

STUDY THE THERAPEUTIC ROLE OF BILATERAL TRANSCRANIAL MAGNETIC STIMULATION IN A SAMPLE OF PATIENTS WITH OBSESSIVE COMPULSIVE DISORDER ATTENDING AL-AZHAR UNIVERSITY HOSPITALS

By

Bahaa Mahmoud Abd El-Wahed, Mohamed Abd El-Fattah Soliman and Amgad Ahmed Meshref

Department of Psychiatry, Faculty of Medicine, Al-Azhar University

Corresponding Author: Bahaa Mahmoud Abd El-Wahed,

Mobile: 01064691668, **E-mail:** bahaa.mahmoud11@gmail.com

ABSTRACT

Background: Obsessive-compulsive disorder (OCD) is a mental disorder in which a person has certain thoughts repeatedly or feels the need to perform certain routines repeatedly to an extent that generates distress or impairs general functioning, affects approximately 2-3% of the world population. The first-line treatments are selective serotonin reuptake inhibitors and cognitive behavioral therapy. Despite that, approximately 40- 60% of patients remain treatment refractive.

Objective: Evaluating the efficacy of low frequency repetitive transcranial magnetic stimulation (rTMS) applied over the supplementary motor area (SMA) on both sides as an adjunctive treatment for OCD.

Methods: Twenty-four patients with OCD were randomly assigned to 2 weeks either active LF (1 Hz, n=12) with parameters (25-minute trains, 1,500 pulses/day each side at 100% of the resting motor threshold RMT, 5 sessions/week) or sham (n=12) (same LF parameters with coil tilting). OCD symptoms were assessed using: Yale-Brown Obsessive Compulsive Scale (Y-BOCS) before and immediately after sessions.

Results: A repeated-measures analysis of variance (ANOVA) revealed a significant reduction in Y-BOCS scores in the active groups compared with the sham group after 2 weeks. There were no reports of serious adverse effects following the active or sham rTMS treatments.

Conclusion: LF rTMS over the supplementary motor area (SMA) on both sides appeared to be superior to sham rTMS for relieving OCD symptoms in patients with OCD. Further trials with larger sample sizes should be conducted to confirm the present findings.

Key words: Bilateral Transcranial magnetic stimulation; Obsessive-compulsive disorder; supplementary motor area.

INTRODUCTION

Obsessive-compulsive disorder (OCD) is a chronic and highly debilitating neuropsychiatric disorder characterized by obsessions and/ or compulsions; that lead to significant distress to the patients and

their families (*American Psychiatric Association, 2014*). Obsessions are persistent, intrusive ego dystonic thoughts, urges or images, while compulsions are repetitive and time-consuming behaviors or mental acts that usually done to prevent the occurrence or limit the distress caused

by the obsession. The prevalence of OCD in the general population is estimated at 2 to 3%, and it affects both sexes equally (Ruscio A *et al.*, 2010).

High doses of SSRIs and clomipramine in addition to CBT are considered as first-line treatments for OCD at present (Stein DJ *et al.*, 2012). Recently, treatment regimens have expanded to include other psychotropic drugs, particularly antipsychotics. Despite that, 40-60% of patients fail to respond to those medications appropriately or unable to tolerate their side effects (Rehn S *et al.*, 2018). Therefore, it was important to develop new treatment strategies based on understanding the abnormalities that contribute to OCD (Elbeh KA *et al.*, 2016).

Repetitive Transcranial Magnetic Stimulation (rTMS) is one of the potential additional treatments for OCD. It is a non-invasive neuromodulator technique in which strong electrical currents are passed through a coil that is placed directly on the scalp to induce magnetic field pulses with sufficient intensity able to pass through the skull and form an electrical current in the cortical region below the coil; consequently, depolarizing or hyperpolarizing the axons of the neurons (Shayganfard M *et al.*, 2016).

