J. Appl. Environ. Biol. Sci., 9(5)11-20, 2019

ISSN: 2090-4274
Journal of Applied Environmental and Biological Sciences
www.textroad.com

A Comparison of the Effectiveness of Adding Neurofeedback to Standard Treatment (SSRIs + CBT) in Patients with Obsessive-Compulsive Disorder (OCD)

Abbas Masjedi Arani[1], Negar Asgharipour[2], Seyedshahab Banihashem[3], Mohsen Saberi Isfeedvajani[4], Naeeme Dorri Mashhadi[5*]

[1]Department of Clinical Psychology, School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran
[2]Research Center for Psychiatry and Behavioral Sciences, Department of Clinical Psychology, Mashhad University of Medical Sciences, Mashhad, Iran
[3]Department of Psychosomatic Medicine, Taleghani Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran
[4]Medicine, Quran and Hadith Research Center & Department of Community Medicine, Faculty of Medicine, Baqiyatallah University of Medical Sciences, Tehran, Iran
[5*]Department of Clinical Psychology, School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran

Received: January 22, 2019
Accepted: April 2, 2019

ABSTRACT

The aim of this study was to investigate the effects of adding neurofeedback to selective SSRIs medication and CBT in patients with obsessive-compulsive disorder (OCD). Ten outpatients were diagnosed with OCD and they were randomized to NFT + SSRIs + CBT and SSRIs + CBT. Repeated-measures ANOVA tests were utilized for statistical analysis. The results showed significant differences in reducing OCD symptoms severity and obsessions in the group that had extra NFT. There were no significant differences in reducing compulsion and depression symptoms. The result of this study obviously showed that adding neurofeedback to standard medication and CBT could improve treatment results in reducing severity of OCD. This improvement could also be seen in Obsessions. Results showed that each one of the standard treatments and neurofeedback could affect reducing compulsion disorder and depression; however, by implementing both the treatments together, we could not see any significant results.

KEYWORDS: Obsessive-compulsive disorder (OCD), Neurofeedback, Cognitive behavior therapy (CBT), Selective serotonin reuptake Inhibitors (SSRIs), Obsession, Compulsion, Depression.

INTRODUCTION

Obsessive-compulsive disorder (OCD) is a penetrating disorder in mental health problem that can affect quality of life and is followed by poor social function [1, 2]. OCD is recognized by obsessions, rituals, preoccupations, and compulsions. These obsessions and compulsions are time-consuming and cause clinically significant distress or impairment in social, occupational or other important areas of functioning [3]. Lifetime prevalence of OCD is seen in about 2 or 3% of general population; OCD is ranked as the fourth prevalent psychiatric disorders [4]. OCD is mostly comorbid with anxiety disorder, mood disorder, and, especially, bipolar disorder [5]. According to studies, OCD includes abnormalities in EEG and QEEG of frontal and frontotemporal areas. Specially, people who have sever OCD in comparison to the slight ones, have less alpha waves in frontal areas and Pz and higher delta and teta waves on the Fz and F7 [6-8]. Researches with LORETTA techniques in OCD patients, show an increase in low frequencies of EEG and beta activities in cingulate cortex while resting state [9, 10]. Increase in the low frequency waves (2-6 Hz) in medial frontal cortex has been observed [7]. Increasing Beta waves (13-30 Hz) can be seen in central frontal of the OCD patients, which can cause general arousal of whole brain [10-12].

Two treatments of choice for OCD are medication with SSRIs and CBT, with emphasis on exposure and response prevention (EX/ RP). These treatments have more empirical evidence and are used more than other treatments [13-16]. About 40-80% of patients respond to this treatment by reducing their Y-BOCS score by 30% after treatment [17-19]. However, researches show that approximately 50% of patients do not respond significantly [15, 20, 21]. Even after treatment many OCD patients still show symptoms, this signifies that standard treatment does not result in a complete treatment [22, 23]. The recurrence rate is more than 20-50% [24, 25], and moreover approximately 25% of patients refuse EX/ RP at first place [26, 27].

Corresponding Author: Naeeme Dorri Mashhadi, Department of Clinical Psychology, School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran. Email: Naeemedorri@gmail.com, Mobile: +989158271737

Studies that used brain imaging techniques showed that in both psychotherapy and medication, glucose metabolism decreases in the lateral rostral caudate nucleus, and the psychological treatment of OCD results in the normalization of brain activity pattern [28, 29]. Psychotherapy also reduces the activity in certain areas of the brain that are bound to forced behavior. However, it decreases the activity of the amygdalohippocampal subcortical region (bottom-up processing) and increases the activity of the frontal cortex regions (top-down processing). Therefore, It can be concluded that the observed changes in the person´s overt behaviors reflect the changes in the brain (covert behaviors) [30, 31].

Neurofeedback therapy is based on the brain physiology and brain wave activity and can modify the neuroplasticity and neurogenesis of the brain through self-regulation. Therefore, it can be a powerful tool for treating this disorder [32]. The functional base of neurofeedback is that the brain regulates emotions, physical symptoms, thoughts, and behaviors that cause many psychological problems [33]. The distinctive feature of neurofeedback treatment is that its side effects are the least harmful and the patient is active in this treatment [34-36]. This means that the patient plays the central role in his treatment, which makes him control his brain activity [37]. In fact, unlike medication that regulates the brain, the neurofeedback helps the brain to self-regulate. During neurotherapy, Individuals reconstruct and reproduce waves, which the changes are initially short termed but gradually, become more stable [38].

