

Research Paper



Effectiveness of Low-frequency rTMS and CBT in Reducing Symptoms Severity and Improving Cognitive Flexibility in Adults With OCD: A Clinical Trial

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ABSTRACT

Introduction: This study aims to assess and compare the effects of low-frequency (LF) repetitive transcranial magnetic stimulation (rTMS) and cognitive-behavioral therapy (CBT) on symptoms and cognitive flexibility of adults with obsessive-compulsive disorder (OCD).

Methods: This is a randomized clinical trial conducted on 24 people with OCD living in Zanjan City, Iran, in two groups of CBT (n=12) and rTMS (n=12). The CBT with exposure and response prevention (ERP) was presented at 20 sessions. The rTMS (1 Hz) was delivered at 100 resting motor thresholds using an 8-shaped coil over the right dorsolateral prefrontal cortex (DLPFC) (F4) for 2 weeks at 10 sessions. They completed the Yale-Brown obsessive-compulsive scale (Y-BOCS) and the cognitive flexibility inventory (CFI) before, immediately, and one month after the intervention. Collected data were analyzed in SPSS software, version 22.

Results: Results showed a significant difference between the two groups in the severity of OCD symptoms (obsessions and compulsions) immediately after the intervention ($P < 0.001$), where higher reductions were observed in the CBT group. There was no significant difference between the two groups in cognitive flexibility ($P > 0.05$). No significant difference was found between the groups in any study variable one month after interventions.

Conclusion: There is a significant difference between CBT and LF-rTMS techniques in reducing the severity of OCD symptoms, while there is no difference between them in improving the cognitive flexibility of the patients.

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Highlights

- Individual CBT is more effective than Lf rTMS in reducing the severity of OCD symptoms.
- The LF rTMS can improve the cognitive flexibility of patients with OCD.
- Individual CBT is not effective in improving the cognitive flexibility of patients with OCD.

Plain Language Summary

Obsessive-compulsive disorder (OCD) is a mental disorder characterized by obsessive thoughts and behaviors. OCD individuals have impaired executive functioning. One of the executive functions impaired in these people is cognitive flexibility. Cognitive-behavioral therapy (CBT) is currently the standard treatment of OCD. However, these patients may refuse this therapy. Therefore, there is a need for new non-invasive treatments. Improvement in dorsolateral prefrontal cortex (DLPFC) function may help improve the symptoms of these patients. Therefore, in this study we aim to assess whether low-frequency repetitive transcranial magnetic brain stimulation is more effective than CBT in reducing symptoms and improving cognitive flexibility in adults with OCD. The results showed that CBT is more effective than Lf rTMS in reducing the severity of OCD symptoms, while repetitive transcranial magnetic brain stimulation is effective in improving the cognitive flexibility. It can help the patients to generate multiple alternative solutions to difficult situations.

Introduction

Obsessive-compulsive disorder (OCD) is a debilitating and severe mental disorder characterized by varying degrees of obsessive thoughts and behaviors. Obsessive thoughts are intrusive, unwanted, and annoying thoughts or images that people experience spontaneously incompatible with the person's obvious and perceived feelings. Compulsions are repetitive and time-consuming behaviors or mental acts that are used to neutralize anxiety caused by obsessive thoughts (Rapinesi et al., 2019; Robbins et al., 2019). According to the World Health Organization (WHO), it is among the 10 disabling disorders (Melchior et al., 2019). Its lifelong prevalence is 1%-3% worldwide (Kessler et al., 2005) and 5.1%-1.8% in Iran (Mohammadi et al., 2004; Vandan Sharifi et al., 2015). OCD has a gradual onset and becomes chronic if people do not receive treatment (Olatunji et al., 2013), and its symptoms change over time due to stressors in life (Stewart et al., 2004). People with OCD tend to engage in obsessive actions, and even if they know that obsessive actions are useless, they cannot stop it (Sternheim et al., 2014). Impaired executive functioning has been observed frequently in OCD individuals (Fournet et al., 2019). Executive functioning is defined as managing intervening components in goal-directed behaviors and predicting the consequences of behavior (Pajouhinia et al., 2020). Executive functions

include cognitive processes, such as working memory, inhibitory control, and cognitive flexibility, essential for goal-directed behavior (Miyake et al., 2000; Nejati et al., 2020). Clinically, people with OCD have difficulty switching between mental processes to generate adaptive behavioral responses to their symptoms. Many neurological studies have shown reduced cognitive flexibility in people with OCD (Gruner & Pittenger, 2017; Vriend et al., 2013). The ability to modify cognitive sets to adapt to variable environmental stimuli is a key component in most operational definitions of cognitive flexibility. It is considered a wide range of behaviors that enable people to adapt adaptively to stressful events instead of having maladaptive behaviors (Kurginyan & Osavolyuk, 2018). Recently, neurological models of OCD have suggested cognitive inflexibility as a significant feature of OCD patients, which can also be present in their relatives (Chamberlain et al., 2007). Although OCD patients have many cognitive impairments, impaired cognitive flexibility may be an essential trait for understanding the neural basis of OCD (Tomiya et al., 2019).

