The Effectiveness of Transcranial Magnetic Stimulation for Obsessive-Compulsive Disorder

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Abstract

Obsessive-compulsive disorder (OCD) is an anxiety-related disorder. Obsessions are experienced as recurring, unwanted thoughts. In response to obsessions, people feel driven to act with repetitive behaviours, known as compulsions. Obsessions and compulsions cause significant distress and impairment in an individual's daily life and relationships. OCD is relatively common, with a lifetime prevalence rate between 2%-3%. Thus, research must find an effective treatment for individuals with OCD. This paper examines a relatively new area of research that explores the use of transcranial magnetic stimulation (TMS) to treat OCD. TMS is a non-invasive brain stimulation that has recently shown promising effects in treating psychological disorders. Studies researching TMS on OCD, primarily with individuals who have not responded to previous treatments, have found it to be effective, with symptoms significantly decreasing post-treatment, and with effects lasting up to 3-months post-treatment. Overall, TMS appears to offer an effective alternative for individuals with treatment-resistant OCD. However, while studies on TMS show significant results, participants with greater OCD symptoms and/or sleep disturbances tend to report a decreased response to treatment. Also, studies using TMS typically have limitations with their sample sizes, lack of control groups, and lack of long-term follow-up assessments. Overall, TMS appears to be effective for OCD, but future research needs to address current limitations to determine the true effectiveness of this new treatment.

Introduction

Individuals with obsessive-compulsive disorder (OCD) experience obsessions, compulsions, or both (American Psychiatric Association, 2013). Obsessions include recurrent or persistent thoughts, urges, or images deemed disturbing and unwanted, which cause anxiety or distress. Compulsions are repetitive behaviour or acts that a person feels they need to perform in response to an obsession or a strictly followed internalized rule (American Psychiatric Association, 2022). OCD has a 12-month prevalence rate of 1.2% and a lifetime prevalence rate of 2.3% (Ruscio et al., 2010). Due to the significant distress or impairment that OCD symptoms cause, a variety of treatment options have been studied. Treatment options for OCD commonly include cognitive behavioural therapy, selective serotonin reuptake inhibitors, or a combination of both. However, cognitive behavioural therapy and selective serotonin reuptake inhibitors as treatment options are ineffective for some individuals with OCD, as around 40-60% of individuals fail to respond to these treatments (Gershkovich, 2017).

The potential therapeutic effects of transcranial magnetic stimulation (TMS) is a new area of research, which uses either repetitive transcranial magnetic stimulation (rTMS) or deep transcranial magnetic stimulation (dTMS) to treat neurological or psychiatric disorders

(Valero-Cabre et al., 2017). TMS induces electrical currents in brain regions, which affects the excitability and activity in the brain depending on the stimulation settings. The frequency and number of electrical pulses can affect excitability and activity differently (Valero-Cabre et al., 2017). Both rTMS and dTMS are conducted through the same process, but dTMS allows for direct stimulation of deeper subcortical structures (Lusicic et al., 2018). Researchers have recently begun studying the effects of rTMS and dTMS in OCD. The present paper aims to examine the effectiveness of TMS on participants with OCD.

Literature Review

Haghighi et al. (2015) aimed to study how active rTMS, compared to a sham condition, improves symptoms in individuals suffering from treatment-resistant OCD—namely, those who do not respond to treatments such as medication, psychotherapy, or both. The study consisted of 21 participants, with a mean age of 35.8 years old, and with 12 participants being female. The Diagnostic and Statistical Manual of Mental Disorders (DSM-IV-TR; American Psychiatric Association, 2000) was used to diagnose OCD. The Yale-Brown Obsessive Compulsive Scale (Y-BOCS; Goodman et al., 1989) and the Clinical Global Impression Scale (CGI; Guy, 1976) were also used to assess the severity of symptoms. The CGI consists of the Clinical Global Impressions-Severity scale and the Clinical Global Impressions-Improvement scale. The CGI-Severity scale allows the clinician to rate the symptom severity of the participant based on observed symptoms and behaviour. In contrast, the CGI-Improvement scale rates the change of severity from baseline until the end of the treatment (Busner & Targum, 2007).

