

## Evaluation of Neurofeedback Therapy in Adolescents with Major Depressive Disorder Who Take Fluoxetine

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### Abstract

**Introduction:** Major depression is one of the most common psychiatric disorders that is with depressed mood and characterized by feelings of sadness, low self esteem and lack of interest or pleasure in daily activities.

**Objective:** The main aim of this article is comparison of efficacy of real neurofeedback therapy versus sham (unreal or placebo) in adolescents with major depressive disorder in Iran, Mashhad.

**Material & Method:** This study included 28 adolescents with major depression that were diagnosed by psychiatric interview according to DSM -V and Hamilton scale. They were randomly divided into two groups. All patients were treated with 20 mg of fluoxetine. Half received neurofeedback treatment on F3 region and the other half received unreal neurofeedback treatment or sham (placebo). Immediately after the 20th session Hamilton test was conducted.

**Results:** The efficacy of treatment with real and unreal neurofeedback on adolescents' depression shows difference in scores. The differences between pre-test and post-test scores within each group and finally between the two groups were compared using independent t-test. According to the results, the index calculated t (-0.9) is not significant. So there is no significant difference between real and unreal neurofeedback effects.

**Conclusion:** This study shows that real neurofeedback therapy was effective; but this efficacy was not significantly different from unreal neurofeedback therapy in adolescent depression. This means that in F3 region, the effect of real neurofeedback therapy was not any different from unreal neurofeedback on adolescents' depression. Experiments on other regions are suggested.

**Keywords:** Neurofeedback; Major depressive disorder; Alfa waves; Theta waves

### Introduction

The basic symptoms of depression include depressed mood, pessimistic thoughts, inability to gain pleasure, loss of energy and mental slowdown. Depressed mood is not always evident. Neurofeedback is a form of biofeedback that changes brain waves' activity. It shows the patient how to train his/her brain waves within a few sessions and as a result improves the natural state. The study is quiet important as Neurofeedback could be a promising tool for avoiding side effects of anti-depressant drugs. Kumano et al. and Rosenfeld in preliminary case studies and Waldkoetter & Sanders in pilot studies showed neurofeedback may decrease depressive symptom [1]. Baehr et al. evaluated an alpha asymmetry neurofeedback protocol in the treatment of mood disorders and also did one to five years post therapy Follow-up. In this study only 3 out of 6 patients with mood disorders was treated by right hemisphere alpha training [2]. Raymond et al. evaluated the effects of alpha/theta neurofeedback on personality and mood [3]. Rosenfeld, proposed EEG biofeedback protocol for affective disorders [4]. Dias and Deussen show that most protocols including Alpha hemispheric asymmetry and theta/beta ratio in the

left prefrontal cortex were useful in depression treatment [5]. In 2005 a study on 15 patients with depression carried out by Hammond showed the use of neurofeedback protocol can endure improvement approximately in 80% of cases with frontal alpha wave asymmetry [6].

Saxby showed decrease in Beck's Depression Inventory in 14 alcoholic patients with depression after sessions of alpha/theta brain wave neurofeedback training [7]. In a study on 16 people with depression, by Linden half received neurofeedback treatment so they could see the positive image of their brain wave and half did not receive neurofeedback. All of them received antidepressant throughout the process. The depression level of the group who has undergone neurofeedback therapy reduced significantly compared with the group who did not receive neurofeedback therapy [8]. Escolano studied alpha intervention via neurofeedback therapy on patients with major depressive disorder which showed the effectiveness of intervention in a variety of cognitive function [9]. This study aims to test the efficacy of real neurofeedback therapy versus unreal in adolescents with major depressive disorder. The null hypothesis was that there was no difference between the result of real and unreal methods.

## Material and Method

The main objective of this study was to determine the effectiveness of neurofeedback in the treatment of major depression in adolescents in Iran, Mashhad. Study samples were adolescents aged 11 to 18 years, who were admitted to child and adolescent psychiatric clinics of Mashhad Medical University in Iran. Simple random sampling was used and number of samples was calculated using G \* Power software. With effect size  $f^2=0.3$  (which is a relatively moderate effect size) and number of groups=2 and  $\alpha$  - value=0.05, 14 subjects in each group were obtained. Ethics committee of Mashhad medical university has approved this research.