The nature of brain activity is electrochemical and the general changes in brain activity can be seen by changing each of these two parts. In disorders, where the function of the brain has been impaired or altered, medication can manipulate the brain's chemistry and the neurofeedback will help the electrical part. CBT, with emphasis on EX/ PR, regulates the thoughts and beliefs and facilitate habituation by exposure. Therefore, it can lead to conscious control of the emotions and cerebral cortex affects the subcortical regions. Adding neurofeedback to cognitive therapy for OCD can probably increase the therapeutic effects and the effectiveness of the treatment remains more stable for the individual. The purpose of this study was to compare the efficacy of adding neurofeedback to standard treatment (Cognitive-behavioral and medication).

METHODS

Participants:

This research is a Quasi-experimental double-blind trial without placebo-controlled group. Around 30 outpatients were referred for the interview and diagnostic stages. A total of 10 outpatients with OCD were selected and placed in two groups for treatment: NFT + SSRIs + CBT group and SSRIs + CBT group, where the sampling was purposeful. Subjects were matched according to age, gender, education, and socioeconomic status. All participants were provided with informed consent form in order to participate in the study. The Y-BOCS and HDRS were administered by trained independent evaluators (licensed psychologists) who were unaware of condition assignment, at pre-, mid-, post-treatment, and two-month follow-up. The SCID was only collected at pretreatment by the therapist. At the end, collected data were analyzed by an independent analyzer.

Inclusion criteria are as follows: (1) primary diagnosis of OCD, based on a structured interview SCID (DSIMIV-TR) by a psychiatrist or master's degree holder in psychology, (2) a minimum score of 16 on the Y-BOCS intensity scale evaluated by the expert rater, (3) at least one year OCD duration, (4) 18-50 years old, (5) high school graduate, (6) outpatient, (7) at least eight weeks duration of SSRIs, and (8) informed consent to participate in research.

Exclusion criteria are as follows: (1) experience a full course of psychotherapy prior to the study, (2) refusal to receive treatment for neurofeedback or medication due to their obsessions and compulsion, (3) concurrent psychotherapy or medications, (4) suicidal thoughts, (5) comorbidity with developmental disorder, (6) psychosis, (7) active episode of mania, (8) substance use disorder, (9) nervous system disorders (10), borderline, antisocial and paranoid personality disorder, (11) pregnancy and lactation, (12) recent experience of physical or surgical trauma, and (13) loss of five sessions.

Measures:

Yale-Brown Obsessive Compulsive Scale (Y-BOCS): it is a 10-item semi-structured interview that assesses the severity of obsessions and compulsions on a five-point scale. The sum of all the items yields a total score (range = 0–40) [39], with scores of 16 or greater generally represents clinically significant levels of OCD symptoms. Internal consistency estimates were excellent for the Y-BOCS across all time points (all $\alpha s \geq .90$) [40-42]. We utilized the translated version of Y-BOCS. Its validity and reliability with Cronbach's alpha, SC and SS were 0.97 and 0.95, respectively. However, the correlation coefficient between the two half-tests was 0.93 and 0.89, respectively [43]. The Y-BOCS was completed at pre-, mid-, and post-treatment as well as at two-month follow-up.

Hamilton Depression Rating Scale (HDRS): HDRS is a multiple item questionnaire used to provide an indication of depression and its symptoms severity. The patient is rated by a clinician on 24 items scored at a 0-3 or 0-4 likert-type score scale (based on scale type). The best Cutting score for screening depression is 12 [44].

This test has a good validity and reliability with Cronbach's alpha ≥ 0.70 [45]. The reported reliability of the Persian version is 0.66 [46].
The Structured Clinical Interview for DSM-IV Axis I and II Disorders (SCID): The SCID is a structured diagnostic interview that assesses DSM-IV Axis I and II diagnoses; it was used to determine patients' diagnoses. The measure shows adequate to excellent inter-rater reliability (Kappa coefficient of 0.71 for axis I and 0.84 for axis II) in prior studies [47]. In this research, the Persian version of SCID, translated by Sharifi et al. and adapted to the Iranian culture, was used [48].
Procedure: All patients are on at least eight weeks duration of SSRIs medication (with at least one pharmaceutical equivalents, such as sertraline 100mg, fluvoxamine 100mg, and fluoxetine 40mg). These are prescribed by the psychiatrist, started before pre-test and continued over treatment [49]. Moreover, all the patients received CBT for 15 weeks, a 1.5 hour session per week on Foa and Yadin protocol [50]. Patients in the NFT group (five patients) received 30 session of neurotherapy, two 45 minute session per week.
Data analyses
Shapiro-Wilk and Levene's methods were used to test for distribution normality and equality of variances and repeated-measures ANOVA tests were utilized for statistical analysis. Demographic data were analyzed employing Exact Fisher test.

RESULTS

The sample consisted of seven women and three men with a mean age of 30.80 years (*SD* = 6.01). The OCD duration mean was 13.90 years (SD = 5.21) and the minimum age of the onset was 14 and the maximum age was 23 (mean = 16.90, SD = 3.07). As many as five patients were randomly assigned to receive NFT+CBT+SSRIs, and five other patients were assigned to receive CBT+SSRIs treatment. A total of 60% participants are married. The mean and standard deviation of the other variables are in table 1.
Independent sample t-test showed no significant pretreatment differences for age (p = 0/ 49), age of onset (p = 0.02) and OCD duration (p = 0.78) between the two treatment groups. Groups did not differ in terms of age, sex or pre-treatment symptom severity.