The 21 participants were treated with active rTMS over the dorsolateral prefrontal cortex (DLPFC) for two weeks and with an rTMS sham condition for two weeks. With a sham condition, participants are assigned to an inactive procedure imitating the procedure of the active treatment. The sham condition is used to account for possible placebo effects. Ten participants were randomly assigned to undergo the rTMS-first-sham-second condition, while 11 were randomly assigned to the sham-first-rTMS-second condition. The DLPFC was targeted because it is believed that OCD is triggered by dysfunctional circuits in the DLPFC. Haghighi et al. (2015) found that the values of Y-BOCS decreased, and CGI scores improved, to a greater degree when the individuals received active treatment compared to the sham treatment. In other words, self-report and clinician reports had shown that ratings of OCD symptom severity had effectively decreased during the TMS condition, but scores did not decrease for the sham condition (Haghighi et al., 2015).

Another early study by Seo et al. (2016) examined rTMS over the right DLPFC to treat OCD. The sample consisted of 27 participants (n = 13 females) with treatment-resistant OCD who were diagnosed using the DSM-IV-TR. The study used the Y-BOCS and a modified version of the CGI scale to assess the severity of OCD symptoms. Participants were randomly assigned to receive a three-week active or three-week sham procedure. A total of 14 participants received the active treatment, while the other 13 received the sham treatment. Participants in the active group had a mean age of 34.6 years old, while the sham group had a mean age of 36.3 years old. OCD symptoms were assessed during the baseline and every week during the treatment period, with the primary outcome being the Y-BOCS score.

After three weeks of treatment, the participants in the active treatment had a more significant improvement in Y-BOCS and CGI scores compared to the sham treatment group (Seo et al., 2016). Like Haghighi et al. (2015), Seo et al. (2016) found that rTMS is effective in

improving the symptoms of OCD in active groups compared to the sham group. Findings from Seo et al. (2015) support the previous paper (Haghighi et al., 2016) and suggest that TMS may be effective in reducing symptoms amongst treatment-resistant participants.

Another study by Lee et al. (2017) examined the effects of rTMS on treatment-resistant OCD in participants using an open-label design (i.e., all participants were aware they were receiving active treatment). Whereas Haghighi et al. (2016) and Seo et al. (2015) targeted the DLPFC, Lee et al. (2017) conducted active rTMS over the supplementary motor area (SMA). The SMA was targeted due to suggestions of the SMA being hyperactive in OCD patients. Two females and seven males, with the mean age of 30.22 years old, were enrolled in the study. The nine participants were diagnosed with OCD using the DSM-IV-TR. Participants received rTMS over the SMA during their sessions over four weeks. The study used the Korean versions of the Y-BOCS and the CGI to assess the severity of OCD symptoms in participants (Lee et al., 2017). Treatment effectiveness was assessed during baseline, after three weeks, and after four weeks using the Y-BOCS and CGI scales.

Lee et al. (2017) found a significant decrease in Y-BOCS scores after the start of the treatment. The Y-BOCS scores had consistently decreased post-treatment. Further, the CGI results improved from 2 to 4 weeks after beginning treatment. Due to improvements in scores, the study implies that targeting the SMA with rTMS may be an effective treatment for OCD. As found in the prior studies (Haghighi et al., 2015; Seo et al., 2016), Lee et al. (2017) found significant effect of rTMS for treatment-resistant OCD.

A study by Carmi et al. (2019) examined OCD treatment with high-frequency deep transcranial magnetic stimulation (dTMS) compared to sham dTMS to assess the therapeutic effects on treatment-resistant individuals with OCD. Carmi et al. (2019) targeted both the medial prefrontal cortex (mPFC) and the anterior cingulate cortex (ACC). Whereas the previous studies (Haghighi et al., 2015; Lee et al., 2017; Seo et al., 2016) failed to include any follow-ups after treatment, Carmi et al. (2019) conducted a follow up assessment after one-month. The study initially consisted of 100 participants, but only 87 completed the study. OCD was diagnosed according to the DSM-IV-TR, with the Y-BOCS and a modified CGI used to assess symptom severity. Of the 87 participants, 42 (*M*age = 41.1 years old) were allocated to the active treatment, while 45 (*M*age = 36.5 years old) were randomly allocated to the sham treatment. The treatment was conducted for 6 weeks, consisting of 29 sessions.

