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Neurofeedback Training as a New Method in Treatment of Crystal Methamphetamine Dependent Patients: A Preliminary Study

R. Rostami[1] · **F. Dehghani-Arani**[2]

Abstract This study aimed to compare the effectiveness of neurofeedback (NFB) plus pharmacotherapy with pharmacotherapy alone, on addiction severity, mental health, and quality of life in crystal methamphetamine-dependent (CMD) patients. The study included 100 CMD patients undergoing a medical treatment who volunteered for this randomized controlled trial. After being evaluated by a battery of questionnaires that included addiction severity index questionnaire, Symptoms Check List 90 version, and World Health Organization Quality of Life, the participants were randomly assigned to an experimental or a control group. The experimental group received thirty 50-min sessions of NFB in addition to their usual medication over a 2-month period; meanwhile, the control group received only their usual medication. In accordance with this study's pre-test–post-test design, both study groups were evaluated again after completing their respective treatment regimens. Multivariate analysis of covariance showed the experimental group to have lower severity of addiction, better psychological health, and better quality of life in than the control group. The differences between the two groups were statistically significant. These finding suggest that NFB can be used to improve the effectiveness of treatment results in CMD patients.

Keywords Crystal methamphetamine dependency · Neurofeedback · Addiction severity · Mental health · Quality of life · Effectiveness

Introduction

Substance dependence disorder (SDD) or addiction has been described as a chronic, relapsing mental disorder that results from the prolonged effects of drugs on the brain (Volkow et al. 2004). This disorder is believed to take control of a patient's brain and behavior by activating and reinforcing behavioral patterns that become excessively attracted to compulsive drug use (Trudeau et al. 2009). Crystal methamphetamine dependency (CMD), as a type of SDD that has been prevalent in recent years (Hunter et al. 2012), has been found to include psychological effects such as euphoria, anxiety, alertness, irritability, aggressiveness, psychosomatic disorders, psychomotor agitation, delusions of grandiosity, hallucinations, excessive feelings of power and invincibility, repetitive and obsessive behaviors, paranoia, and with chronic use and/or high doses, amphetamine psychosis can occur (Brands et al. 2011).

As Gossop et al. (2002) mentioned, while major pharmacotherapy and psychotherapy approaches have been employed to treat SDD, there has been little significant improvement in treatment and the relapse rate has remained high. They reported that 60 % of heroin addicts relapsed 1 year following SDD treatment. This rate could be even higher in methamphetamine addicts as Brands et al. (2011) mentioned that treatment of methamphetamine dependency is more complex than other substances. Also, most of these patients have comorbid neuro-psycho-physiological conditions which may require comprehensive assessments during the course of therapy to determine the

✉ F. Dehghani-Arani
f.dehghani.a@ut.ac.ir

[1] University of Tehran, 1445983861 Tehran, Iran

[2] Department of Psychology, University of Tehran, Dr Kardan Street, Nasr Bridge, Jalal Al Ahmad Street, Chamran Highway, 1445983861 Tehran, Iran

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need for adding different treatments, i.e., neurotherapy, medication or psychotherapy to integrate into the treatment plan (Trudeau et al. 2009).

Accordingly, in recent years, the neuro-psycho-physiological dimensions of SDD have attracted a great deal of scientific attention (Sokhadze et al. 2008, 2011). Volkow et al. (1988) were the first to use positron emission tomography (PET), as a new neurophysiological method, to study the effects of cocaine on the human brain. Recently quantitative electro-encephalo-graphy (QEEG) has been employed as a type of brain mapping technique that is capable of identifying some neurophysiological abnormalities (Newton et al. 2003). The QEEG activity of CMD patients is characterized by alterations mainly within the alpha, theta, SMR and beta bands (Alper et al. 1998; Sokhadze et al. 2008). These studies have played vital roles in ascertaining the interactions between the SDD, brain, and human behavior. Certain symptoms of SDD such as craving, impulsiveness, psychological and psychological problems are believed to be the result of pathological neurophysiology; and on the other hand this pathological neurophysiology is a kind of damaged brain function which can be the result of prolonged substance abuse (Sokhadze et al. 2011; Trudeau et al. 2009; Volkow et al. 2004).

