Interventions. The Grading of Recommendations, Assessment, Development and Evaluation (GRADE) includes five aspects (study limitations (risk of bias), unexplained heterogeneity and inconsistency of effect, imprecision, indirectness and publication bias) to assess the certainty of the body of evidence for each outcome. There are four levels of quality of evidence: high, moderate, low and very low.

To assess the certainty of the NMA, we will use the Confidence in Network Meta-Analysis (CINeMA) framework.[48] Based on CINeMA, six domains are specific to NMA, including within-study bias, reporting bias, indirectness, imprecision, heterogeneity and incoherence to assess how much information each study contributes to the results from NMA. There are four confidence levels: very low, low, moderate and high.

Patient and public involvement

None.

ETHICS AND DISSEMINATION

This systematic review and NMA does not require ethics approval. The results will be submitted for publication in a peer-reviewed journal. In the event of any changes to the protocol during the conduct of the study, details of the changes, including the date of each amendment, description of the change and the rationale, will be indicated in the reporting of the study results.

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Contributors YT, HL, JH and JiW devised the study. SW and GK drafted the protocol, will carry out data extraction and analysis, and draft the results and discussion sections. All authors contributed to developing the selection criteria, the risk of bias assessment strategy and data extraction criteria. YT, HL, JH, JiW, GK, ZQ, GW, LX, HC, JuW and YW revised the protocol and provided statistical expertise, and will carry out most of the data collection. All authors read, provided feedback and approved the final manuscript.

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Appendix1. Draft search strategy for different databases

English databases

PubMed

#1 Search: (((((((depression[MeSH Terms]) OR (depress*[Title/Abstract])) OR (dysthymi*[Title/Abstract])) OR (adjustment disorder*[Title/Abstract])) OR (mood disorder[Title/Abstract])) OR (affective disorder[Title/Abstract])) OR (affective symptoms[Title/Abstract])) OR (MDD[Title/Abstract])

#2 Search: ((((Transcranial Magnetic Stimulations[MeSH Terms]) OR (TMS[Title/Abstract])) OR (repetitive tms[Title/Abstract])) OR (rtms[Title/Abstract]))

#3 Search: (((((((neuroimaging[Title/Abstract]) OR (coregistration techniques[Title/Abstract])) OR (neuro-navigat*[Title/Abstract])) OR (MRI-neuronavigat*[Title/Abstract])) OR (MRI based neuro-navigat*[Title/Abstract])) OR (connectivity-guided[Title/Abstract])) OR (connectivity analysis[Title/Abstract])) OR (MR-image guided[Title/Abstract])

#4 Search: (((((((F3[Title/Abstract]) OR (beam F3[Title/Abstract])) OR (10-20 EEG system[Title/Abstract])) OR (10-20 system[Title/Abstract])) OR (EEG[Title/Abstract])) OR (electroencephalogram*[Title/Abstract])) OR (10-20 EGG coordinat*[Title/Abstract])) OR (Scalp-targeting[Title/Abstract])

5 Search: (((((((((5 cm[Title/Abstract]) OR (5.5 cm[Title/Abstract])) OR (6 cm[Title/Abstract])) OR (7 cm[Title/Abstract])) OR (abductor pollicis brevis[Title/Abstract])) OR (anatomical landmark[Title/Abstract])) OR (fixed distance* targeting rules[Title/Abstract])) OR (standard procedure[Title/Abstract])) OR (motor hotspot[Title/Abstract])) OR (motor cortex[Title/Abstract])

#6 Search: (randomized controlled trial[pt] OR controlled clinical trial[pt] OR randomized[tiab] OR placebo[tiab] OR drug therapy[sh] OR randomly[tiab] OR trial[tiab] OR groups[tiab]) NOT (animals[mh] NOT humans[mh])

#7 Search: #3 OR #4 OR #5

#8 Search: #1 AND #2 AND #6 AND #7

Embase

#1 'depression'/exp

#2 'depress*':ab,ti OR 'dysthymi*':ab,ti OR 'adjustment disorder*':ab,ti OR 'mood disorder':ab,ti OR 'affective disorder':ab,ti OR 'affective symptoms':ab,ti OR 'MDD':ab,ti

#3 'transcranial magnetic stimulation'/exp

#4 'TMS':ab,ti OR 'repetitive tms':ab,ti OR 'rtms':ab,ti

#5 'neuroimaging':ab,ti OR 'coregistration techniques':ab,ti OR 'neuro-navigat*':ab,ti OR 'mri-neuronavigat*':ab,ti OR 'mri based neuro-navigat*':ab,ti OR 'connectivity-guided':ab,ti OR 'connectivity analysis':ab,ti OR 'mr-image guided':ab,ti

#6 'F3':ab,ti OR 'beam F3':ab,ti OR '10-20 EEG system':ab,ti OR '10-20 system':ab,ti OR 'EEG':ab,ti OR 'electroencephalogram*':ab,ti OR '10-20 EGG coordinat*':ab,ti OR 'scalp-targeting':ab,ti

#7 '5 cm':ab,ti OR '5.5 cm':ab,ti OR '6 cm':ab,ti OR '7 cm':ab,ti OR 'abductor pollicis brevis':ab,ti OR 'anatomical landmark':ab,ti OR 'fixed distance* targeting':ab,ti OR 'standard procedure':ab,ti OR 'motor hotspot':ab,ti

#8 'crossover procedure':de OR 'double-blind procedure':de OR 'randomized controlled trial':de OR 'single-blind procedure':de OR (random* OR factorial* OR crossover* OR cross NEXT/1 over* OR placebo* OR doubl* NEAR/1 blind* OR singl* NEAR/1 blind* OR assign* OR allocat* OR volunteer*):de,ab,ti