Table 1. mean and standard deviation of variables

Measure	NFT+CBT+SSRI's				CBT+SSRI's			
	Pre	Mid	Post	Follow up	pre	mid	Post	Follow up
Y-BOCS	30.80	19.20	10	10.20	30.40	24.60	18.60	19.60
	4.43	1.92	2.73	1.92	3.28	3.43	3.36	7.76
Obsession	16	10	5.40	5.20	15.60	13.40	10.20	10.40
	2	0.7	1.67	1.30	1.81	1.51	1.78	3.20
Compulsion	14.80	9.20	4.60	5	14.80	11.20	8.40	9.20
	2.58	1.64	1.14	0.70	1.92	3.03	1.81	4.60
HDRS	44.40	21.60	13.80	9	36	23.20	15.40	13.40
	7.33	4.15	4.32	1.73	7.17	3.27	2.19	7.12

OCD symptom severity: Repeated-measures ANOVA analysis indicated a significant Time Intervention Effect, F(2) = 75.95, p=0, Cohen's d = 0.90 and significant Time × Condition interaction for Y-BOCS scores, F(2) = 5.94, p=0.01, Cohen's d = 0.42. Between-group comparisons indicated significant difference between the conditions post treatment, F(1) = 10.35, p=0.01, Cohen's d = 0.56, significant differences were found with follow-up, F(1) = 10.23, p=0.01. These findings indicated that both the treatment conditions had a large, significant impact on reducing OCD symptoms over the treatment period that continued through follow-up. However, the NFT + SSRI + CBT condition had significantly larger improvements post-treatment and during the follow-up than under the SSRI + CBT condition. Moreover, from the baseline to follow-up, there was an average of 66.26% improvement in Y-BOCS scores under NFT + SSRI + CBT condition, as compared to a 36.23% improvement under SSRI + CBT condition (Figure1).

Obsession severity: Repeated-measures ANOVA analysis indicated a significant Time Intervention Effect, F(2) = 92.32, p=0, Cohen's d = 0.92 and significant Time × Condition interaction for Obsession scores, F(2) = 10.44, p=0, Cohen's d = 0.56. Between-group comparisons indicated significant difference between the conditions post treatment, F(1) = 11.06, p=0.01, Cohen's d = 0.58, significant differences were found with follow up, F(1) = 13.18 , p=0. These findings indicated that both the treatment conditions had a large, significant impact on reducing obsession symptoms over the treatment period that continued through follow-up. However, the NFT + SSRI + CBT condition had significantly larger improvements post-treatment and follow-up than under the SSRI + CBT condition. Moreover, from the baseline to follow-up, there was an average of 67.07% improvement in the Obsession scores under NFT+SSRI+CBT condition, as compared to a 33.75% improvement under SSRI+CBT condition (Figure 2).

Compulsion severity: Repeated-measures ANOVA analysis indicated a significant Time Intervention Effect, $F(2) = 45.00$, $p=0$, Cohen's $d = 0.84$. However, no significant Time × Condition interaction for compulsion scores, $F(2) = 2.35$, $p=0.12$, Cohen's $d = 0.22$, was seen. Between-group comparisons indicated no significant difference between the conditions post treatment $F(1) = 4.86$, $p=0.05$, Cohen's $d = 0.37$ and at follow up $F(1) = 5.74$, $p=0.04$ was found. These findings indicate that both the treatment conditions had a large, significant impact on reducing compulsion symptoms over the treatment period that continued through follow-up. However, differences between the treatment conditions were not significant. Moreover, from the baseline to follow-up, there was an average of 65.35% improvement in the compulsion scores under NFT + SSRI + CBT condition, as compared to a 38.64% improvement under SSRI + CBT condition (Figure 3).

Depression severity: Repeated-measures ANOVA analysis indicated a significant Time Intervention Effect, $F(2) = 111.74$, $p=0$, Cohen's $d = 0.93$ and significant Time × Condition interaction for Depression severity scores, $F(2) = 5.40$, $p=0.01$, Cohen's $d = 0.40$. Between-group comparisons indicated no significant difference between the conditions post treatment $F(1) = 0.47$, $p=0.51$, Cohen's $d = 0.05$ and during the follow up, $F(1) = 0.007$, $p=0.93$. These findings indicated that both the treatment conditions had a large, significant impact on reducing depression severity over the treatment period that continued through follow-up. However, differences between the treatment conditions were not significant. Moreover, from the baseline to follow-up, there was an average of 79.02% improvement in the Depression scores under NFT + SSRI + CBT condition, as compared to a 63.88% improvement under SSRI + CBT condition (Figure 4).