These neuro-psycho-physiological abnormalities in SDD and CMD, as well as those mentioned limitations of pharmacotherapy and psychotherapy, underline the need for complementary therapeutic methods for this disorder, which contain long-lasting effects and minimal side effects (Trudeau et al. 2009; Unterrainer et al. 2014). Neurofeedback (NFB), as a form of EEG biofeedback, appears to be one of these promising complementary therapeutic methods. NFB is an operant conditioning technique that trains the mind to act in a more optimal way in order to improve emotional, cognitive, behavioral, and physical experiences. It can be used to turn abnormal rhythms and frequencies into relatively normal rhythms and frequencies and subsequently turn abnormal psychological states into normal ones (Scott et al. 2005; Simkin et al. 2014). This method has been used as a therapeutic method for SDD and as the literature reported its use has been associated with reformed negative neuropsychological consequences of substance abuse, reduced drug-seeking symptoms, improved psychological and neurophysiological variables, and longer abstinence (Burkett et al. 2005; Dehghani-Arani et al. 2013; Kaiser et al. 1999; Peniston and Kulkosky 1989; Peniston and Saxby 1995; Sokhadze et al. 2008; Unterrainer et al. 2014).

The first NFB protocol was alpha training that was employed in SDD by Passini et al. (1977), who showed the effects of alpha NFB training in reducing anxiety and improvement in the personality measuring scales in SDD patients. Goldberg et al. (1976) also pointed out that the alpha conditioning program reduced drug use and increased self-control in four addicted patients. Thereafter, the treatment of addictive disorders by NFB was popularized by the work of (Peniston and Kulkosky 1989) in which 10 alcoholic patients underwent approximately 40 alpha/theta brain wave training sessions. Eight of them remained generally abstinent at least 3 years after NFB treatment. Fahrion, Walters, Coyne and Allen repeated these results in 1992 in a controlled case study. The same results were repeated in studies conducted by Bodehnamer and Callaway (2004) and Burkett et al. (2005) on crack-cocaine abusers. They found that the addition of Peniston alpha/theta protocol to crack cocaine treatment regimens may promise to be an effective intervention for treating crack cocaine abuse and increasing treatment retention. In another study by Raymond et al. (2005), subjects who received alpha-theta training showed significant improvement in mood and Minnesota multiphase personality inventory-2 (MMPI-2) scores. Follow-up studies also reported consistent treatment outcomes in alcohol- or drug-addicted clients who completed an alpha/theta NFB protocol (Kelley 1997; Trudeau 2000). Trudeau (2005) showed the same results on the effectiveness of NFB in adolescents with SDD.

In 2005 Scott et al. extended the Pension's traditional alpha/theta NFB protocol to treat patients with mixed SDD, rich in stimulant abusers. Chronic EEG abnormalities and high incidence of pre-existing ADHD in stimulant abusers suggest that they may be less able to engage in the hypnagogic and auto-suggestive Peniston protocol. Furthermore, eyes-closed alpha feedback as a starting protocol may be deleterious in stimulant abusers because their most common QEEG abnormality is excess frontal alpha (Scott et al. 2005; see also Simkin et al. 2014; Trudeau et al. 2009). According to this explanation, in Scott et al. (2005) study, patients who had abused stimulants were treated using attention-deficit type NFB protocols (beta and/or SMR augmentation with theta suppression), followed by the Peniston Protocol. The beta and/or SMR protocol used to normalize attention, and then the standard Peniston protocol without temperature training apply. This treatment approach is now widely known as the Scott–Kaiser modifications of the Peniston Protocol (Sokhadze et al. 2008). In their study, Scott et al. (2005) found that this protocol doubled the recovery rate for drug dependence. They documented significant improvements in psychological functioning and the ability of the experimental group to focus their thoughts and to process information. In addition, findings revealed substantial improvement in long-term abstinence rates in these patients. After only 45 days of treatment, almost one-third of the control group had dropped out of treatment residential facility compared with only 6 % of the experimental group.

Table 1 Demographic data for the experimental and control groups

Group	N	Age			Abstinence (months)			Education (years)		
		Mean	SD	Range	Mean	SD	Range	Mean	SD	Range
Experimental	50	29.2	7.07	17–50	3	1.87	1–5	14.41	1.72	12–16
Control	50	28.89	7.65	18–50	3.1	2.1	1–5	14.3	1.01	12–16
Total	100	28.5	7.32	17–50	3	1.98	1–5	14.35	1.36	12–16

Next studies have evaluated the treatment outcomes of Scott–Kaiser NFB Protocol in SDD. Burkett et al. (2005) study showed that the addition of this NFB protocol to crack cocaine treatment regimens caused a significant decrease relapse, depression, and anxiety rates compared to conventional forms of SDD treatment. At follow-up, participants regularly reported no uses, or one through nine uses. Dehghani-Arani et al. (2013) also compared results of 30 sessions of NFB being provided to opioid dependent patients undergoing outpatient treatment (methadone or Buprenorpine maintenance), in comparison with a control group that received outpatient treatment alone. Patients receiving NFB showed significantly more improvements in general health and craving. The last study is the Unterrainer et al. (2014) study in which a mixed substance misuse case received 11 sessions including a 2-month follow-up of NFB protocol combined with short-term psychodynamic psychotherapy. Pre/post-treatment and follow-up assessment confirmed a significant psychopathology reduction. Furthermore, there was no relapse during the follow-up phase of the study.

