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Transcranial Magnetic Stimulation of Dorsolateral Prefrontal Cortex in Treatment-Resistant Obsessive Compulsive Disorder: A Mini-Review

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Abstract

Introduction: *Approximately two-thirds of patients with Obsessive-Compulsive Disorder (OCD) exhibit inadequate responses to current standard therapies. A previous meta-analysis has shown the potential benefit of repetitive transcranial magnetic stimulation (rTMS) of the dorsolateral prefrontal cortex (dlPFC) area in patients with OCD. However, the analysis also included patients who had not previously failed first-line treatments. This mini-review aims to explore the therapeutic effects of rTMS applied to the dlPFC area in patients with treatment-resistant OCD.*

Methods: *We conducted a comprehensive search for randomized controlled trials (RCTs) and observational studies across various databases (PubMed, EMBASE, Ebsco, Web of Science, and Cochrane Central). Eligible studies encompassed rTMS administered to the dlPFC area in cases of treatment-resistant OCD. Studies that did not focus on using the Yale-Brown Obsessive-Compulsive Scale (Y-BOCS) to assess the efficacy of rTMS were excluded. Quality assessments were conducted based on the Cochrane risk-of-bias tool.*

Results: *Our review identified five RCTs involving 132 patients that met the established criteria. The application of high-frequency (HF) and low-frequency (LF) rTMS to the dlPFC region yielded controversial post-treatment Y-BOCS findings due to factors such as small sample sizes, short-term study durations, variations in rTMS protocols, and four studies exhibiting a high risk of bias.*

Discussion: *The available data is constrained by a scarcity of high-quality, large-scale trials with extended follow-up periods and optimized protocols. Further research is warranted to establish the efficacy of rTMS administered to the dlPFC in this patient population.*

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Introduction

Obsessive Compulsive Disorder (OCD) is a chronic and often severe psychiatric disorder characterized by obsessive thoughts and compulsive behaviors affecting 2 - 3% of the US population (Rapinesi et al., 2019; Ruscio et al., 2010). OCD can lead to significant impairment of interpersonal relationships and occupational functioning, resulting in economic consequences (Moritz et al., 2005).

Cognitive-behavioral therapy (CBT) and high-dose selective serotonin reuptake inhibitors (SSRIs) are considered the first-line treatments for OCD. They can be used as stand-alone therapy or in combination when there is no response within 13 to 20 weeks. However, around two-thirds of OCD patients are considered resistant to treatment (Abudy et al., 2011; Simpson et al., 2006; Pallanti et al., 2002). Thus, it is essential to explore other interventions that are efficacious and well–tolerated for treatment-resistant OCD.

Repetitive transcranial stimulation (rTMS) is a non-invasive, safe, and well-tolerated intervention that modulates prefrontal cortical circuits involved in OCD. Therefore, it provides a practical option for treatment-resistant OCD patients (Saba et al., 2015). The two main areas in the brain involved in the pathophysiology of OCD are the dorsolateral prefrontal cortex (dlPFC) and the pre-supplementary motor area (pre-SMA). While the pre-SMA regulates inhibition in the motor cortex, the dlPFC is essential for executive and emotional function (Gowda et al., 2019). A recent meta-analysis by Fitzsimmons et al. (2022) found that both low-frequency (LF) and high-frequency (HF) rTMS to the dlPFC can reduce OCD symptoms (Figure 1); however, their analysis included patients of all severity levels.

Therefore, our review focused on examining the efficacy of rTMS over the dlPFC only in treatment-resistant OCD patients from studies that compared rTMS against a control group and used the Yale-Brown Obsessive-Compulsive Scale (Y-BOCS) as an outcome predictor. The findings could support future research and clinical decision-making.