Carmi et al. (2019) found a reduction in the Y-BOCS score from baseline to after the treatment phase in both the active and sham group. However, it was found that the reduction in Y-BOCS score was significantly sustained in the active group when compared with the sham group 4-weeks after treatment. Overall, while Carmi et al. (2019) initially found that dTMS over the mPFC and ACC may not be more effective than a sham treatment, the follow-up indicates that the effects of active dTMS did last, whereas any effects of sham treatment did not. The decrease in Y-BOCS and CGI scores from Carmi et al. (2019) corroborate previous findings (Haghighi et al., 2015; Lee et al., 2017; Seo et al., 2016), suggesting that dTMS treatment is effective for improving OCD symptoms while also indicating the effects last 4-weeks after treatment.

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Another recent study conducted by Joshi et al. (2022) studied the use of rTMS in an early augmentation of OCD. An early augmentation refers to individuals who have not responded to first-line treatment, such as selective serotonin reuptake inhibitors, and quickly begin a new treatment simultaneously. Joshi et al. (2022) hypothesized that early rTMS treatment with medications would lead to a more significant reduction in OCD symptoms compared to medications with sham treatment. A total of 24 treatment-resistant individuals participated, and OCD was diagnosed based on the International Classification of Diseases, Tenth Revision (World Health Organization, 2004). A total of 13 participants (Mage = 31.85, n = 7 females) received active rTMS, and 11 participants (Mage = 25.36, n = 3 females) received the sham treatment. The treatment was delivered six times a week for 20 sessions over the SMA. Participants were assessed using the Y-BOCS before treatment and were reassessed every sixth rTMS session and at the end of therapy (Joshi et al., 2022). The patients in both groups initially were on 10mg/d of escitalopram, which was then increased to 20mg/d after 10 days.

There was a significant reduction in the Y-BOCS scores at the end of the therapy sessions (Joshi et al., 2022). The researchers found that the active group had a more significant reduction in Y-BOCS scores than the sham group. Due to the augmentation strategy used and the reduction of Y-BOCS, the findings suggest that augmentation of medications with rTMS in early phases of treatment could be beneficial to reduce OCD symptoms.

Rostami et al. (2020) studied the efficacy of rTMS over the SMA and DLPFC to reduce OCD symptoms, while also examining if baseline symptom severity influenced response to the treatment. Compared to previous studies (Carmi et al., 2019; Haghighi et al., 2015; Lee et al., 2017; Seo et al., 2016), Rostami et al. (2020) also chose to treat two brain regions to examine which region would respond more effectively to the treatment. A total of 65 treatment-resistant participants were included in the study, with 35 participants being female and 30 being male, with a mean age of 32.25 years old. Of the participants, 38 received rTMS over the SMA, and 27 received rTMS over the DLPFC. All the participants received a clinical assessment using the Y-BOCS one week before treatment and at the end of the rTMS treatment. Participants underwent 20 rTMS sessions over seven weeks (Rostami et al., 2020).

Rostami et al. (2020) found no significant difference in the treatment based on targeting the DLPFC or SMA. After treatment, participants reported significantly reduced Y-BOCS scores in both conditions. However, the participants who had higher Y-BOCS scores prior to treatment responded less effectively to the rTMS treatment (Rostami et al., 2020). Rostami et al. (2020) found that rTMS was effective whether delivered to the SMA or DLPFC, corroborating previous studies (Carmi et al., 2019; Haghighi et al., 2015; Lee et al., 2017; Seo et al., 2016). The findings also indicate that rTMS may not be as effective for individuals with more severe OCD symptoms.