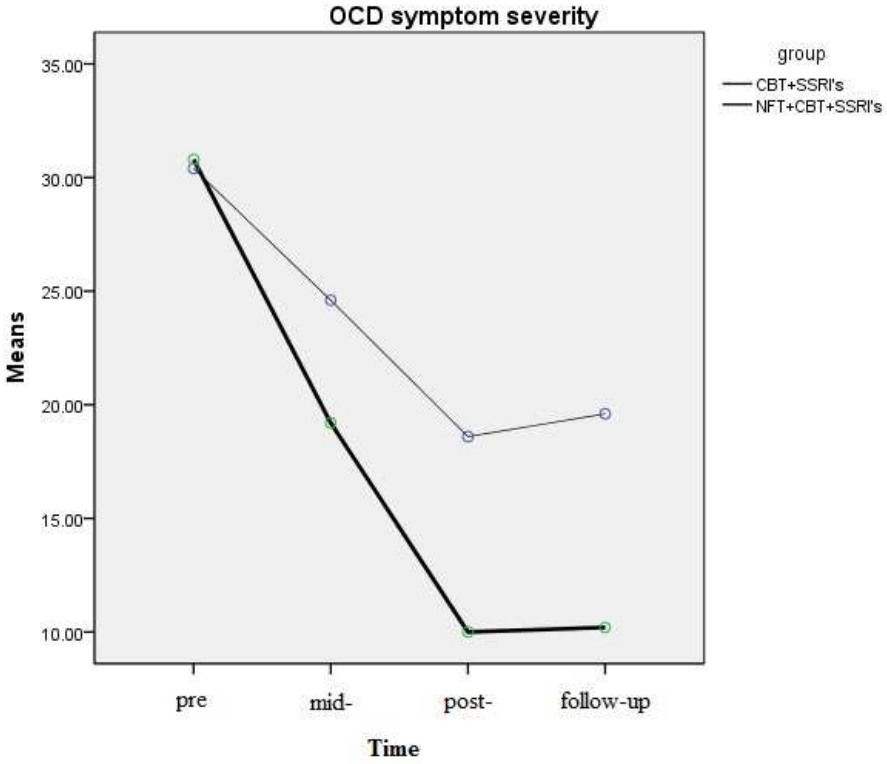

Figure 1. OCD symptom severity

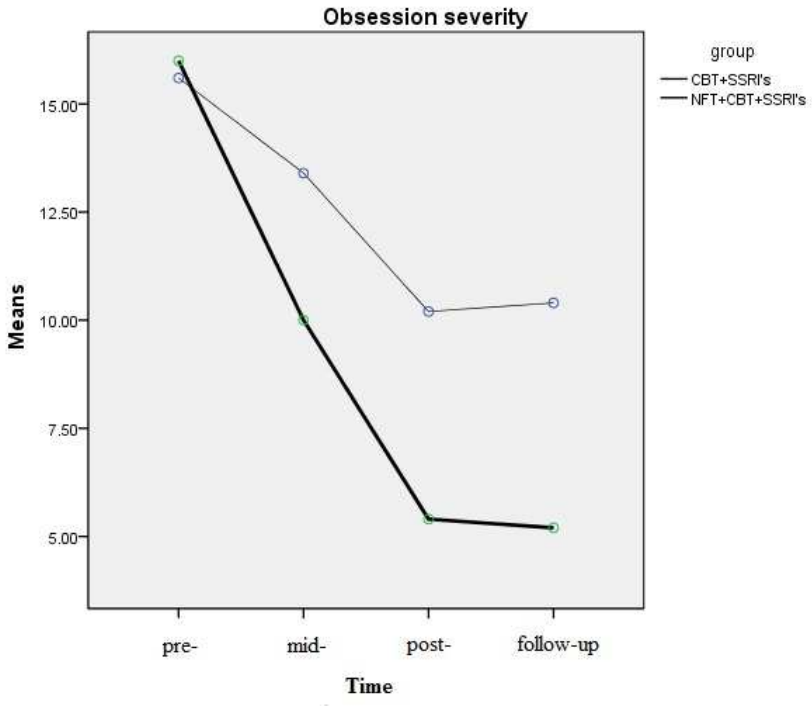

Figure 2. Obsession severity

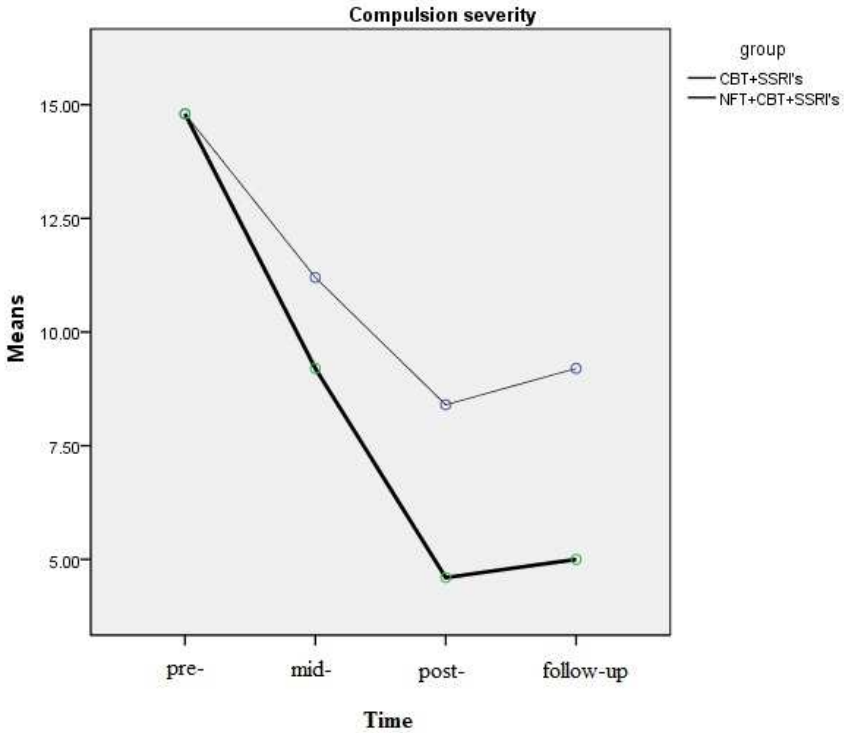

Figure 3. compulsion severity

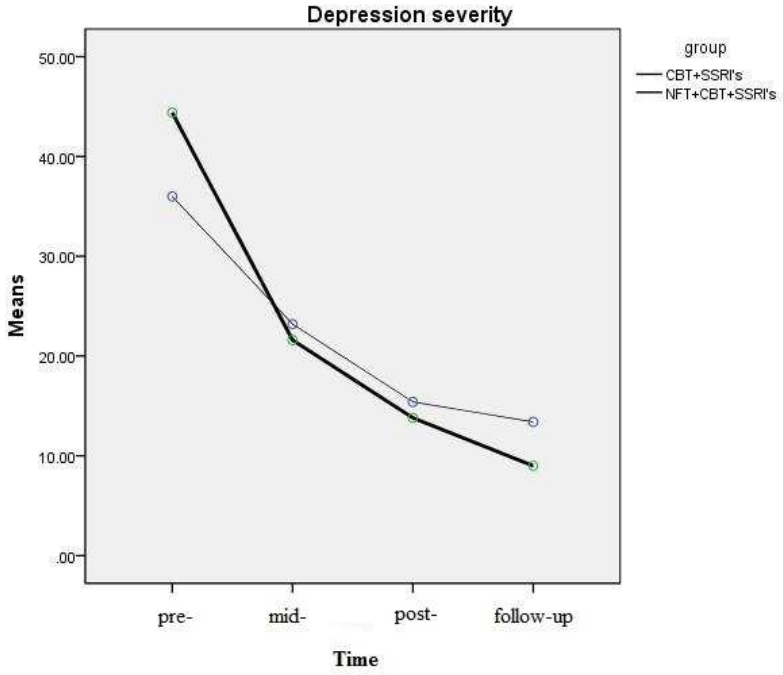

Figure 4. depression severity

DISCUSSION

Our findings provided clear evidence that adding Neurofeedback in the treatment of OCD patients can improve the effects of standard treatment with SSRIs medication and CBT. Greater improvement was observed in OCD symptoms -specifically in Obsessions- in the group that had extra treatment with neurofeedback. Their improvement was statistically significant by the end of treatment and in follow up. Reduction of compulsions and depression symptoms had a significant trend throughout the treatment in each group. However, there were no significant differences found between groups.

These findings were consistent with previous reports. According to those reports, neurofeedback alone [51, 52], as well as the addition of neurofeedback to medication [38], reduces the OCD symptoms. Moreover, our results were consistent with other findings, which indicated that different types of neurofeedback were effective in reducing contamination-related obsessions [53-55]. The findings of the present study were similar to that of Deng et al. (2014). Their study investigated the effectiveness of adjunctive treatment with neurofeedback to standard treatment with psychotherapy and medication and observed a reduction of 50% in OCD symptoms [56]. The main differences between the present study and Deng's research were the number of treatment sessions in both neurofeedback and psychotherapy treatments as well as sample size.

Based on each section of treatment, we could explain how adding neurofeedback to medication and CBT could result in decreasing OCD severity. Cognitive behavioral therapy and medication were common in both groups. Therefore, the significant difference observed in reducing the severity of OCD and obsessions between the two treatment groups could be explained by the effectiveness of adding neurofeedback to the treatment. In this study, neurotherpay had two parts: the first part consisting of training SMR, Alpha, and High Beta (18-22 Hz) on C4 and the second part on Fz-Pz by normalizing High Beta wave (18-30 Hz).

Sensory motor rhythm was associated with physical relaxation, attention processing, physical activity preparation before it begins, and mental consciousness. In other words, with increasing SMR, the mobility of a person decreases and physical relaxation increased [57]. People with OCD experienced problems, such as tension, tachycardia, increasing blood pressure, brain wave changes, negative emotions, panic attacks, etc. These were due to the high level of anxiety they experienced when exposed to obsessive-compulsive stimuli [56]. According to the cognitive behavioral theory, anxiety plays an essential role in formation and continuation of OCD. The person makes compulsive behavior merely to reduce anxiety [58, 59]. Positive treatment outcome in the neurofeedback group could be attributed to the fact that in the part of neurotherapy of individuals, we trained SMR waves. By learning to adjust this wave, they could improve their relaxation skills and reduce muscle tension, thereby modify part of their anxiety symptoms. By reducing anxiety during treatment, symptoms of OCD would also be reduced.