Materials and Methods

Study Criteria

We used the following inclusion criteria: (1) randomized controlled trials (RCTs), (2) observational studies, (3) use of rTMS of the dlPFC, (4) symptom improvement assessed by the Y-BOCS score, (5) adults with treatment-resistant OCD, and (6) full-text available in English, Spanish, Portuguese, Arabic, and French. We excluded studies that evaluated (1) other neuromodulation techniques, (2) patients with non-treatment resistant OCD, (3) patients under 18 years, (3) studies with incomplete results, (4) studies evaluating rTMS for other indications, as well as (6) case reports, systematic reviews, and meta-analyses.

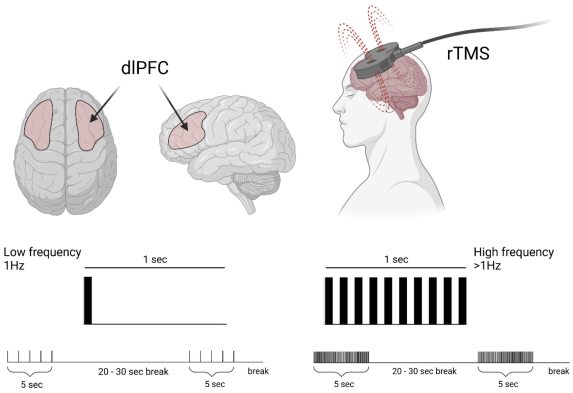

Figure 1: *Scheme of low- and high-frequency rTMS.*

Search Strategy

We conducted an electronic search on August 16th, 2023, using the databases PubMed (Medline), EMBASE, EBSCO, Web of Science, and Cochrane Central. We used the Mesh terms "Obsessive-Compulsive Disorder" and "Transcranial Magnetic Stimulation" and searched with a broad combination of synonyms entered in the title or abstract. Table S1 in the supplemental data reports the detailed search strategy per database.

Data Extraction

Two independent investigators screened titles and abstracts according to the selection criteria. Articles of potential relevance were allocated to the next stage to be reviewed in detail (n=27). Subsequently, the full text of the selected articles was screened according to the inclusion and exclusion criteria (Figure 2). In case of initial disagreement, the article was discussed. A consensus was reached on the eligibility. Rayyan web app for systematic reviews (Qatar Computing Research Institute, Doha, Qatar) (Ouzzani et al., 2016), Zotero software (Corporation for Digital Scholarship, USA), and Google Sheets online editor (Google Docs, GoogleLLC, CA, USA) were used for the screening process.

From each study, we extracted the characteristics of the population (e.g., age, sex, and level of non-response), details of the intervention (e.g., rTMS parameters and the site of stimulation), outcome measures (e.g., Y-BOCS mean scores