Cognitive-behavioral therapy (CBT) based on exposure and response prevention (ERP) is currently the standard treatment for OCD. In CBT, individuals are believed to respond to the cognitive representation of stressful events instead of responding to these events (Porto et al., 2009). ERP involves gradual and long-term exposure to intimidating stimuli and avoiding obsessive actions (Olatunji et al., 2013). CBT can reduce

cortico-striato-thalamo-cortical circuit hyperactivity and ultimately help improve the symptoms of OCD (Moody et al., 2017). However, CBT is much less common than drug therapy. According to surveys in the United Kingdom and USA, only 5% of adults with OCD receive CBT (O'Neill & Feusner, 2015). On average, 30% of these patients refuse ERP therapy or drop out of treatment (Olatunji et al., 2010; Melchior et al., 2019). Therefore, complementary interventions have been suggested as an alternative to overcome CBT limitations in treating OCD. A potential new treatment option, repetitive transcranial magnetic stimulation (rTMS), can modulate neural activity in brain circuits (Elbeh et al., 2016; Husain et al., 2002). First introduced by Barker et al. in 1985, rTMS is a non-invasive technique that delivers electromagnetic pulses to selected areas of the cerebral cortex (Barker et al., 1985; Jaafari et al., 2012). The stimulation can be applied at either high (≥ 5 Hz) or low (≤ 1 Hz) frequencies, which have stimulatory and inhibitory effects on cortical excitability, respectively (Lefaucheur et al., 2014). Studies have shown that the dorsolateral prefrontal cortex (DLPFC) is essential in cognitive flexibility (Borwick et al., 2020; Quiñones-Camacho et al., 2019). Thus, improvement in DLPFC neuronal function may help improve the cognitive flexibility of patients with OCD. In a clinical trial, Seo et al. reported the effectiveness of low-frequency rTMS (LF-rTMS) over the right DLPFC in relieving the symptoms of OCD and depression in OCD patients (Seo et al., 2016).

Due to the high involvement of networks in the pathophysiology of OCD and the rTMS's ability to adjust cortical and subcortical structures and its potential therapeutic effectiveness in modulating inactive or hyperactive areas of the brain by targeting cortical circuits in patients with OCD, and lack of study on comparing the efficacy of CBT and LF-rTMS in treating OCD patients, the present study aims to compare the effects of CBT with ERP and rTMS over the right DLPFC on symptoms and cognitive flexibility in people with OCD. It is hypothesized that (a) there is a difference between LF-rTMS and CBT in reducing the severity of OCD symptoms and (b) there is a difference between LF-rTMS and CBT in improving the cognitive flexibility of OCD patients.

Materials and Methods

Study design and participants

This randomized clinical trial employed a pre-test/post-test/follow-up design. The study population consists of all adults with OCD referred to the clinic of Shahid Beheshti Hospital in Zanjan City, Iran, in 2020 (during

the COVID-19 pandemic) ($n=41$). The sample size was determined to be 13 for each group using G*Power software by considering $\alpha=0.05$, an error probability of 0.95, and an effect size of 0.6 according to previous studies in the literature which reported middle-size to large-size effects of rTMS and CBT on patients with OCD (Perera et al., 2021; Hoppen et al., 2021). Due to the COVID-19 pandemic and considering the 20% dropout, the sample size was increased to 17 for each group. In this regard, 34 patients were selected using a convenience sampling method and randomly (by drawing cards) assigned into two parallel groups of CBT ($n=17$) and rTMS ($n=17$). Each group of patients was acknowledged which group s/he was assigned to. The randomization was conducted using a lottery method by the last author. All samples were diagnosed with OCD by a psychiatrist and re-evaluated by a psychologist through a structured clinical interview for diagnostic and statistical manual of mental disorders, fifth edition (DSM-5) (SCID-5) and using the Millon clinical multi-axial inventory-III (MCMI-III). The inclusion criteria were as follows: Having OCD according to the psychiatrist and based on SCID-5, bearing at least a middle-school education, being 18-50 years old, signing a written consent, and lacking a history of psychological therapies, transcranial direct current stimulation, or neurofeedback.

On the other hand, the exclusion criteria were the existence of suicidal thoughts, personality disorders according to the SCID-5 and MCMI-III, psychotic disorders, history of seizures and epilepsy, the existence of an electrical or metal object in the body (e.g. pacemaker), and having bipolar disorder. Before entering the study, the participants received medication whose dosage had been stabilized for four weeks. After and during the study, the psychiatrist kept the dosage the same. Ten patients were excluded from the study (5 from the rTMS group and 5 from the CBT group). Therefore, 12 patients in each group completed the study. Figure 1 shows the sampling and allocation processes.