Furthermore, in another part of the neurotherapy of the patients (as in the study of [51]), we normalized the High Beta wave (18-30). Beta wave was related to thinking, concentration, sustained attention, tension, vigilance, and excitement [57]. In addition, the High Beta wave was associated with obsessions, negative thoughts, rumination, anxiety, general arousal of the brain, worry, and disturbance in attention and concentration [60, 61]. The increase in Beta and High Beta was associated with anxiety, obsession, anger, rumination and hyper vigilance. During treatment, patients learnt to regulate this wave and might have been able to improve part of their OCD symptoms, which are associated with obsessions, negative thoughts, anxiety, and general arousal of the brain. Different components of neurofeedback treatment in this study focused on the reducing obsessions and training to maintaining physical relaxation. This might be the most important reason for the effectiveness of neurofeedback therapy to reduce OCD symptoms and obsessions.

The results of this study was consistent with various other studies [36, 62-64] that have shown that beta wave training was effective in reducing anxiety, over thinking, obsessions, and enhancing SMR on C4 to reduce arousal. Moreover, our results were consistent with the findings of Paquette et al. (2009) and Hammond et al. (2003). These studies showed that normalized High Beta wave decreased obsessions, negative thoughts, rumination, and worries [60, 65]. In describing how to reduce obsessive-compulsive disorder with neurotherapy, the role of normalization of the High Beta wave in the neurofeedback treatment protocol could be noted. As already mentioned, the High Beta wave was associated with obsessions, negative thoughts, ruminations, and so on.

Treatment of exposure and prevention of response was the most effective treatment for OCD [14, 16]. EX/ RP was more effective in treating compulsions than obsessions [21, 66]. In line with these studies, our results showed a significant trend in reducing the symptoms of OCD in both treatment groups. Our results were consistent with the studies which showed that neurofeedback with medication was effective in reducing compulsions and rituals [8, 38, 56]. Since in both the groups compulsions were reduced, this contradiction with the previous studies could be attributed to differences in neurofeedback protocols and sample size. In the study of Kopřivová et al. (2013), neurotherapy was based on QEEG and possibly the clinically significant results of this study was related to this protocol. Moreover, due to the difference observed in our finding (but not significant), we could mention the role of sample size in this section. From the result of previous studies and the present study, it could be concluded that both the psychotherapy and neurofeedback was effective in reducing compulsions. However, significant differences could not be expected to be seen by simultaneous provision of two treatments.