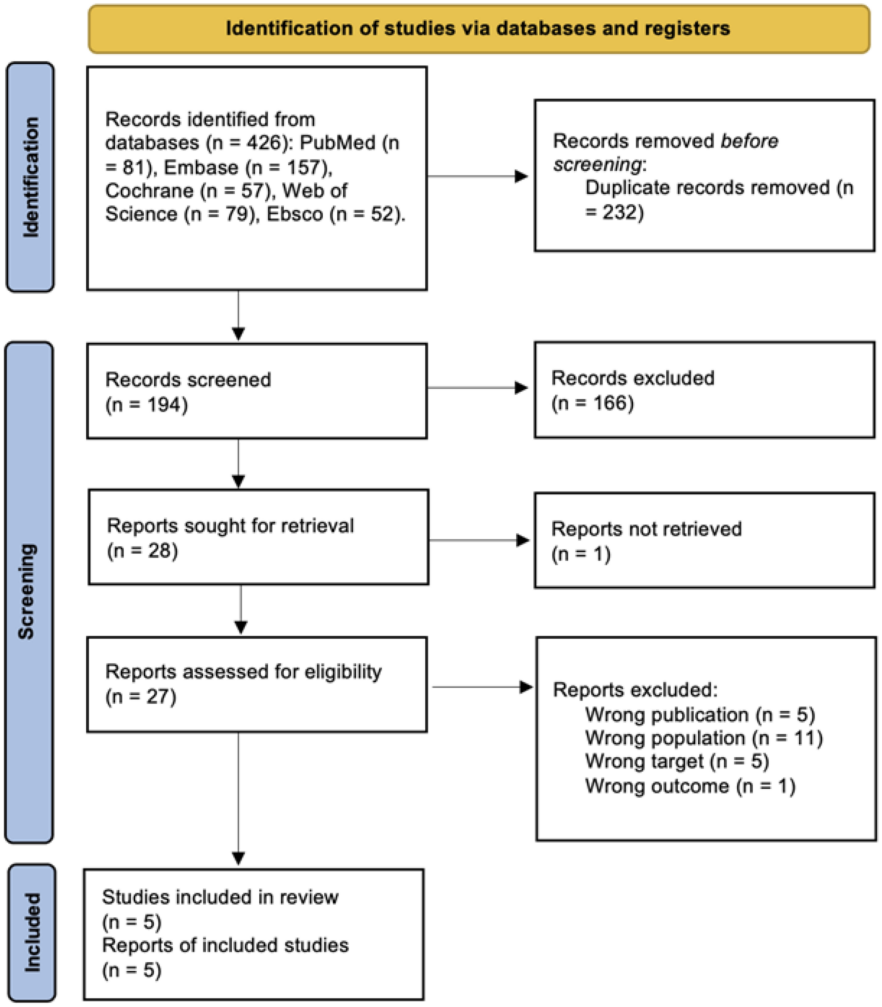

Figure 2: *PRISMA diagram.*

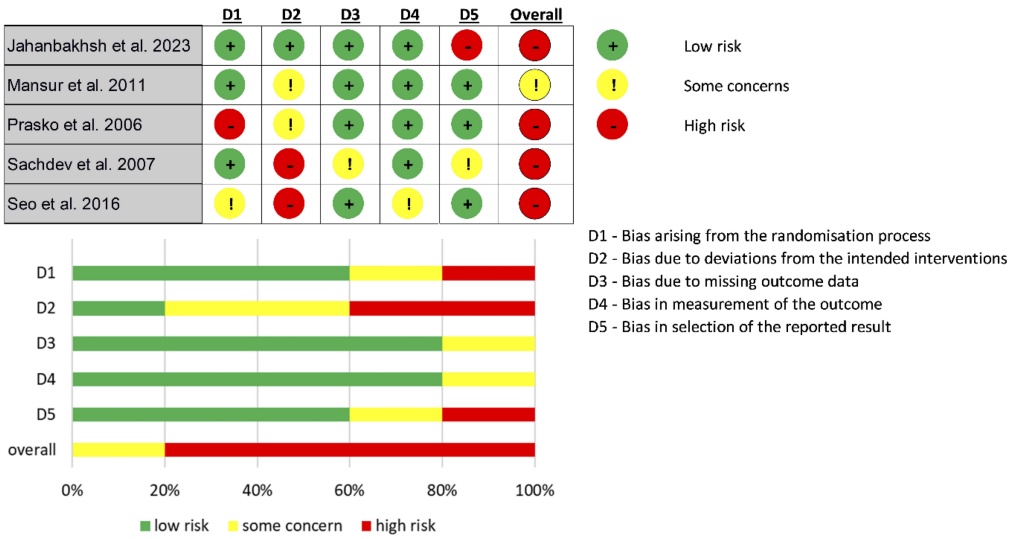

Figure 3: *Scheme of risk of bias assessment for included studies.*

and percent reduction), and study characteristics such as sample size, country site, control group, blinding strategy, and follow-up period. In addition, a risk bias assessment was performed using the RoB 2 Cochrane risk-of-bias tool for randomized trials (Higgins et al., 2011). This tool assesses five different domains of bias through different questions, which are differently weighted. These five domains include the risk of bias from randomization, intervention, missing data, outcome measurement, and discrimination in selecting the reported results. A detailed description can be found here: https://methods.cochrane.org/bias/resources/rob-2-revised-cochrane-risk-bias-tool-randomized-trials. Consensus between the two raters resolved disagreements about the risk of bias.