Study measures

After obtaining written informed consent from the participants, they completed a demographic form, the Yale-Brown obsessive-compulsive scale (Y-BOCS) to assess their OCD symptoms, and the cognitive flexibility inventory (CFI) to evaluate their cognitive flexibility. The Y-BOCS is a semi-structured interview and the gold standard for assessing OCD symptoms. It has two primary scales: Symptom checklist (SC) and severity scale (SS). The SC has 16 self-report items rated on a 5-point scale. In the SS, the severity of obsessions and

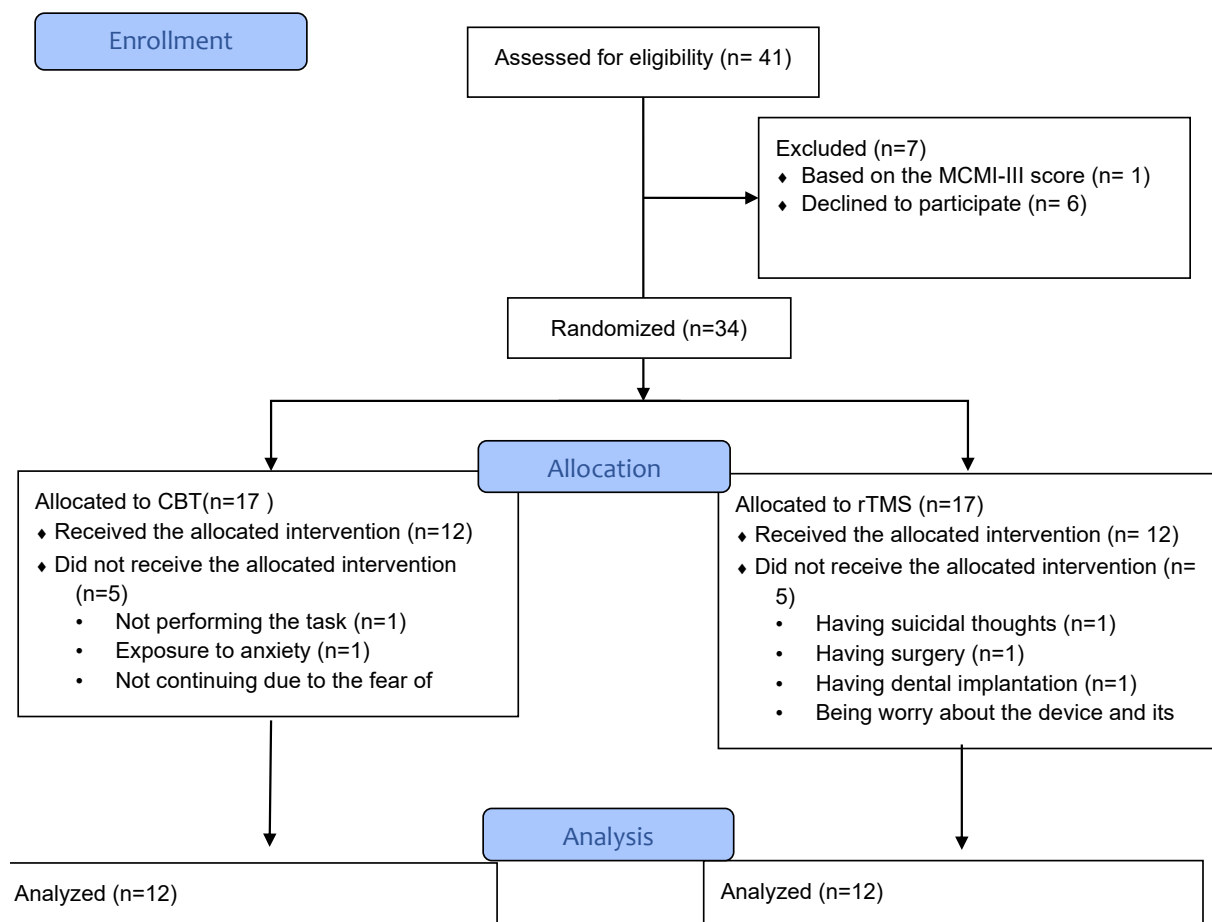


Figure 1. Flowchart of sampling and allocation

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ArTMS: Repetitive transcranial magnetic stimulation; CBT: Cognitive behavioral therapy.

compulsions is measured in five areas: Distress, frequency, intervention, resistance, and symptom control. In this study, we used the Persian version of Y-BOCS validated by [Rajezi Esfahani et al. \(2021\)](#), who reported internal consistency of 0.97 for the SC and 0.95 for the SS, a split-half reliability of 0.93 for the SC and 0.89 for the SS, and a test re-test reliability of 0.99. In our study, patients completed the SS scale only.

[Dennis and Vander Wal \(2010\)](#) developed the CFI, which is a 20-item self-report tool using a 7-point Likert scale to measure three aspects of cognitive flexibility, including the ability to perceive multiple alternative explanations for life occurrences and human behavior, the ability to generate multiple alternative solutions to difficult situations, and the desire to perceive difficult situations as controllable (Control subscale). The CFI has excellent internal consistency and high test re-test reliability ([Dennis & Vander Wal, 2010](#)). They reported Cronbach α values of 0.90, 0.86, and 0.91, as well as

test re-test reliability values of 0.81, 0.77, and 0.75 for the overall scale, control, and alternatives subscales, respectively. For its Persian version, [Shareh et al. \(2014\)](#) reported a three-factor structure: control, alternative solutions, and alternative explanations. They reported the Cronbach α and test re-test coefficients for the Persian CFI reliability as 0.90 and 0.71, respectively. The mentioned tools were completed again immediately and one month after the intervention.

Study interventions

The CBT group individually received CBT with ERP at 20 sessions twice a week, each for 45-90 minutes, according to the protocol proposed by [Leahy et al. \(2011\)](#) (Table 1). According to [Jaurieta et al. \(2008\)](#), individual CBT is more effective in reducing OCD symptoms than group CBT. Treatment was performed by the researcher (MS student in clinical psychology) under the supervision of a therapist.