The findings of this study were consistent with the results of the previous studies, which showed that QEEG-guided neurotherapy was effective in reducing depression symptoms associated (comorbid) with OCD [61, 65]. However, the finding of the present study were inconsistent with that of Joseph et al. (2009) that did not show significant improvement in addition of neurofeedback to medication in reducing obsessive compulsive symptoms and depression [67]. Of course, this discrepancy is partly justifiable. The number of neurofeedback sessions in the present study was twice the number in Joseph's research (2009). In studies such of Kopřivová et al. (2013) and Deng et al. (2014), which added neurofeedback to medication and CBT, there was no information on the reduction of comorbid depression with OCD [8, 56]. To explain the efficacy of adding neurofeedback to medication and CBT to reduce depression symptoms without targeting these symptoms in treatment, we could point that symptoms of depression might be secondary to OCD symptoms, resulting in helplessness and feeling of being unable to control obsessive compulsive symptoms. By reducing symptoms of OCD, depression symptoms were also reduced. Reduced OCD symptoms were associated with increased availability of time, ability to return to work and education, increasing self-esteem due to overcoming OCD, etc. Each of these achievements could also contribute to reducing the symptoms of depression. Previous studies on the effectiveness of treatment on reducing the severity of depression with OCD did not report the effectiveness of CBT, medication, and neurofeedback. Therefore, it could be concluded that psychotherapy and neurofeedback separately could reduce the severity of comorbid depression with OCD. However, simultaneous provision of these two treatments could not be significantly different.

Limitations and implications:

Several limitations were noticed while interpreting the findings of this study. First, our study included small sample size that might have reduced the power to detect the true differences. Therefore, we suggest larger sample size to enhance the generalizability of the findings and the application of results in the treatment of patients with OCD for future studies. Second, in our study there was no placebo control of neurofeedback (e.g. shamfeedback). Therefore, it is possible that greater improvement in neurofeedback group was due to the placebo effect of 30 additional contacts with therapist. Hence, implementing various control group such as medication + neurofeedback or medication + CBT + SHAM feedback were suggested for future studies in order to clarify these observed differences.

Acknowledgement:
This article was extracted from the thesis written by Naeeme Dorri in school of Medicine Shahid Beheshti University of Medical science (Registeration No: IR.SBMU.MSP.REC.1395.460).

Compliance with Ethical Standards:
Funding: This study was not funded by any company.
Ethical approval: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.
Informed consent: Informed consent was obtained from all individual participants included in the study.
Competing Interests: The authors declare that they have no competing interests.

REFERENCES

.1 Eisen, J.L., et al., *Impact of obsessive-compulsive disorder on quality of life.* Comprehensive psychiatry, 2006. **47**(4): p. 270-275.
.2 Zandberg, L.J., et al., *Change in obsessive-compulsive symptoms mediates subsequent change in depressive symptoms during exposure and response prevention.* Behaviour research and therapy, 2015. **68**: p. 76-81.
.3 AmericanPsychiatricAssociation, *Diagnostic and statistical manual of mental disorders (DSM-5)*. 2013: American Psychiatric Pub. 227.
.4 BJ Saddock, V.S., Pedro Ruiz, *Obsessive-compulsive and related disorders*, in *Kaplan BJ. Kaplan and Sadock's Synopsis of Psychiatry. Behavioral Sciences/Clinical Psychiatry*. 2016, Wolters Kluwer: Philadelphia
.5 Fineberg, N.A., et al., *A prospective population-based cohort study of the prevalence, incidence and impact of obsessive-compulsive symptomatology.* International journal of psychiatry in clinical practice, 2013. **17**(3): p. 170-178.
.6 Budzynski, T.H., et al., *Introduction to quantitative EEG and neurofeedback: Advanced theory and applications*. 2nd ed. 2009: Academic Press.
.7 Kopřivová, J., et al., *EEG source analysis in obsessive–compulsive disorder.* Clinical Neurophysiology, 2011. **122**(9): p. 1735-1743.
.8 Kopřivová, J., et al., *Prediction of treatment response and the effect of independent component neurofeedback in obsessive-compulsive disorder: a randomized, sham-controlled, double-blind study.* Neuropsychobiology, 2013. **67**(4): p. 210-223.
.9 Pascual-Marqui, R.D., *Standardized low-resolution brain electromagnetic tomography (sLORETA): technical details.* Methods Find Exp Clin Pharmacol, 2002. **24**(Suppl D): p. 5-12.
.10 Velikova, S., et al., *Dysfunctional brain circuitry in obsessive–compulsive disorder: source and coherence analysis of EEG rhythms.* Neuroimage, 2010. **49**(1 :(p. 977-983.
.11 Olbrich, S., et al., *Altered EEG lagged coherence during rest in obsessive–compulsive disorder.* Clinical Neurophysiology, 2013. **124**(12): p. 2421-2430.
.12 Micoulaud-Franchi, J.-A., et al., *Electroencephalographic neurofeedback: Level of evidence in mental and brain disorders and suggestions for good clinical practice.* Neurophysiologie Clinique/Clinical Neurophysiology, 2015. **45**(6): p. 423-433.
.13 Abramowitz, J.S., S. Taylor, and D. McKay, *Obsessive-compulsive disorder.* The Lancet, 2009. **3** :(9688)74p. 491-499.
.14 Foa, E.B., *Cognitive behavioral therapy of obsessive-compulsive disorder.* Dialogues in Clinical Neuroscience, 2010. **12**(2): p. 199.
.15 Krebs, G. and I. Heyman, *Treatment-resistant Obsessive-compulsive Disorder in Young People: Assessment and Treatment Strategies.* Child and Adolescent Mental Health, 2010. **15**(1): p. 2-11.
.16 McKay, D., et al., *Efficacy of cognitive-behavioral therapy for obsessive–compulsive disorder.* Psychiatry research, 2015. **227**(1): p. 104-113.
.17 Hand, I., *Ambulatory behavior therapy in obsessive-compulsive disorders.* Fortschritte der Neurologie-Psychiatrie, 1995. **63**: p. 12-18.
.18 Foa, E.B., M.E. Franklin, and J. Moser, *Context in the clinic: how well do cognitive-behavioral therapies and medications work in combination?* Biological psychiatry, 2002. **52**(10): p. 987-997.
.19 Abramowitz, J.S., *The Psychological Treatment of Obsessive—Compulsive Disorder.* The Canadian Journal of Psychiatry, 2006. **51**(7): p. 407-416.
.20 Stanley, M.A. and S.M. Turner, *Current status of pharmacological and behavioral treatment of obsessive-compulsive disorder.* Behavior therapy, 1996. **26**(1): p. 163-186.