Results

The search yielded 194 relevant studies, of which five RCTs met the inclusion criteria, reporting 132 patients (Jahanbakhsh et al., 2023; Mansur et al., 2011; Prasko et al., 2006; Sachdev et al., 2001; Seo et al., 2016). Their inclusion criteria ranged from age 18 to 45, 60, 65, or open end, with an overall mean age between 28.90 and 42.10 (Table 1). Each study included 8 to 15 patients per treatment group. The level of non-response was assessed according to Pallanti et al. 2002. This varied largely from Level I (one SSRI, Prasko et al., 2006) to Level III (two SSRI and CBT, Jahanbakhsh et al., 2023), Level IV (three SSRI and CBT, Mansur et al., 2011) or Level $\geq$ III (Sachdev et al., 2001). The remaining study by Seo et al. (2016) included patients with at least two anti-OCD medications but did not specify which ones.

For the localization of the dlPFC, all studies used the 5-cm rule first described by George et al. (1995). Two studies used the 10-Hz HF rTMS on the right and left dlPFC, respectively (Mansur et al., 2011; Sachdev et al., 2007). In both, the patients were treated five days weekly; however, in the study by Sachdev et al. (2007), the double-blinded phase lasted two weeks, and after that, an open treatment continued for up to 20 sessions with a total of 4 weeks of rTMS to all subjects with 1500 pulses per day in 12-minute sessions with an intensity of 110% of the motor threshold (MT). The patients in the study by Mansur et al. (2011) received the same intensity treatment for six consecutive weeks with 2000 pulses per 20-minute session. While Mansur et al. (2011) used a sham coil without magnetic stimulation, Sachdev et al. (2007) placed a sham coil on the patient and had an active coil 1 meter away while running the same settings as the treatment group.

The participants in the three other studies received 1-Hz LF treatment, using sham coils for their controls, two to the left dlPFC (Jahanbakhsh et al., 2023; Prasko et al., 2006) and one to the right dlPFC (Seo et al., 2016). The patients in the study by Jahanbakhsh et al. (2023) received 1200 pulses per 20-minute session five times weekly for five consecutive weeks. The same treatment was given for three weeks in the study by Seo et al. (2016), with an intensity of 100% of the MT. Participants in the study by Prasko et al. (2016) received 1800 pulses in a daily 30-minute session with an MT of 110% for two consecutive weeks.

None of the studies except Prasko et al. (2006) showed significant differences between the intervention and the control groups at baseline in Y-BOCS. Regarding follow-up, there was a significant difference among the studies, ranging from zero weeks (Seo et al., 2016) to two (Sachdev et al., 2007; Prasko et al., 2016), six weeks (Mansur et al., 2011), and 3-6 months, respectively (Jahanbakhsh et al. 2023). Neither the HF study by Sachdev et al. (2007) nor the one by Mansur et al. (2011) showed any significant difference in the Y-BOCS between the groups at the end of the study. However, using analysis of variance (ANOVA), the latter observed a considerable difference ($p=0.002$) in time. In the LF studies, Prasko et al. (2006) also found no significant differences between the groups at the end of the study. In the report by Seo et al. (2016), a significant difference was observed between the groups at the end of the survey ($p=0.008$), revealing a significant effect of time and a group-by-time interaction effect. Finally, Jahanbakhsh et al. (2023) reported a substantial decrease in the Y-BOCS between the groups ($p=0.042$). Furthermore, a highly significant difference was found between baseline and follow-up in time, intervention, and interaction groups (all $p<0.001$)

An additional analysis of the risk of bias in these studies revealed severe concerns. Four of the studies demonstrate a high bias risk (Jahanbakhsh et al. 2023, Sachdev et al. 2007, Prasko et al. 2016, Seo et al. 2016) and one some concerns (Mansur et al. 2011) (Figure 3). The main concerns in Domain 2 (D2) of the Risk of bias assessment using the Rob2 tool result from the unblinded administrator of the rTMS treatment. The high risk in the study from Jahanbakhsh et al. (2023) is due to inadequate use of a t-test instead of a post hoc test after ANOVA. The article by Prasko et al. (2016) needs more information on the concealment of randomization. Due to the study design of the trial by Sachdev et al. (2007), after two weeks of a double-blinded treatment, all patients were aware of their allocations and had the choice to complete up to 20 sessions of rTMS.