Although pathophysiology of OCD is not fully understood, many studies suggested that OCD is associated with dysfunction in the orbitofronto-striato-pallido-thalamic circuitry. This includes dorsolateral prefrontal cortex (DLPFC), anterior cingulate gyrus, supplementary motor area (SMA), orbitofrontal cortex (OFC) and caudate nucleus (Seo HJ *et al.*, 2016).

The aims of the present study are evaluating the therapeutic effect low frequency (1 Hz) repetitive transcranial magnetic stimulation (rTMS) applied over the supplementary motor area (SMA) on both sides versus sham stimulation in the treatment of OCD patients.

MATERIALS AND METHODS

The present study has included 24 patients with a primary diagnosis of OCD according to DSM-5 criteria from those attending psychiatric clinic at Sayed Galal Hospital, Faculty of Medicine, Al-Azhar University and accepted to participate in this study by obtaining prior informed consent during the period from March 2020 to September 2020. The ethical Committee of the Faculty of Medicine, Al-Azhar University approved the experimental protocol.

Inclusion criteria:

Patients aged from 18 to 65 years old of both sexes with Yale-Brown Obsessive Compulsive Scale (Y-BOCS) score: ≥ 16 .

Exclusion criteria:

Patients with history of other comorbid neuropsychiatric disorder; drug abuse, history of epilepsy, serious head injury or neurosurgical procedure; metal implants and pacemakers.

Procedure:

The stimulation was carried out using an 8-figure shape coil (Magstim rapid 2), which placed with its center Parallel above the optimal position of the supplementary motor area (SMA) on both sides.

The supplementary motor area (SMA) on both sides was identified at points 3-

cm anterior to the leg motor area in the sagittal midline. The Resting Motor Threshold (RMT) has been determined using visualization method via the stimulation of the primary motor cortex area for leg muscles in 5 successful trials of 10 TMS.

The patients were randomly classified into two groups to receive either a sham or active LF rTMS.

The 1st group: included 12 patients received rTMS with (1 Hz frequency, 1500 pulses/session at 100% of RMT applied in 150 trains, with 5 seconds inter-train interval). **The 2nd (sham) group:** included 12 patients received stimulation with the same parameters of the 1st group and the coil was placed over the same area but perpendicular to the scalp.

Every patient received 10 sessions, each session lasting 25 minutes, 1 session/day for 5 consecutive days for two weeks and continued pharmacological treatments with the same doses throughout the study. Neither the patient nor the rater knew

whether the patients were receiving real or sham rTMS.

All patients were assessed before rTMS procedure, after 2 weeks later with Yale-Brown obsessive compulsive scale (Y-BOCS) (Goodman WK et al., 1989).

Statistical analysis:

Data was analyzed using SPSS version 23.0. Quantitative data were expressed as mean ± standard deviation (SD). Qualitative data were expressed as percentage. The demographic and clinical data were compared using t-tests, chi-square tests. A repeated-measures analysis of variance (ANOVA) was used to evaluate the group- and time-dependent effects of rTMS on the mean scores of the psychometric scales. Patients with a reduction ≥25% in Y-BOCS score were classified as responders. P value <0.05 was considered to indicate statistical significance.

RESULTS

Of the 24 patients who were initially included in this study, 12 patients in each group. All patients completed treatment sessions, and the procedure was well tolerated.

The difference between the active and the sham groups according to demographic data wasn't statistically significant (**Table 1-a, b, c, d, e**).

Table (1-a): Age of the studied patients

		Active group N=12	Sham group N=12	T	p-value
Age	Mean	27.4	31.7	1.1	0.265
	SD	7.5	10.4		

Table (1-b): Sex of the studied patients

		Active group N=12		Sham group N=12		X ²	p-value
Sex	Male	7	58.3%	6	50%	0.16	0.682
	Female	5	41.7%	6	50%		

X²: Chi square test**Table (1-c): Marital state of the studied patients**

		Active group N=12		Sham group N=12		X ²	p-value
Marital status	Married	6	50%	6	50%	0.0	1.0
	Single	6	50%	6	50%		