Khedr et al. (2022) aimed to study the effectiveness of low frequency rTMS for treating OCD when used over the orbitofrontal cortex (OFC) and the DLPFC. A total of 60 individuals, consisting of 28 males and 32 females, participated in the study, with a mean age of 35.4 years old. The participants were diagnosed with OCD using the fifth edition of the DSM (American Psychiatric Association, 2013). All participants were evaluated at baseline using the Y-BOCS and the CGI. Participants were randomly allocated to the OFC rTMS condition, the DLPFC rTMS condition, or a sham DLPFC rTMS condition. Each patient received ten sessions over five

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days. The participants were evaluated with the Y-BOCS and the CGI again after the treatment phase and three months after the end of treatment.

Khedr et al. (2022) found that the scores of participants allocated to the active group improved significantly compared to the sham group. Like Rostami et al. (2020), there were no differences between the two active groups (OFC or DLPFC) at the end of treatment. Further, it was found that the effects of rTMS treatment over the DLPFC were maintained at the three-month follow-up, but the effects of rTMS treatment over the OFC were lost. Like Carmi et al. (2019), the results imply that treatment effects last after the end of treatment. However, findings from Khedr et al. (2022) suggest that treatment over the OFC may not be as effective as the DLPFC treatment by three months post-treatment. Khedr et al. (2022) also found that the lower the Y-BOCS score a participant had at baseline, the better the response to rTMS, as poor responders were found to have higher Y-BOCS score at baseline. In other words, individuals with higher symptom severity prior to treatment may experience a muted response to TMS.

In a study by Donse et al. (2017), the researchers aimed to study correlations between sleep disturbances in OCD with response to rTMS. The researchers investigated sleep disturbances between OCD and non-OCD individuals, along with the predictive values of rTMS responders and non-responders. A total of 51 participants were included in the study, 25 individuals with OCD and 26 healthy participants as a control group. The patient group had nine females and 16 males, while the control group had 14 females and 12 males. The mean age for the patient group was 39.3 years old, while the control group had a mean age of 34.2 years old. The patient group completed the Y-BOCS assessment, while both groups completed the Holland Sleep Disorders Questionnaire (HSDQ; Kerkhof et al., 2013) to measure sleep disorder severity and the Pittsburgh Sleep Quality (PSQI; Buysse et al., 1989) to assess sleep quality. The healthy patients did not participate in the treatment, thus only completing the questionnaires at baseline. Questionnaires for OCD patients were assessed every fifth session and post-treatment. The patient group completed at least ten sessions of rTMS over the SMA combined with psychotherapy (Donse et al., 2017).

As Donse et al. (2017) hypothesized, the OCD patients had a higher degree of sleep issues compared to the control group. When comparing OCD participants and healthy participants, the HSDQ indicated higher sleep disturbances in the OCD participant group and higher PSQI scores. Overall, rTMS was an effective treatment as the Y-BOCS scores decreased for responders, but 10 of the 25 participants did not respond to treatment. It was found that these non-responders reported more issues with sleep disturbances. However, when comparing responders and non-responders, the HSDQ had no significant difference, implying that the HSDQ may not be a viable predictor for treatment response. The PSQI revealed significant differences, as non-responders had higher rates of sleep disturbances, which implies that higher PSQI scores at baseline may predict non-response to rTMS treatment (Donse et al., 2017). Overall, Donse et al. (2017) found that while rTMS is effective, it is less effective for individuals reporting lower sleep quality.

In an open-label study, Gajadien et al. (2023) studied sleep disturbances and their predictive response to OCD participants undergoing rTMS treatment. A total of 43 males and 18 females participated in the study, with the Y-BOCS score assessing the severity of OCD symptoms. The sleep disturbances were measured using the PSQI and the HSDQ. Participants received at least ten treatment sessions of low frequency rTMS over the SMA and/or DLPFC. A

total of 35 participants received the SMA protocol, and 26 received both SMA and DLPFC protocols. Both protocols were combined with cognitive behavioural therapy. Participants were then assessed post-treatment with the Y-BOCS (Gajadien et al., 2023).

Overall, a significant reduction in OCD symptom severity was found post-treatment. Furthermore, no significant differences in effectiveness were found between treatment protocols based on targeting over the SMA or both DLPFC and SMA, supporting previous findings on protocol targeting (Gajadien et al., 2023; Khedr et al., 2022; Rostami et al., 2020). Gajadien et al. (2023) also found that the PSQI and the HSDQ were able to predict response to rTMS, as non-responders had more sleep disturbances at baseline compared to responders. Thus, severity of sleep disturbances may be able to predict response to treatment, supporting the results of Donse et al. (2017).