Regarding safety, the most common side effect reported in 4 of these Studies was headache (Jahan-

bakhsh et al. 2023, Mansur et al. 2011, Sachdev et al. 2007, Seo et al. 2016). A second adverse event reported after the procedure was scalp discomfort or localized scalp pain without persistence after active stimulation in 2 of these studies (Mansur et al. 2011; Seo et al. 2016). In none of the studies, there were statistical differences between the treatment and sham groups in the total number of events and no cognitive or worsening of depressive symptoms.

Discussion

Effective pharmacological therapies are currently lacking for treatment-resistant OCD patients to improve their symptoms and quality of life. A promising therapeutic option for these patients is rTMS, which is clinically effective in treatment-resistant major depressive disorder (MDD) (Rizvi & Khan, 2019). Therefore, rTMS may also be a potential solution for treatment-resistant OCD. We identified five RCTs, including treatment-resistant OCD patients who underwent rTMS of the dlPFC. Two used HF rTMS (Prasko et al., 2006; Mansur et al., 2011) and showed no significant differences in the Y-BOCS outcome. The meta-analyses by Berlim et al. (2013) and Rehn et al. (2018) described similar observations for trials with HF therapy. In contrast, these studies showed significant improvement for LF rTMS, consistent with two of our three LF studies (Jahanbakhsh et al., 2023; Seo et al., 2016). Prasko et al. (2006) found no significant differences between the treatment groups in the Y-BOCS at the end of the study. However, this result may not be solid since patients had a significant baseline difference.

Ma and Shi (2014) provide support for the positive outcome in the studies by Jahanbakhsh et al. (2023) and Seo et al. (2016), as their subgroup analysis of SSRI-treatment-resistant OCD patients revealed differences in treatment time. While four weeks of consecutive treatment did not show significant benefits, this differs from 2-weeks and 6-weeks of treatment. However, Seo et al. (2016) presented a significant difference between the groups ($p=0.008$) with a 3-week treatment time. Nonetheless, this difference lost strength when evaluated using ANOVA ($p=0.572$), unlike Jahanbakhsh et al. (2023), who found statistically significant results for this variable ($p<0.001$). The differences in the follow-up time after the treatment may explain this finding. Rehn et al. (2018) analyzed the effect of short (4 weeks) vs. long (12 weeks) follow-up time in 18 papers. Excluding one paper in each case due to visualized outlying, they found no benefit for active rTMS in the short-term follow-up, compared to a positive effect towards rTMS in the long-term follow-up (Rehn et al. 2018). This is also a possible explanation for the non-significant findings in the studies from Mansur et al. (2011), Sachdev et al. (2007), and Prasko et al. (2006).

Another explanation for the lack of significance in the studies by Mansur et al. (2011), Sachdev et al. (2007), and Prasko et al. (2006) could be the level of non-response to the treatment of the included patients. The latter included patients with Level I non-response, meaning they failed treatment with just one SSRI. On the other hand, Mansur et al. (2011) included only patients with Level IV non-response, meaning at least 3 SSRIs and CBT failed to reach a positive response to the symptoms. Sachdev et al. (2007) also included patients with a Level III or higher non-response. Interestingly, while Level I could be considered as not severe enough for TMS therapy to have an impact, Level IV may be too severe for TMS to improve the symptoms.

In addition, inconsistencies among the five studies included in our review could have been due to the inaccuracy in using the 5-cm rule to localize the dlPFC. In patients with MDD, Zhang et al. (2021) found that the dlPFC was only accurately localized in 31.8% to 54%, identified by magnetic resonance imaging (MRI). A better alternative, therefore, is to use MRI with neuronavigation to guide the exact location of the stimulation target in real-time. This technology provides more precise and accurate positioning of the rTMS coil (Caulfield et al., 2022). Therefore, it may reduce variability among and within the study participants, improving the consistency of results across the studies.