.21 Vyskocilova, J., et al., *Group CBT for Patients with Obsessive Compulsive Disorder–Predictors of Therapeutic Efficacy*. European Psychiatry, 2015. **30**: p. 1496.

.22 PIGOTT, T.A. and S. Seay, *Pharmacotherapy of obsessive-compulsive disorder.* International Review of Psychiatry, 1997. **9**(1): p. 133-148.

.23 Ackerman, D.L. and S. Greenland, *Multivariate meta-analysis of controlled drug studies for obsessive-compulsive disorder.* Journal of clinical psychopharmacology, 2002. **22**(3): p. 309-317.

.24 Simpson, H.B., et al., *Standard criteria for relapse are needed in obsessive–compulsive disorder.* Depression and Anxiety, 2005. **21**(1): p. 1-8.

.25 Anand, N., et al., *Cognitive behavior therapy in medication non-responders with obsessive–compulsive disorder: A prospective 1-year follow-up study.* Journal of anxiety disorders, 2011. **25**(7): p. 939-945.

.26 Riggs, D.S. and E.B. Foa, *Obsessive-compulsive disorder*, in *COMPREHENSIVE HANDBOOK OF PERSONALITY AND PSYCHOPATHOLOGY*, M. Hersen and J.C. Thomas, Editors. 1993, John Wiley & Sons, Inc. p. 169-182.

.27 Foa, E.B., M.E. Franklin, and M.J. Kozak, *Psychosocial treatments for obsessive–compulsive disorder: Literature review*, in *Obsessive-compulsive disorder: Theory, research, and treatment*, R.P. Swinson, et al., Editors. 1998, Guilford Press: New York. p. 258-276.

.28 Linden, D., *How psychotherapy changes the brain–the contribution of functional neuroimaging.* Molecular psychiatry, 2006. **11**(6): p. 528.

.29 Barsaglini, A., et al., *The effects of psychotherapy on brain function: A systematic and critical review.* Progress in neurobiology, 2014. **114**: p. 1-14.

.30 Clark, D.A. and A.T. Beck, *Cognitive theory and therapy of anxiety and depression: Convergence with neurobiological findings.* Trends in cognitive sciences, 2010. **14**(9): p. 418-424.

.31 Nakao, T., K. Okada, and S. Kanba, *Neurobiological model of obsessive–compulsive disorder: evidence from recent neuropsychological and neuroimaging findings.* Psychiatry and clinical neurosciences, 2014. **68**(8): p. 587-605.

.32 Myers, J.E. and J.S. Young, *Brain wave biofeedback: Benefits of integrating neurofeedback in counseling.* Journal of Counseling & Development, 20 :(1)90 .12p. 20-28.

.33 Hammond, D.C., et al., *Adverse reactions and potential iatrogenic effects in neurofeedback training.* Journal of Neurotherapy, 2001. **4**(4): p. 57-69.

.34 Hammond, D.C. and L. Kirk, *First, do no harm: Adverse effects and the need for practice standards in neurofeedback.* Journal of Neurotherapy, 2008. **12**(1): p. 79-88.

.35 Hammond, D.C., *What is neurofeedback: An update.* Journal of Neurotherapy, 2011. **15**(4): p. 305-336.

.36 Magda, Z. and M. Pelc. *Using Neurofeedback as an Alternative for Drug Therapy in Selected Mental Disorders*. in *International Scientific Conference BCI 2018 Opole*. 2018. Springer.

.37 Fovet, T., R. Jardri, and D. Linden, *Current issues in the use of fMRI-based neurofeedback to relieve psychiatric symptoms.* Current pharmaceutical design, 2015. **21**(23): p. 3384-3394.

.38 Barzegary, L., H. Yaghubi, and R. Rostami, *The effect of QEEG-guided neurofeedback treatment in decreasing of OCD symptoms.* Procedia-Social and Behavioral Sciences, 2011. **30**: p. 2659-2662.

.39 Goodman ,W.K., et al., *The yale-brown obsessive compulsive scale: II. Validity.* Archives of general psychiatry, 1989. **46**(11): p. 1012-1016.

.40 Fisher, P.L. and A. Wells, *How effective are cognitive and behavioral treatments for obsessive–compulsive disorder? A clinical significance analysis.* Behaviour Research and Therapy, 2005. **43**(12): p. 1543-1558.