Table 1. The protocol of CBT with ERP therapy

Session	Content
1-2	Acquaintance, a psychological interview, assessing current problems, symptoms, obsessions/compulsions, avoidance behaviors, feared consequences, internal and external triggers of obsessive thoughts, impairments in social, academic, and occupational functioning; informing of diagnosis and treatment options; having patient write out goals for treatment (homework)
3-4	Reviewing homework and all obsessions/compulsions and avoided situations, assessing motivation for treatment, building motivation, describing cognitive-behavioral conceptualization of OCD and CBT, obtaining patient's commitment to proceed with treatment, introducing cognitive model, identifying automatic thoughts, obsessional anxiety, compulsions, and triggering situations; evaluating automatic thoughts, asking the patient to list advantages and disadvantages of proceeding with treatment (homework)
5-6	Reviewing homework, administrating self-report questionnaires to assess mood and track progress, educating the patient regarding intrusive thoughts as normal phenomena, evaluating the validity of automatic thoughts, helping the patient devise behavioral experiments and begin constructing hierarchies of obsessions and avoided situations, having the patient continue modifying automatic thoughts and assumptions, conducting behavioral experiments and practice in disrupting rituals (homework)
7-10	Reviewing homework, administrating self-report questionnaires to assess mood and track progress, continuing modifying automatic thoughts and dysfunctional assumptions, helping the patient complete exposure hierarchies, planning initial exposure sessions, conducting exposure to initial items on hierarchies of obsessions and avoided situations, teaching postponing, slowing, and changing repetition, helping the patient block all rituals, having the patient continue modifying automatic thoughts, and assigning daily repetition of exposure (homework)
11-16	Reviewing homework, administering self-report questionnaires to assess mood and track progress, challenging any thoughts related to exposure avoidance and lapses in rituals, continuing exposure to items higher up hierarchies of obsessions and avoided situations, continuing to help patient block ritual, examining any lapses in response prevention, having patient continue modifying automatic thoughts, and assigning daily repetition of exposure (homework)
17-20	Reviewing homework, administering self-report questionnaires to assess mood and track progress, assessing attainment of goals to determine whether treatment may be tapered, tracking progress in identifying and modifying thoughts, assessing any life problems related to OCD or patient recovery, continuing with cognitive challenges to schemas of danger, responsibility and the like; ensuring that the exposure is performed to items highest in the hierarchy, monitoring any lapses, teaching to use lapses to practice skills, encouraging the patient to continue practicing all skills learned

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The rTMS group received rTMS for 2 weeks at 10 sessions (5 consecutive days per week, each for 20 minutes) according to the protocol proposed by [Gomes et al. \(2012\)](#). Each person received 1-Hz rTMS at 100% of resting MT (1200 pulses per day with a 10-min rest interval between each 300 pulses) using a focal 8-shaped 70-mm coil (Neuro-MS/D Advanced Therapeutic, Neurosoft Ltd., Russia), which was positioned on the right DLPFC (F4, according to the EEG 10–20 International System) such that there was no space between the skin and the coil. The rTMS was conducted by an expert who was unaware of the results.

Data analysis

Descriptive statistics such as Mean±SD, frequency, and percentage were used to analyze the collected data. Also, inferential statistics such as the chi-square test and independent t-test (to examine the differences in demographic factors and pre-test means), multivariate analysis of covariance (MANCOVA) (to compare the groups in terms of Y-BOCS and CFI scores), repeated-measures analysis of variance (ANOVA) (to compare the means of Y-BOCS and CFI between the time points), and the Fisher least significant difference (LSD) test for pairwise comparison were used in SPSS software, version

22. According to the results of the Kolmogorov-Smirnov test, the assumption of normal distribution of data in all three stages of pre-test, post-test, and follow-up was confirmed ($P>0.05$). According to the results of Levene's test, the assumption of the quality of variances in the studied groups was not observed in the post-test data of obsessions (a component of Y-BOCS) and the pre-test data of alternatives subscale of CFI ($P<0.05$). Therefore, the degree of corrected freedom was used to compare the two groups in the mentioned variables. In other variables, the equality of variances was confirmed ($P>0.05$).

Results

Characteristics of participants

Table 2 presents the demographic characteristics of patients. In the CBT group, with a mean age of 32.83 ± 9.43 years, there were two males and 10 females; 7 were single, 5 were married, and most had a bachelor's degree ($n=7$, 58.3%). In the rTMS group with a mean age of 30.17 ± 11.26 years, there were 6 males and 6 females; 5 were single, 7 were married, and most had a high school diploma ($n=5$, 41.7%). No significant difference was found between the two groups in terms of gender

Table 2. Demographic characteristics of the study participants

Characteristics		No. (%)			Pearson Chi-square	P*
		CBT Group (n=12)	rTMS Group (n=12)	Total		
Gender	Male	2(16.7)	6(50)	8(33.3)	3	0.083
	Female	10(83.3)	6(50)	16(66.7)		
Marital status	Single	7(58.3)	5(41.7)	12(50)	0.67	0.414
	Married	5(41.7)	7(58.3)	12(50)		
Educational level	Lower than high school	1(8.3)	2(16.7)	3(12.5)	6.22	0.183
	Diploma	4(33.3)	5(41.7)	9(37.5)		
	Associate's degree	0(0)	1(8.3)	1(4.2)		
	Bachelor's degree	7(58.3)	2(16.7)	9(37.5)		
	Master's degree	0(0)	2(16.7)	2(8.3)		
Characteristics		Mean±SD			t	P**
Age (y)		32.83±9.43	30.17±11.26	31.50±10.25	0.63	0.536

*Chi-square test, **Independent t-test.