X²: Chi square test**Table (1-d): Working state of the studied patients**

		Active group N=12		Sham group N=12		X ²	p-value
Work	Work	3	25%	4	33.3%	0.2	0.653
	No work	9	75%	8	66.7%		

X²: Chi square test**Table (1-e): Handedness of the studied patients**

		Active group N=12		Sham group N=12		X ²	p-value
Handedness	Rt	11	91.7%	10	83.3%	0.38	0.537
	Lt	1	8.3%	2	16.7%		

X²: Chi square test**Table (2): Y-BOCS of the studied patients before sessions**

		Active group N=12	Sham group N=12	T	p-value
Y-BOCS before	Mean	29.08	27.75	0.55	0.588
	SD	6.02	5.9		

The comparison between the 2 groups according to mean Y-BOCS isn't significantly different immediately after sessions (P=0.641) (**Table 3**).

Table (3): Y-BOCS of the studied patients after sessions

		Active group N=12	Sham group N=12	T	p-value
Y-BOCS after	Mean	23.5	24.5	0.47	0.641
	SD	5.5	4.9		

As regard OCD symptoms according to Y-BOCS, there is reduction in the active groups immediately after sessions with

statistically significant difference (p=0.027) (**Table 4**).

Table (4): Y-BOCS of the active group patients before and after sessions

		Before N=12	After N=12	T	p-value
Y-BOCS Active group	Mean	29.08	23.5	2.37	0.027
	SD	6.02	5.5		

DISCUSSION

The present study aimed to evaluate the effect of low frequency repetitive transcranial magnetic stimulation (rTMS) applied over the supplementary motor area (SMA) on both sides as an adjunctive treatment for OCD compared to sham TMS. This was in line with studies which indicated that rTMS of the supplementary motor area (SMA) on both sides was more effective for treating OCD than sham stimulation (*Shivakumar V et al., 2019*).

The study included 24 OCD patients whom divided into a sham or active rTMS groups. The demographical and clinical data of the 2 groups were monitored at the baseline and there was no significant difference in the scores of Y-BCOS. The side effects of the rTMS were acceptable as what was mentioned in many previous studies (*Seo HJ et al., 2016*).

It was clear that OCD more common among males (58.3% males) also most of the patients were in the third and fourth decade of life as the most representative age category in the two groups was (21-38 years). The difference between groups according to sex (p =0.682) and age (p =0.265) has no statistical significance (**Table 1a, b**).

This is consistent with Kang et al. study (17 males/ 3 females) with mean

age (28.6), *Sarkhel et al., 2010* (male/female 23/19), mean age (30.67) and many other studies which indicate that symptoms in more than 80% of cases started before the age of 35 Years (*Rehn Set al., 2018*).

Regarding the marital and occupation status, the percentage of non-workers people were higher in the 2 groups without statistical significance difference (p = 0.653) (**Table 1-d**). This can be explained by the presence of OCD as a mental disorder that causes a deterioration of social and occupational performance (*Elbeh KA et al., 2016*).

Our result found that LF-rTMS (1 Hz) applied over the supplementary motor area (SMA) improves symptoms and severity of OCD with significant reduction of Y-BOCS score at the end of 2nd week of treatment (**Table 4**) (P=0.027) and three patients were considered as responders to the treatment (defined as having decrease in the score of Y-BOCS ≥ 25% of the baseline) versus none in the sham group. The difference between groups in Y-BOCS wasn't statistically significant at the end of sessions (**Table 3**) (p=0.641).

Our results are consistent with that of *Mantovani et al.,* study, where they found that LF-rTMS over the supplementary motor area (SMA) produces significant

improvement of OCD ($P < 0.01$). Also results agreed with that of Gomes *et al.* as there were significant differences over 2nd weeks between the active and sham groups on Y-BOCS ($P < 0.0001$) (Mantovani *et al.*).

While Pelissolo *et al.* who studied the effect of LF-rTMS over SMA in OCD for 4 weeks and there were no statistically significant differences between the active and sham groups on Y-BOCS at the end of the 4th week. Perhaps this is due to the difference in the stimulation period as well as the nature of sham stimulation.