#9 #1 OR #2

#10 #3 OR #4

#11 #5 OR #6 OR #7

#12 #8 AND #9 AND #10 AND #11

Cochrane Central Register of Controlled Trials

#1 MeSH descriptor: [Depression] explode all trees

#2 MeSH descriptor: [Transcranial Magnetic Stimulation] explode all trees

#3 (depress* OR dysthymi* OR adjustment disorder* OR mood disorder* OR affective disorder* OR affective symptoms OR MDD):ab,ti

#4 (TMS OR repetitive tms OR rtms):ab,ti

#5 (neuroimaging OR coregistration technique* OR neuro-navigat* OR mri-neuronavigat* OR mri based neuro-navigat* OR connectivity-guided OR connectivity analysis OR mr-image guided):ab,ti

#6 (F3 OR beam F3 OR EEG OR electroencephalogram* OR scalp-target*):ab,ti

#7 (5 cm OR 5.5 cm OR 6 cm OR 7 cm OR abductor pollicis brevis OR anatomical landmark OR fixed distance* targeting OR standard procedure OR motor hotspot):ab,ti

#8 #1 OR #3

#9 #2 OR #4

#10 #5 OR #6 OR #7

#11 #8 AND #9 AND #10

PsycINFO

S1 MA depression OR TI depress* OR TI dysthymi* OR TI adjustment disorder* OR TI mood disorder* OR TI affective disorder* OR TI affective symptoms OR TI MMD

S2 AB depress* OR AB dysthymi* OR AB adjustment disorder* OR AB mood disorder* OR AB affective disorder* OR AB affective symptoms OR AB MDD

S3 MA transcranial magnetic stimulation OR TI TMS OR TI repetitive tms OR TI rtms OR AB TMS OR AB repetitive tms OR AB rtms

S4 TI neuroimaging OR TI mr-image guided OR TI coregistration technique* OR TI neuro-navigat* OR TI mri-neuronavigat* OR TI mri based neuro-navigat* OR TI connectivity-guided OR TI connectivity analysis

S5 AB neuroimaging OR AB mr-image guided OR AB coregistration technique* OR AB neuro-navigat* OR AB mri-neuronavigat* OR AB mri based neuro-navigat* OR AB connectivity-guided OR AB connectivity analysis

S6 TI F3 OR TI beam F3 OR TI EEG OR TI electroencephalogram* OR TI scalp-target* OR TI 10-20 EEG system OR TI 10-20 system OR TI 10-20 EGG coordinat*

S7 AB F3 OR AB beam F3 OR AB EEG OR AB electroencephalogram* OR AB scalp-target* OR AB 10-20 EEG system OR AB 10-20 system OR AB 10-20 EGG coordinat*

S8 AB 5 cm OR AB 5.5 cm OR AB 6 cm OR AB 7 cm OR AB abductor pollicis brevis OR AB anatomical landmark OR AB fixed distance* targeting OR AB standard procedure OR AB motor hotspot

S9 TI 5 cm OR TI 5.5 cm OR TI 6 cm OR TI 7 cm OR TI abductor pollicis brevis OR TI anatomical landmark OR TI fixed distance* targeting OR TI standard procedure OR TI motor hotspot

S10 SU.EXACT("Treatment Effectiveness Evaluation") OR SU.EXACT.EXPLODE("Treatment Outcomes") OR SU.EXACT("Placebo") OR SU.EXACT("Followup Studies") OR placebo* OR random* OR "comparative stud*" OR clinical NEAR/3 trial* OR research NEAR/3 design OR evaluat* NEAR/3 stud* OR prospectiv* NEAR/3 stud* OR (singl* OR doubl* OR trebl* OR tripl*) NEAR/3 (blind* OR mask*)

S11 S1 OR S2

S12 S4 OR S5 OR S6 OR S7 OR S8 OR S9

S13 S3 AND S10 AND S11 AND S12

Chinese databases：

中文文献库：

CNKI

(TI='抑郁症' + ‘抑郁障碍’ + '抑郁' or SU='抑郁症' + ‘抑郁障碍’ + '抑郁') AND (TKA='经颅磁刺激' + ‘TMS’ + '无创脑刺激' + ‘非侵入性脑刺激’) AND (TKA=‘PFC’ + ‘前额叶’ + ‘DLPFC’ + ‘背外侧前额叶’)

万方

主题:(“抑郁症” or “抑郁障碍” or “抑郁”) and 主题:(“经颅磁刺激” or “TMS” or “无创脑刺激” or “非侵入性脑刺激”) and 摘要:(“PFC” or “前额叶” or “DLPFC” or “背外侧前额叶”)

维普

(M=抑郁症 OR 抑郁障碍 OR 抑郁) AND (M=经颅磁刺激 OR TMS OR 无创脑刺激 OR 非侵入性脑刺激) AND (U=DLPFC OR 背外侧前额叶 OR PFC OR 前额叶)

中国生物医学文献

("抑郁症"[常用字段:智能] OR "抑郁障碍"[常用字段:智能] OR "抑郁"[常用字段:智能]) AND ("经颅磁刺激"[常用字段:智能] OR "TMS"[常用字段:智能] OR "无创脑刺激"[常用字段:智能] OR "非侵入脑刺激"[常用字段:智能]) AND ("DLPFC"[全部字段:智能] OR "背外侧前额叶"[全部字段:智能] OR "PFC"[全部字段:智能] OR "前额叶"[全部字段:智能])