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(P=0.083), marital status (P= 0.414), and level of education (P=0.183) according to the results of the chi-square test, and in terms of age (P=0.536) according to the results of independent t-test (Table 2). In the CBT group, 9 patients (75%) had contamination obsessions with washing/cleaning compulsions, 2(16.16%) had harm obsessions with checking compulsions, and one (8.33%) had symmetry obsessions with ordering. In the rTMS group, 9(75%) had contamination obsessions with washing/cleaning compulsions, and 3(25%) had harm obsessions

with checking compulsions. However, this difference between groups was not significant according to the chi-square test results (P>0.05).

Comparing OCD symptoms in two study groups

As seen in Figure 2, the pre-test scores of Y-BOCS and its components were higher in the CBT group than in the rTMS group. This difference was statistically significant only in the total score (P=0.011) and

Table 3. Test of between-subject effects (dependent variable: post-test OCD symptoms)

Source	Dependent Variables	Sum of Squares	df	Mean Square	F	P	η_p^2
Pre-test	Compulsions	225.054	1	225.054	22.700	0.000	0.519
	Total	508.763	1	508.763	15.353	0.001	0.422
Group	Obsessions	238.007	1	238.007	23.645	0.000	0.530
	Compulsions	207.401	1	207.401	20.920	0.000	0.499
	Total	847.182	1	847.182	25.565	0.000	0.549
	Obsessions	211.383	21	10.066	-	-	-
Error	Compulsions	208.196	21	9.914	-	-	-
	Total	695.903	21	33.138	-	-	-

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Table 4. Test of within-subject effects for OCD symptoms (Greenhouse-Geisser test)

Dependent Variables		Sum of Squares	df	Mean Square	F	Sig.	η_p^2
Obsessions	Time	663.528	1.834	361.834	65.249	0.000	0.748
	Time×Group	166.083	1.834	90.568	16.332	0.000	0.426
	Error	223.722	40.343	5.545	-	-	-
Compulsions	Time	498.111	1.991	250.145	48.251	0.000	0.687
	Time×Group	210.778	1.991	105.850	20.418	0.000	0.481
	Error	227.111	43.808	5.184	-	-	-
Total	Time	2310.194	1.949	1185.289	69.867	0.000	0.761
	Time×Group	751.028	1.949	385.329	22.713	0.000	0.508
	Error	727.444	42.879	16.965	-	-	-

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the compulsions domain ($P=0.017$). Immediately after the intervention, the scores decreased significantly in both groups, whereas the decrease was higher in the CBT group. Results of MANCOVA (Table 3) showed that, after controlling the pre-test scores, the difference between groups was statistically significant in post-test obsessions ($F_{1,21}=23.645$, $P<0.001$, $\eta^2=0.53$); post-test compulsions ($F_{1,21}=20.920$, $P<0.001$, $\eta^2=0.45$); and post-test total score ($F_{1,21}=25.565$, $P<0.001$, $\eta^2=0.55$). One month after the intervention, these scores slightly increased in both groups. Results of repeated-measures ANOVA (Table 4) showed a significant difference in the Y-BOCS scores within three time points of pre-test, post-test, and follow-up, where the main and interaction effects were significant ($P<0.001$). To assess be-

tween which time points this difference was observed, the LSD test was conducted. In the CBT group, the results (Table 5) showed a significant difference between pre-test and post-test scores and between pre-test and follow-up scores of obsessions, compulsions, and total scores ($P<0.001$). Still, there was no significant difference between post-test and follow-up scores ($P>0.05$). In the rTMS group, there was a significant difference between pre-test and post-test scores and between pre-test and follow-up scores of obsessions and total score ($P<0.05$) but not in compulsions. No significant differences between the post-test and follow-up scores of any variables were observed in this group (Table 5).