In our study there were statistically significant differences between the active and the sham groups, patients treated with active rTMS had a somewhat greater reduction in OCD symptoms.

The obstacles that we have met may be related to many limitations such; the short stimulation period (two weeks), dependence on the manual targeting in coil localization, relying on the tilting method in sham stimulation, relatively small sample size, the nature of the target group with OCD in COVID restrictions and finally choosing SMA as the target region for stimulation which is only one of the neural circuits involved in the occurrence of OCD symptoms, or a starting point to induce remote stimulation of other circuits also involved in OCD and persistence of symptoms, such as OFC and DLPFC which can't be stimulated directly using rTMS techniques used in the present study.

So, we recommend that; Conducting more studies involving larger numbers of patients with a less chronic form of OCD, taking into account that there are other regions involved in the occurrence of

OCD, the impact of psychiatric drugs, neuroimaging and computer modeling of TMS to determine optimal stimulation targets and the change in brain activity in OCD during rest than exposure to stimuli.

CONCLUSION

The two-week treatment with rTMS applied over the SMA on both sides as an adjunctive treatment does outweigh the sham stimulation in relieving OCD symptoms, reducing clinical severity or improving treatment response.

REFERENCES

1. **American Psychiatric Association. Diagnostic and statistical manual of mental disorders (2013):** DSM-5. Washington, D.C: American Psychiatric Association; 2013.
2. **Abudy A, Juven-Wetzler A, Zohar J. (2011):** Pharmacological management of treatment-resistant obsessive-compulsive disorder. *CNS Drugs* 2011; 25:585-596.
3. **Elbeh KA, Elserogy YM, Khalifa HE, Ahmed MA, HafezMH, Khedr EM. (2016):** Repetitive transcranial magnetic stimulation in the treatment of obsessive-compulsive disorders: double blind randomized clinical trial. *Psychiatry Res.* 2016; 238:264–9.
4. **Goodman WK, Price LH, Rasmussen SA, et al. (1989):** The Yale-Brown Obsessive Compulsive Scale. I. Development, use, and reliability. *ArchGen Psychiatry* 1989; 46:1006-1011.
5. **Mansur CG, Myczkowski ML, Cabral SD, (2011):** Sartorelli MDB, et al. Placebo effect after prefrontal

- magnetic stimulation in the treatment of resistant obsessive-compulsive disorder: RCT. *Int J Neuropsychopharmacol.* 2011; 14(10):1389–97.
6. **Rehn S, Eslick GD, Brakoulias V. (2018):** A meta-analysis of the effectiveness of different cortical targets used in rTMS for the treatment of OCD. *Psychiatr Q.* 2018; 89:645–65.
 7. **Ruscio A, Stein D, Chiu W, Kessler R. (2010):** The epidemiology of obsessive-compulsive disorder in the national comorbidity survey replication. *Mol Psychiatry.* 2010; 15(1):53–63.
 8. **Shivakumar V, Dinakaran D, Narayanaswamy JC, Venkatasubramanian G. (2019):** Noninvasive brain stimulation in obsessive-compulsive disorder. *Indian J Psychiatry* 2019; 61, Suppl S1:66-76.
 9. **Stein DJ, Koen N, Fineberg N, Fontenelle LF, Matsunaga H, Osser D, et al. A (2012):** evidence-based algorithm for the pharmacotherapy for obsessive-compulsive disorder. *Curr Psychiatry Rep* 2012; 14:211-219.
 10. **Shayganfard M, Jahangard L, Nazaribadie M, et al. (2016):** Repetitive Transcranial Magnetic Stimulation Improved Symptoms of Obsessive-Compulsive Disorders but Not Executive Functions: Results from a RCT with Crossover Design and Sham Condition. *Neuropsychobiology* 2016; 74(2):115-24.
 11. **Seo HJ, Jung YE, Lim HK, Um YH, Lee CU, Chae JH. (2016):** Adjunctive low-frequency repetitive transcranial magnetic stimulation over the right dorsolateral prefrontal cortex in patients with treatment-resistant obsessive-compulsive disorder: a randomized controlled trial. *Clinical Psychopharmacology and Neuroscience.* 2016; 14(2):153–60.
 12. **Sarkhel S, Sinha VK, Praharaj SK. (2010):** Adjunctive high-frequency right prefrontal repetitive transcranial magnetic stimulation (rTMS) was not effective in obsessive-compulsive disorder but improved secondary depression. *J Anxiety Disord.* 2010; 24(5):535–9.