Our assessment of the risk of bias reveals potential problems in the evaluated studies. As 4 of 5 of the included papers showed a potentially high risk of bias and the other some concerns, we may consider there is a significant knowledge gap in our specific population. One of the biases found was related to the blinding of the treatment allocator (Domain D2, Figure 2), which may be mitigated, as shown in the most recent paper in our study (Jahanbakhsh et al., 2023). Although challenging, blinding the allocator would reduce the performance bias. The blinding procedure has been reported as difficult since the administrator needs to set the stimulation parameters. A purpose-built sham coil identical to the active coil may enable blinding and decrease performance bias. This type of bias might be the main concern in the study by Prasko et al. (2011), where unbalanced groups in terms of age, baseline OCD severity, and disease duration after randomization likely led to a false negative result. Besides improvement of the blinding, increasing the sample size or using a stratified randomization method could result in better-balanced groups. Lastly, there were issues with the statistical analysis in the study by Jahanbakhsh et

Study	Age Mean (SD), years (Exp/Ctr)	Sex (M:F) (Exp/Ctr)	Duration of illness Mean (SD), years (Exp/Ctr)	Total Y-BOCS Mean (SD) (Exp/Ctr)	Level of non-response to treatment*	Trial of medication Mean (SD) (Exp/Ctr)	Currently on Medication (Exp/Ctr)	Currently under psychotherapy, n or previously (yes/no) (Exp/Ctr)	Additional psychiatric disorder, n (%)
Jahanbakhsh et al. (2023)	34.07 (8.34)/34.53 (9.75)	(6:9)/(4:11)	13.53 (8.44)/13.87 (6.99)	27.53 (4.61)/27.40/(4.92)	III**	NA/NA	15/15	0/0 No/No	0(0)/0(0)
Mansur et al. (2011)	42.10 (11.90)/39.30 (13.9)	(7:6)/(6:8)	26.2 (14.0)/15.6 (11.5)	30.0 (3.7)/29.0(4.9)	IV	4.2 (1.1)/4.9(1.7)	13/14	NA/NA No/No	Unipolar depression 11(85)/12(86) Bipolar depression 1(8)/2(14) Social phobia 2(15)/1(7) Panic disorder 0(0)/2(14) General anxiety disorder 0(0)/2(14) Alcohol abuse 1(8)/1(7) History of motor tics 3(23)/2(14)
Prasko et al. (2006)	28.9 (7.7)/33.2 (8.7)	(13:5)/(5:7)	14.6 (7.3)/16.3 (7.9)	29.82 (5.876)/23.42 (4.999)	I***	NA/NA	18/12.	NA/NA	0(0)/0(0)
Sachdev et al. (2007)	29.5 (9.9)/35.8 (8.3)	(3:7)/(5:3)	12.6 (5.7)/12.3 (5.4)	25.8 (5.7)/23.9 (9.9)	≥III	4.6 (1.6)/4.1(2.0)	9/4.	NA/NA Yes/yes	0(0)/0(0)
Seo et al. (2016)	34.60 (9.80)/36.3 (12.5)	(8:6)/(6:7)		32-34/32-34	Treatment with two anti-OCD medications	NA/NA	14/13	NA/NA NA/NA	Major Depressive Disorder 12(85.7)/10(76.9)

Ctr, Control group; **Exp**, experimental group; **M:F**, Male:Female; **NA**, Not Available; **n,** number; **SD**, standard deviation; **Y-BOCS**, Yale-Brown Obsessive-Compulsive Scale.
* Level of non-response to treatment according to Pallanti et al. (2002).
** Two trials with selective serotonin reuptake inhibitors (but without combination with psychotherapy, such as Cognitive Behavioral Therapy).
*** One trial with serotonin reuptake inhibitor (eventually in combination with low doses of adjuvant antipsychotics, in a frequency of 13:5(Exp)/4:8(Ctr)).