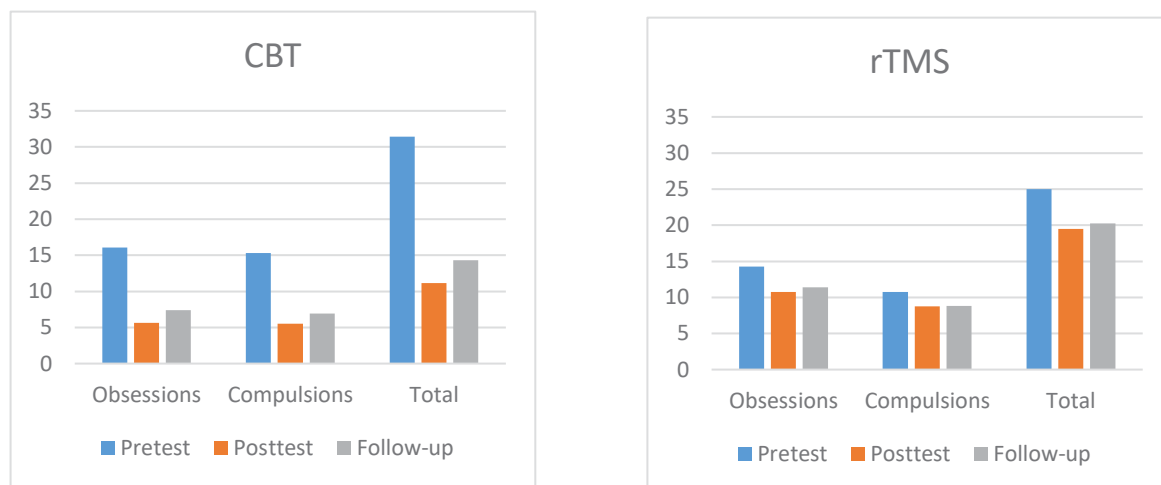


Figure 2. Mean scores of Y-BOCS for two study groups at three time points

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Table 5. Pairwise comparison for OCD symptoms LSD test

Group	(I) Time	(J) Time	Mean Difference (I-J)	Std. Error	Sig.	95% CI		
						Lower Bound	Upper Bound	
CBT	Obsessions	Pre-test	Post-test	10.417*	1.003	0.000	8.208	12.625
		Follow-up	Post-test	8.667*	1.150	0.000	6.135	11.199
			Pre-test	-10.417*	1.003	0.000	-12.625	-8.208
		Post-test	Follow-up	-1.750	0.871	0.070	-3.668	0.168
			Pre-test	-8.667*	1.150	0.000	-11.199	-6.135
		Follow-up	Post-test	1.750	0.871	0.070	-0.168	3.668
	Compulsions	Pre-test	Post-test	9.833*	1.021	0.000	7.586	12.081
		Follow-up	Post-test	8.417*	.848	0.000	6.550	10.283
			Pre-test	-9.833*	1.021	0.000	-12.081	-7.586
		Post-test	Follow-up	-1.417	0.821	0.112	-3.223	0.390
			Pre-test	-8.417*	0.848	0.000	-10.283	-6.550
		Follow-up	Post-test	1.417	0.821	0.112	-0.390	3.223
	Total	Pre-test	Post-test	20.250*	1.943	0.000	15.974	24.526
		Follow-up	Post-test	17.083*	1.885	0.000	12.935	21.232
			Pre-test	-20.250*	1.943	0.000	-24.526	-15.974
		Post-test	Follow-up	-3.167	1.609	0.075	-6.708	0.374
			Pre-test	-17.083*	1.885	0.000	-21.232	-12.935
		Follow-up	Post-test	3.167	1.609	0.075	-.374	6.708
rTMS	Obsessions	Pre-test	Post-test	3.500*	0.783	0.001	1.776	5.224
		Follow-up	Post-test	2.833*	0.920	0.010	0.809	4.858
			Pre-test	-3.500*	0.783	0.001	-5.224	-1.776
		Post-test	Follow-up	-0.667	0.732	0.382	-2.277	0.944
			Pre-test	-2.833*	0.920	0.010	-4.858	-0.809
		Follow-up	Post-test	0.667	0.732	0.382	-0.944	2.277
	Compulsions	Pre-test	Post-test	2.000*	0.826	0.034	0.183	3.817
		Follow-up	Post-test	1.917	1.048	0.095	-0.389	4.223
			Pre-test	-2.000*	0.826	0.034	-3.817	-0.183
		Post-test	Follow-up	-0.083	0.973	0.933	-2.224	2.058
			Pre-test	-1.917	1.048	0.095	-4.223	0.389
		Follow-up	Post-test	0.083	0.973	0.933	0.183	3.817
	Total	Pre-test	Post-test	5.500*	1.264	0.001	2.717	8.283
		Follow-up	Post-test	4.750*	1.670	0.016	1.074	8.426
			Pre-test	-5.500*	1.264	0.001	-8.283	-2.717
		Post-test	Follow-up	-0.750	1.493	0.625	-4.036	2.536
			Pre-test	-4.750*	1.670	0.016	-8.426	-1.074
		Follow-up	Post-test	0.750	1.493	0.625	-2.536	4.036

*The mean difference is significant at the 0.05 level.