In this study, 28 adolescents (13 boys and 15 girls) were diagnosed of major depression by psychiatric interview, according to DSM-V. All subjects had no other psychiatric disorders or any neurological disorders. All participants obtained at least 70 in Wechsler IQ test. This would rule out any intellectual disability.

Before treatment, parents have completed the informed consent form. Hamilton depression scale test and Wechsler IQ test have been done for all adolescents before the first session and then they were divided into two groups randomly. All patients were treated with 20 mg of fluoxetine. One group (N=14) received Neurofeedback treatment and the other group (N=14) received unreal neurofeedback treatment or sham (placebo). Hamilton test is performed immediately after 20th session. In the first session, baseline was determined and threshold was changed every three minutes. Mean of alpha / theta ratio for each person was obtained in every session. Data was analyzed by covariance and t-test in SPSS software (version 20). Statistical analysis of data is presented in two parts. The descriptive statistics of the indicators is used to describe mean and standard deviation. The inferential statistics is used to compare the mean and variance of depression in real and unreal neurofeedback treatment groups with t-test and Levene's test. Paired t-test (dependent) and independent t-test were used for evaluation of significance of hypothesis (Table 1).

Neurofeedback treatment were done using PROCAMP 2 neurofeedback device. In subsequent meetings, mean threshold of the previous session was used as the first threshold. Alpha/ theta ratio is calculated every 20 ms (millisecond), with an interval of 5 ms and was compared with a threshold. If the ratio is less than the threshold, an auditory and visual reward was given. Each person had undergone 20 sessions, and each session lasted 30 minutes. Treatment period was 10-12 weeks. During the treatment period, the proportion of alpha / theta at the beginning and the end of each session was determined in F3 region. Conditions for sham group were exactly the same as in real neurofeedback except that EEG signals were from another person. Mean difference scores were used (difference between pre-test score and post-test score) to compare effectiveness of neurofeedback and sham group.

## Results

The sample consisted of 28 adolescents, 13 boys and 15 girls that were randomly assigned into two groups of real and unreal neurofeedback. T-independent test shows the difference in age between the two groups is not significant ( $t=0.88$  &  $P=0.387$ ). There was no significant difference between the average education level (in terms of years of education) between the two groups ( $t=1.33$  &  $P=0.198$ ). In pretest, the difference in depression scores of the two groups was less than 1, But after the intervention, mean depression score was decreased 7.33 score (improved) in real neurofeedback group and 5.67 score in sham group (improved). Therefore, mean depression score at baseline (in pre-test) are match. For evaluation of homogeneity of baseline in both groups, independent t-test was used. Homogeneity of variances was checked using Levene's test, which was not significant. Consequently equality of variances in the two groups has also been met.

This study shows that treatment of major depression in adolescents by real neurofeedback is effective.

Effect size	Sig	Degrees of freedom	t-index	Post-test	Pre-test	*MDD
74.0	0.000	11	**5.41	17	24.33	Real neurofeedback group
0.49	0.001	11	** 4.49	19.33	25	Sham group

**Table 1:** Effectiveness of real and sham neurofeedback in adolescents with major depression by Dependent t-test, \*MDD: Major Depressive Disorder, \*\* P-Value  $\leq 0.01$

Cohen's d as a measure of effect size, shows efficacy of real neurofeedback on depression is high in adolescents but efficacy of sham group (placebo) is moderate in major depression disorder in adolescents.

Sig	Degrees of freedom	index t	Mean difference	variable
0.387	22	-0.9	33-.7	MDD
			67-.5	

**Table 2:** Independent t-tests between real and unreal neurofeedback effects in treatment of major depression in adolescents

According to the above result, the calculated t index (-0.9) is not significant.

## Discussion

This study shows that both real and unreal neurofeedback treatments are effective in reducing major depression in adolescents; but the effect sizes are different. The effectiveness of real neurofeedback treatment in adolescents' depression was high but that of unreal neurofeedback (sham treatment) was moderate. Moreover, result of Cohen's d shows that sham (unreal) neurofeedback treatment is also effective in reducing depression. However, the efficacy of treatment of neurofeedback on major depression in adolescents is different between real and sham group. Table 2 shows that there is no significant difference between the effect of real and unreal neurofeedback therapy.

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## Conclusion

In this study, the efficacy of Neurofeedback treatment in adolescents' depression, whether it is real or sham was proved; but there is no significant difference between real and unreal (sham) neurofeedback in the treatment of MDD in adolescents.

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