Table 1: *Demographics of the studies (extraction data).*

Study (RCT)	Site (Country) No. of Participants (Exp/Ctl)	Intervention	Control group	Blinding strategy	Main Outcome Measures (Y-BOCS)	Post-rTMS (or sham) evaluation and follow-up duration	Main findings	Side Effects
Jahanbakhsh et al. (2023)	Single center (Iran) 30 (15/15)	rTMS Protocol: 1 Hz, 1200 pulses/day, three 20min sessions per week over 5 consecutive weeks (15 sessions). Coil: F-8 coil (MAG PRO X100). Brain target: Left dlPFC ("5-cm rule").	Sham coil	Participants, rTMS administrator and outcome assessors	Y-BOCS mean difference	After 5-, 10- and 15-session treatment, after 3-6 months follow-up	Unilateral low-frequency rTMS over the left dlPFC area in combination with drug therapy showed significant improvement of clinical symptoms on drug-resistant OCD after 15 sessions, which persisted 3-6 months after intervention. Antipsychotic drugs enhanced the effect of rTMS. Evidence of placebo effect at the beginning of the study.	No major side effects,4 patients in the treatment group and 2 patients in the control group reported mild headaches for several hours after the treatment sessions.
Mansur et al. (2011)	Single center (Brazil) 27 (13/14)	rTMS Protocol: 10 Hz, 2000 pulses/day, five 20min sessions per week over 6 consecutive weeks (30 sessions).	Sham coil	Participants and outcome assessors	Definition of a positive response to treatment and response (Exp:Ctr). Reduction ≥ 30% in Y-BOCS. 4/13 vs 2/14 (p=0.385)	After 2- and 6-weeks treatment, and after 2- and 6-weeks follow-up	Unilateral high-frequency rTMS over the right dlPFC area in combination with drug therapy did not show significant improvement of clinical symptoms or treatment response on drug-resistant OCD.	Side effects included mild headache, scalp discomfort, cervical pain, mood swings, and other less common events without major implications.
Prasko et al. (2006)	Single center (Czech Republic) 30 (18/12)	rTMS Protocol: 1 Hz, 110% MT, 1800 pulses/day, five 30min sessions per week over 2 consecutive weeks (10 sessions). Coil: F-8 coil (Magstim Super rapid stimulator). Brain target: Left dlPFC ("5-cm rule").	Sham coil rotated to 90 degrees	Participants and outcome assessors	Y-BOCS mean score	After 2-weeks treatment and after 2 weeks follow-up	Unilateral low frequency rTMS over the left dlPFC area in combination with drug therapy did not show significant improvement of clinical symptoms or treatment response on drug-resistant OCD during 10 sessions.	No seizures, headaches, or neurological and cognitive difficulties occurred after rTMS.
Sachdev et al. (2007)	Single center (Australia) 18 (10/8)	rTMS Protocol: 10 Hz, 110% MT, 1500 pulses/day, five 12 min sessions per week over 4 consecutive weeks (10 sessions). Coil: F-8 coil (Magstim Super Rapid device). Brain target: Left dlPFC ("5-cm rule").	Sham coil and an active coil 1m away from the participant.	Participants up to 2 weeks and outcome assessors during the entire study.	Y-BOCS mean score and percent reduction. Definition of a positive response to treatment and response. (Exp:Ctr) Reduction > 40% in Y-BOCS 3/10 vs 2/8 (p=ns)"	After 2-weeks treatment (double-blind phase) and 4-weeks treatment (open treatment continued for up to 20 sessions of rTMS to all subjects).	Unilateral high frequency rTMS over the left dlPFC area did not show significant improvement of clinical symptoms on drug-resistant OCD after 10 sessions (with or without correction for depression ratings). Possibility of placebo effect and antidepressant effect of rTMS in first 2 weeks.	Headaches - report in 3, immediately after the treatment, warranted analgesic treatment with good response. No seizures, no adverse effects on memory or concentration occurred.
Seo et al. (2016)	Single center (South Korea) 27 (14/13)	rTMS Protocol: 1 Hz, 100% MT, 1200 pulses/day, five 20min sessions per week over 3 consecutive weeks. Coil: F-8 coil (TAMAS stimulator) Brain target: Right dlPFC ("5-cm rule").	Sham coil	Participants, rTMS administrator and outcome assessors	Definition of a positive response to treatment and response (Exp:Ctr) Reduction ≥25% in Y-BOCS 7/14 vs 3/13 (p=0.148)	After 1-, 2- and 3-weeks treatment	Unilateral low-frequency rTMS over the right dlPFC area in combination with drug therapy showed significant improvement of clinical symptoms on drug-resistant OCD (as well as concomitant comorbid depressive symptoms) after 15 sessions.	No serious adverse effects following the procedure. Localised scalp pain (n=3), without persistence after the active stimulation. Headache was reported in 2 patients in the active group, resolving spontaneously within a few hours.