Limitations and Future Directions

The studies reviewed in the present paper had recurrent limitations, such as small sample sizes and follow-up assessments. The studies conducted by Haghighi et al. (2015), Seo et al. (2016), Lee et al. (2017), and Joshi et al. (2022) had small samples of less than 30 participants, hindering the generalizability of the studies. Future studies are encouraged to incorporate larger sample sizes for studies to be generalizable.

Other studies (Donse et al., 2017; Lee et al., 2017; Rostami et al., 2020) lacked a control group, which may allow placebo effects to influence the results. Specific to Lee et al. (2017), the study was an open-label study, which made it difficult to prevent a placebo effect. Future studies should always include a control group to counter the possibility of placebo effects accounting for any results.

As well, studies that did not include a follow-up period made it challenging to understand the long-term effects of TMS (Donse et al., 2017; Haghighi et al., 2015; Joshi et al., 2022; Lee et al., 2017; Seo et al., 2016). Studies that conducted short follow-up periods found that effects sustained for up to three months, but long-term effects are still unknown (Carmi et al., 2019; Khedr et al., 2022). Future studies are encouraged to implement more long-term follow-up assessments to understand effects after three months.

Studies were consistent in showing that TMS can reduce OCD symptoms, but researchers have also found that symptom severity (Khedr et al., 2022; Rostami et al., 2020) or sleeping disturbances (Donse et al., 2017; Gajadien et al., 2023) may play a role in treatment effectiveness. Since few studies have explored what factors influence treatment response, future studies should consider examining baseline symptom severity, as well as pre-existing sleep disturbances, and whether they influence treatment response.

Other limitations include the lack of reporting information that may influence treatment effectiveness. In Donse et al. (2017) and Gajadien et al. (2023), the participants had access to psychotherapy alongside rTMS treatment, but details regarding the psychotherapy were not included in both papers. For Donse et al. (2017), the type of therapy and its effects were not explained. In both studies, because the participants had access to psychotherapy it is unclear whether the decrease in symptom severity was due to rTMS or psychotherapy. Thus, it is unclear how adding psychotherapy may have altered the results found by Donse et al. (2017) and Gajadien et al. (2023).

Conclusion

In conclusion, this paper examined the effectiveness of TMS on OCD. Overall, compared to sham treatments, both rTMS and dTMS lead to a greater reduction in OCD symptoms amongst individuals with treatment-resistant OCD (Carmi et al., 2019; Donse et al., 2017; Gajadien et al., 2023; Haghighi et al., 2015; Joshi et al., 2022; Khedr et al., 2022; Lee et al., 2017; Rostami et al., 2020; Seo et al., 2016). Moreso, TMS appeared to be effective when used over the SMA or DLPFC (Donse et al., 2017; Gajadien et al., 2023; Haghighi et al., 2017; Gajadien et al., 2023; Haghighi et al., 2017; Rostami et al., 2020; Seo et al., 2017; Gajadien et al., 2023; Haghighi et al., 2015; Khedr et al., 2022; Lee et al., 2017; Rostami et al., 2020). There is also preliminary evidence that the reduction in OCD symptoms due to TMS may last up to three months post-treatment (Khedr et a., 2022). TMS also appears to be effective when used alongside medication or cognitive behavioural therapy and could potentially be used sooner in the therapeutic process (Joshi et al., 2022; Gajadien et al., 2023).

Although TMS appeared to be effective for OCD symptoms, there were findings to indicate it may be less effective amongst individuals with more severe symptoms, as well as individuals with sleep disturbances (Rostami et al., 2020; Khedr et al., 2022; Donse et al., 2017; Gajadien et al., 2023). Subsequent studies that aim to study TMS should also consider individuals who failed to respond to the treatment and examine its correlation with symptom severity and/or sleep disturbances. Although there is evidence that TMS is effective for treating OCD, many of these studies exhibit significant limitations, and future research is strongly encouraged to strengthen the evidence of TMS for OCD.

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