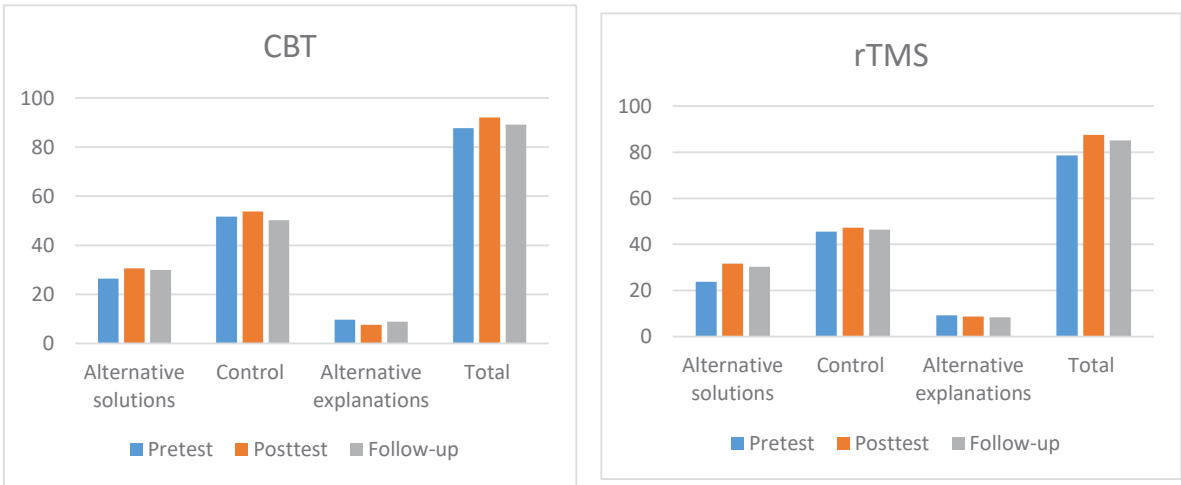


Figure 3. Mean scores of CFI for two study groups at three time points

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Comparing cognitive flexibility in two study groups

As seen in [Figure 3](#), the pre-test scores of total CFI and its three subscales were higher in the CBT group than in the rTMS group, but there was no significant difference between the pre-test CFI scores of the two groups ($P>0.05$). Immediately after the intervention, both groups' total scores and scores of "alternative solutions" and "control" increased. In contrast, the "alternative explanations" subscale score decreased in both groups. Results of MANCOVA ([Table 6](#)) showed that these differences between groups were not statistically significant in any domains ($P>0.05$). One month after intervention, a slight decrease was reported in the total score of CFI and its subscales in both groups. Results of repeated-measures ANOVA ([Table 7](#)) showed no significant overall difference between the two groups in any variables over three time points of pre-test, post-test, and follow-up ($P>0.05$).

Discussion

The purpose of this study was to compare the effectiveness of CBT with ERP (presented individually) and low frequency (1-Hz) rTMS in reducing symptom severity (Y-BOCS score) and improving cognitive inflexibility (CFI score) in 24 patients with OCD. The results showed that both treatment methods highly reduced the severity of OCD symptoms immediately after intervention, where CBT had a higher effect. The difference between the results of the two methods was statistically significant. This finding confirms our first hypothesis. After one month, the severity of symptoms was slightly increased in both groups, but it was not statistically significant. [Grassi et al. \(2018\)](#) evaluated the potential CBT-enhancing effect of high-frequency rTMS over the left DLPFC in patients with OCD. They reported that the rTMS could be an adequate tool to enhance the impact

Table 6. Test of between-subject effects (dependent variable: Cognitive flexibility)

Source	Dependent Variables	Sum of Squares	df	Mean Square	F	Sig.	η_p^2
Group	Alternative solutions	45.929	1	45.929	0.614	0.442	0.028
	Control	51.146	1	51.146	0.517	0.480	0.024
	Alternative explanations	6.782	1	6.782	1.811	0.193	0.079
	Total	9.756	1	9.756	0.048	0.829	0.002
Error	Alternative solutions	1572.145	21	74.864			
	Control	2075.998	21	98.857			
	Alternative explanations	78.625	21	3.744			
	Total	4261.878	21	202.947			

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Table 7. Test of within-subject effects for cognitive flexibility

Dependent Variables		Sum of Squares	df	Mean Square	F	Sig.	η_p^2
Alternative solutions	Time	498.694	1.576	316.330	3.281	0.060	0.130
	Time×group	45.028	1.576	28.562	0.296	0.693	0.013
	Error	3343.611	34.683	96.405			
Control	Time	71.861	1.577	45.557	0.759	0.447	0.033
	Time×group	24.694	1.577	15.655	0.261	0.719	0.012
	Error	2082.778	34.702	60.019			
Alternative explanations	Time	20.361	2	10.181	2.057	0.140	0.086
	Time×group	8.528	2	4.264	0.861	0.430	0.038
	Error	217.778	44	4.949			
Total	Time	539.583	1.550	348.174	1.722	0.198	0.073
	Time×group	95.583	1.550	61.677	0.305	0.683	0.014
	Error	6895.500	34.095	202.247			

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of CBT with ERP technique in these patients. In their study, at the end of the 16 CBT sessions (once a week), patients showed a 35% and 30% symptom reduction in obsessions and compulsions, respectively. In our study, the means of obsessions and compulsions were reduced from 16.08 to 5.67 and from 15.33 to 5.50, respectively, after 20 CBT sessions. In a meta-analysis by Reid et al. (2021), the effect of CBT with ERP on reducing OCD symptoms was reported as high, which is consistent with our results. Elbeh et al. (2016), in a clinical trial, evaluated the effect of 1-Hz (low frequency) and 10-Hz (high frequency) rTMS on the right DLPFC in people with OCD. Their results showed that LF-rTMS significantly reduced the Y-BOCS score, while this effect was insignificant at 10 Hz. Hence, they concluded that 1Hz-rTMS, targeting the right DLPFC, is a promising tool for treating OCD. Shayganfard et al. (2016), Liang et al. (2021), and Khedr et al. (2022) also reported that LF rTMS over right DLPFC improved symptoms of OCD. These are consistent with our results. Seo et al. (2016) examined the effect of rTMS on the right DLPFC (1 Hz, 1200 pulses per session, 100% of resting motor threshold) for three weeks at 15 sessions in people with OCD. Their results also showed a significant decrease in the Y-BOCS score. In Alonso et al.'s study (2001), each OCD patient was given LF-rTMS (1 Hz, 110% of resting motor threshold) over the right DLPFC three times a week for 6 weeks. Their results did not show a significant decrease in the Y-BOCS score at the post-