.41 Rufer, M., et al., *Dissociation and symptom dimensions of obsessive–compulsive disorder.* European archives of psychiatry and clinical neuroscience, 2006. **256**(3 :(p. 146-150.

.42 Rufer, M., et al., *Symptom dimensions in obsessive–compulsive disorder: prediction of cognitive-behavior therapy outcome.* Acta Psychiatrica Scandinavica, 2006. **113**(5): p. 440-446.

.43 RajeziEsfahani, S., et al., *Reliability and validity of the Persian version of the Yale-Brown Obsessive-Compulsive Scale.* Iranian Journal of Psychiatry and Clinical Psychology, 2012. **4**(17): p. 297-303.

.44 Kobak, K.A., *Hamilton depression rating scale.* Corsini Encyclopedia of Psychology, 2010.

.45 Bagby, R.M ,.et al., *The Hamilton Depression Rating Scale: has the gold standard become a lead weight?* American Journal of Psychiatry, 2004. **161**(12): p. 2163-2177.

.46 Fata, L., *Comparison of exposure and response prevention, clomipramine and the combination of these two methods in the treatment of obsessive-compulsive disorder*, in *Tehran Psychiatric Institute*. 1991: Iran University of Medical Sciences.

.47 Lobbestael, J., M. Leurgans, and A. Arntz, *Inter-rater reliability of the Structured Clinical Interview for DSM-IV Axis I disorders (SCID I) and Axis II disorders (SCID II).* Clinical psychology & psychotherapy, 2011. **18**(1): p. 75-79.

.48 Sharifi, V., et al., *Reliability and feasibility of the Persian version of the structured diagnostic interview for DSM-IV (SCID).* ADVANCES IN COGNITIVE SCIENCE, 2004. **6**(1-2): p. 10-22.

.49 Bandelow, B., et al., *Guidelines for the pharmacological treatment of anxiety disorders, obsessive–compulsive disorder and posttraumatic stress disorder in primary care.* International journal of psychiatry in clinical practice, 2012. **16**(2): p. 77-84.
.50 Foa, E.B., E. Yadin, and T.K. Lichner, *Exposure and response (ritual) prevention for obsessive compulsive disorder: Therapist guide*. 2012, New York, NY, US: Oxford University Press.
.51 Moradi ,A., et al., *Treatment of anxiety disorder with neurofeedback: case study.* Procedia-Social and Behavioral Sciences, 2011. **30**: p. 103-107.
.52 Sürmeli, T. and A. Ertem, *Obsessive compulsive disorder and the efficacy of qEEG-guided neurofeedback treatment :A case series.* Clinical EEG and Neuroscience, 2011. **42**(3): p. 195-201.
.53 Hampson, M., et al., *Real-time fMRI biofeedback targeting the orbitofrontal cortex for contamination anxiety.* Journal of visualized experiments: JoVE, 2012(59.(
.54 Scheinost, D ,.et al., *Orbitofrontal cortex neurofeedback produces lasting changes in contamination anxiety and resting-state connectivity.* Translational psychiatry, 2013. **3**(4): p. e250.
.55 Scheinost, D., et al., *Resting state functional connectivity predicts neurofeedback response.* Frontiers in behavioral neuroscience, 2014. **8**: p. 338.
.56 Deng, X., et al., *Randomized controlled trial of adjunctive EEG-biofeedback treatment of obsessive-compulsive disorder.* Shanghai archives of psychiatry, 2014. **26**(5): p. 272.
.57 Marzbani, H., H.R. Marateb, and M. Mansourian, *Neurofeedback: a comprehensive review on system design, methodology and clinical applications.* Basic and clinical neuroscience, 2016. **7**(2): p. 143.
.58 Rosso, G., et al., *Stressful life events and obsessive–compulsive disorder: clinical features and symptom dimensions.* Psychiatry research, 2012. **197**(3): p. 259-264.
.59 Rego, S.A., *Treatment Plans and Interventions for Obsessive-compulsive Disorder*. 2016: Guilford Publications.
.60 Paquette, V., M. Beauregard, and D. Beaulieu-Prévost, *Effect of a psychoneurotherapy on brain electromagnetic tomography in individuals with major depressive disorder.* Psychiatry Research: Neuroimaging, 2009. **174**(3): p. 231-239.
.61 Saremi, A.A., et al., *The Effectiveness of Psychoneurotherapy on Reducing Symptoms Severity in Treatment Naïve Patients With Obsessive-Compulsive Washing.* 2016.
.62 Bahrami Kohshahi, S., *Neurofeedback and treatment of obsessive-compulsive disorder.* International Journal of Humanities and Cultural Studies) IJHCS) ISSN 2356-5926, 2016. **1**(1): p. 1915-1926.
.63 Ros, T., et al., *Neurofeedback tunes scale-free dynamics in spontaneous brain activity.* Cerebral Cortex, 2016. **27**(10): p. 4911-4922.
.64 Arns, M., et al., *Neurofeedback: One of today's techniques in psychiatry?* L'Encéphale, 2017. **43**(2): p. 135-145.
.65 Hammond, D.C., *QEEG-guided neurofeedback in the treatment of obsessive compulsive disorder.* Journal of Neurotherapy, 2003. **7**(2): p. 25-52.
.66 Starcevic, V. and V. Brakoulias, *Symptom subtypes of obsessive–compulsive disorder: are they relevant for treatment?* Australian & New Zealand Journal of Psychiatry, 2008. **42**(8): p. 651-661.
.67 Joseph, G.A., et al., *EFFICACY OF NEUROFEEDBACK IN OBSESSIVE COMPULSIVE DISORDER.* Indian Journal of Social Psychiatry, 20 :(3-4)25 .09p. 101-105.