دراسة الدور العلاجي للتحفيز المغناطيسي المتكرر عبر الجمجمة على الجانبين في عينة من المرضى المصابين باضطراب الوسواس القهري المترددين على مستشفيات جامعة الأزهر

بهاء محمد عبد الواحد ، محمد عبد الفتاح سليمان ، أمجد أحمد
قسم الطب النفسي بكلية الطب جامعة الأزهر

الهدف من الدراسة:

1. هذه الدراسة تهدف إلى تقييم فعالية التحفيز المغناطيسي المتكرر عبر الجمجمة على الجانبين rTMS في علاج الوسواس القهري، ووضع معايير مناسبة للعلاج.
2. دراسة ومقارنة التأثير العلاجي للتردد المنخفض لجلسات التحفيز المغناطيسي المتكرر على الجانبين في مرضى الوسواس القهري.

العينة وطرق البحث:

أولاً: العينة:

الاشخاص الذين يعانون من اضطراب الوسواس القهري المترددين على عيادات الطب النفسي بمستشفيات جامعة الأزهر اعتماداً على الخصائص التشخيصية لمرض الوسواس القهري طبقاً للدليل التشخيصي والاحصائي الأمريكي الخامس (DSM-5) في الفترة من مارس الى سبتمبر 2020.

شروط الادراج في العينة:

- كلا الجنسين.
- العمر من 18 - 65 عاماً.

- قبول المشاركة في هذه الدراسة، عن طريق الحصول على الموافقة الكتابية المسبقة.
- أن يكون مريض بالوسواس القهري طبقاً للدليل التشخيصي والإحصائي الأمريكي الخامس (DSM-5).

معايير الاستبعاد:

- رفض المشاركة في هذه الدراسة.
- وجود اضطراب يحول دون إجراء المقابلة الإكلينيكية أو تطبيق المقاييس السيكومترية.
- وجود اضطراب نفسي آخر (اضطراب القلق العام، اضطراب الهلع، الفصام...).
- وجود مرض طبي أو عصبي أو تاريخ للتشنجات (الصرع).
- موانع استخدام جهاز الحث المغناطيسي المتكرر مثل وجود تاريخ لزراعة أجسام معدنية داخل المخ.

ثانياً: طرق البحث:

- مقياس يال براون للوسواس القهري (Y-BOCS).
- (Goodman et al., 1989).
- مقابلة إكلينيكية شبه مقننة وفقاً لمحكات دليل التشخيص الإحصائي الخامس (DSM-5(2013).

(American Psychiatric Association, 2013).

- جهاز التحفيز المغناطيسي المتكرر عبر الجمجمة (rTMS) (Magestim rapid2).

الاستنتاج:

من خلال هذه الدراسة ، يتضح لنا أن التحفيز المغناطيسي المتكرر عبر الجمجمة rTMS منخفض التردد المطبق علي المنطقة الحركية التكميلية SMA علي الناحيتين نجح في احداث تحسن ملحوظ في الوسواس القهري وعمل فرق ذو دلالة احصائية بينه وبين التحفيز الوهمي sham rTMS.

ومع وجود فروق ذات دلالة إحصائية بين المجموعة العلاجية والمجموعة الضابطة، فإن المرضى الذين عولجوا بـ rTMS الحقيقي كان لديهم انخفاض أكبر وملحوظ إلى حد ما في أعراض الوسواس القهري.

الكلمات الدالة: التحفيز المغناطيسي المتكرر عبر الجمجمة، الوسواس القهري، المنطقة الحركية التدمعية.