test and follow-up phases, which is against our results. The discrepancy may be due to the shape of the coil used for stimulation. They used a circular coil, while we used a figure-of-eight butterfly coil. The difference in the shape of coils can affect the inhibitory effect of 1-Hz rTMS (Lang et al., 2006). According to Ørskov et al. (2021), the figure-of-eight coil may have better applicability in patients due to the lower incidence of lack of inhibition in healthy subjects and the lower experience of pain or discomfort. Another reason for the discrepancy can be the difference in treatment sessions (10 sessions vs 18 sessions) and stimulation intensity (100% vs 110% of resting motor threshold). In our study, the LF-rTMS could significantly reduce obsessions in patients (from 14.25 to 10.75) but had no significant effect on their compulsions from the pre-test to follow-up phases; this may be due to the stimulated area (right DLPFC), which is related to the cognitive circuit that influences obsessive thoughts, or not stimulating the left DLPFC which has a role in inhibitory control of OCD patients (Menzies et al., 2008). Fremont et al. (2022) showed that volume loss in the left DLPFC is associated with developing compulsive behaviors.

In comparing the effects of CBT and LF rTMS on the cognitive flexibility of adults with OCD, our results showed no significant difference between the two methods in improving the cognitive flexibility of patients. This finding rejects the second hypothesis of this study.

Although the total and scores of “alternative solutions” and “control” components of the cognitive flexibility increased in both groups, the difference was not statistically significant. In one study, [Shayganfard et al. \(2016\)](#) found that executive functions (Wisconsin card sorting test performance) did not improve after rTMS in 10 adults with OCD, which is consistent with our results. No more related studies on OCD patients were found for the comparison of the results. The non-significant effect of LF-rTMS on the cognitive flexibility of OCD patients in our study may be because the ability of rTMS is limited to penetrate and stimulate the subcortical regions, such as the thalamus and caudate nucleus, which have been suggested as anatomical neural substrates involved in OCD ([Menzies et al., 2008](#)).

Regarding the non-significant effect of LF-rTMS on the cognitive flexibility of OCD patients, the reason may be that a self-report tool is used to assess cognitive flexibility (i.e. the CFI). Compared to neuropsychological tests, self-report tools assess a different aspect of cognitive flexibility ([Johnco et al., 2014](#)). People with lower cognitive flexibility can still benefit from CBT, even though they cannot use cognitive restructuring ([Johnco et al., 2014](#)).

The present study had limitations, such as a low sample size, no placebo or control group (since it was difficult to recruit patients during the COVID-19 pandemic), and not using objective assessment tools for assessing cognitive flexibility in patients. Most tests used in neuropsychological assessments to measure cognitive flexibility, such as the Wisconsin test, may not show the more subtle cognitive problems that occur due to mental disorders well ([Eling et al., 2008](#)). Moreover, significant practical limitations reduce the clinical application of these tests. The Wisconsin test, for example, is time-consuming in execution and scoring, has a training effect, and requires an interactive relationship between the rater and the subject. As a result of the training effect, patients' responses are not solely due to the intervention effect. In this regard, we used a questionnaire (CFI) to measure the cognitive flexibility of OCD patients. Moreover, the existence of comorbid diseases (i.e. depression) was not assessed. The parameters of LF-rTMS (10 sessions, 1 Hz, 100% of motor threshold, and 1200 pulses/day) may be suboptimal. They may also not be enough to generate antidepressant effects in patients. Furthermore, the generalization of the results to all OCD patients in Iran should be done with caution since this study was conducted on patients attending a clinic in a city of Iran (Zanjan). Further studies are recommended by stimulating emotional and cognitive circuits in the brain and using

a larger sample size, a control/placebo group, and objective measurement tools such as functional magnetic resonance imaging and electroencephalography. We applied LF-rTMS over the right DLPFC of patients. Future studies can use high-frequency rTMS or apply it over the left DLPFC to assess its efficacy compared to CBT with ERP.

Conclusion

There is a significant difference between CBT and LF-rTMS techniques in reducing the severity of OCD symptoms. Still, there is no difference between them in improving the cognitive flexibility of patients with OCD.

Ethical Considerations

Compliance with ethical guidelines

All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975. Written informed consent was obtained from all patients to be included in the study. Ethical approval was obtained from the Research Ethics Committee of [Zanjan University of Medical Sciences](#), Zanjan, Iran (Code: IR.ZUMS.REC.1399.180). This study was registered by the [Iranian Registry of Clinical Trials \(IRCT\)](#) (Code: IRCT20200805048316N1).

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Authors' contributions

Conceptualization, data analysis, review and editing: Mohsen Dadashi; Supervision: Mohsen Dadashi, Ahmad Zolghadriha, and Reza Pirzeh; Methodology, data collection and investigation: Arash Fazeli; Writing the original draft: Arash Fazeli, and Shokoufe Ramezani.

Conflict of interest

The authors declared no conflict of interest.

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