Ctr, Control group; **dlPFC,** dorsolateral prefrontal cortex; **Exp,** experimental group; **Hz,** Hertz; **MT**, Motor Threshold; **ns,** not significant; **No,** number; **OCD**, Obsessive-compulsive disorder; **rTMS**, repetitive transcranial magnetic stimulation; **Y-BOCS**, Yale-Brown Obsessive-Compulsive Scale.

Table 2: *Characteristics of the studies (extraction data).*

al. (2023), as the authors used the ANOVA for an overall analysis but changed to a t-test comparing two groups instead of performing an adequate post hoc test. Lastly, the main concern in the paper by Prasko et al. (2011) appears to be the randomization, leading to unbalanced groups concerning Y-BOCS at baseline.

The biases in the findings of the selected studies limit our overall interpretation of the use of rTMS at the dlPFC in treatment-resistant OCD patients. Additional limitations are due to the studies' heterogeneous inclusion and exclusion criteria, which are the differences in age ranges, the diagnostic procedures of OCD, the level of non-response, and the inclusion and exclusion criteria of patients with other psychiatric disorders (Table 1, 2).

To establish whether rTMS is a valid therapeutic option for OCD, these methodological issues should be addressed in large-scale RCTs, including a representative sample with balanced characteristics among the groups, which are keys to increasing statistical power and enhancing the generalizability of the findings. Moreover, incorporating MRI-based neuronavigation will facilitate the accurate localization of the dlPFC, and an appropriate follow-up allow for the evaluation of the effects of the rTMS, which may be delayed. Finally, standardizing the stimulation protocols, including frequency, number of sessions, and duration, is essential to facilitate comparisons among the studies in the future.

RTMS provides a non-invasive, non-pharmacological, and safe alternative for patients who suffer from treatment-resistant OCD. Side effects are primarily short-lasting headaches and scalp discomfort (Table 2), as previously described in other studies using TMS (Krishnan et al., 2016). Moreover, MRI-based neuronavigation enables more precise localization, providing the possibility to apply treatment both for the compulsive and the obsessive features of the disorder by targeting either the dlPFC or the pre-SMA more accurately.

Conclusion

In this review, we identified five studies using rTMS to the dlPFC of treatment-resistant OCD patients. Inconsistencies within and among these studies included problems using the 5-cm rule to accurately localize the dlPFC, blinding strategies, the type of frequency and treatment durations, and the follow-up times. These have led to heterogeneous conclusions unrelated to the effectiveness of dlPFC rTMS in the study population. Our findings suggest that further research is needed to investigate the efficacy of rTMS to the dlPFC using neuronavigation techniques and a follow-up duration of $\geq$ 12 weeks in treatment-resistant OCD patients to overcome the limitations of previous studies.

Supplementary materials

Supplementary Table 1: Search strategy and results by database, performed on the 16th of August 2023.

Author Contributions

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Conflicts of Interest

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