Altogether, Sokhadze et al. (2011) have validated the immense potential that NFB protocols have to likely double if not triple the outcome rates in alcoholism and SDD treatment when they are added as an additional component to a comprehensive treatment program. It is because of this method's potential to improve attention, emotion, and behavior self-regulation skills in patients with SDD. Interventions that incorporate NFB techniques are aimed to reeducate patients to control and self-regulate their emotional and motivational states, and to reestablish the normal biological, cognitive, behavioral, and hedonic homeostasis distorted by SDD (Sokhadze et al. 2008; White and Richards 2009; Unterrainer et al. 2014).

Despite these promising findings, no study has focused specially on CMD, while the prevalence of this substance abuse is increasing (Brands et al. 2011). Previous studies that used NFB as a treatment method showed positive results, but typically possessed an important limitation that reduced their usefulness in treating methamphetamine disorders: most of these studies involved alcoholic or mixed abuse patients, and no experimental studies included a control group on methamphetamine disorders. Present study is the first to have examined the effectiveness of NFB especially in CMD patients, in which the effectiveness of NFB plus pharmacotherapy with pharmacotherapy alone in two experimental and control group of CMD patients has been compared. Pre- and post-treatment questionnaires provided data for the evaluation of patients' addiction severity, psychological symptoms and quality of life. In this simple randomized controlled study it has been hypothesized that the experimental group will show more improvement in addiction severity, psychological symptoms and quality of life in comparison with the control group. Accordingly, this study was designed to evaluate the notion that NFB can improve abnormalities of CMD.

Materials and Methods

Participants

Subjects were 100 men aged 17–50 years who were recruited from an outpatient clinic for treatment of SDD. Inclusion criteria were having CMD disorder according to DSM-IV-R criteria, receiving at least 5 months of psychopharmacotherapy for SDD, and at least 1 month of abstinence from substance abuse. Exclusion criteria were comorbidities such as anoxia, head trauma, stroke, encephalitis, or HIV. After providing signed informed consent, during the pretreatment phase, the participants underwent blood and urine tests for abstinence; passed structured clinical interview for aforementioned comorbidities; and responded to questionnaires on addiction severity, psychological health, and quality of life (i.e., ASI, SCL-90, and WHOQOL). The participants were then randomly assigned to an experimental group or a control group. There were no significant differences between the groups at demographic characteristics including age ($t = .21$, ns), abstinence ($t = -.25$, ns), and education ($t = .39$, ns) (see also Table 1). Both groups were receiving pharmacotherapy for SDD. On this purpose, all participants had a medical file included a SSRI regimen in an SDD outpatient clinic in Tehran. This file was being checked every week by our psychiatrist who was expert in MCD treatment. The experimental group also received 30 sessions of NFB in addition to their pharmacotherapy. All stages of the study had been administered and reviewed by "study, research and instruction board of Iran Drug Control Headquarters".

Experimental Procedure

The duration of the NFB program administered to the patients in the experimental group was 2 months of thirty 50-min sessions. The patients in the control group spent the 2 months waiting for the program. As crystal methamphetamine is a subtype of stimulant substances, in our study we applied the Scott–Kaiser modification of the Peniston protocol which is dedicated for a population of subjects with a history of stimulant abuse. Based on this protocol, the NFB training protocols in the first 10 sessions were bipolar sensory motor rhythm (SMR) training protocols in the C_4 (the central brain cortex) and Pz (the central parietal cortex) areas, and bipolar beta training protocols in the C_3 (the left central cortex) and FPz (the central fronto-parietal cortex) areas, with each protocol lasting 25 min. After these beginning sessions, we decreased the time of SMR and beta training protocols and added 20 min of monopolar alpha/theta training protocols in the Pz (the central parietal brain cortex) area and continued to increase the time of this protocol until the final sessions. All these protocols were performed using the Thought Technology ProComp 2 system, a single-subject EEG used for self-training, research, and for working with others. The Thought Technology ProComp 2 system displayed the brain's electrical activity (via electodes placed on the patient's scalp) on a monitor in the form of an audio/visual exercise. The feedback informed the patients of his success in making changes. The training was introduced as a computer game in which patients could score points using their brain. Subjects were advised to be attentive to the feedback and to find the most successful mental strategy to get as many points as possible; They received no other specific instructions.

In the SMR and beta training protocols, the feedback was audio/visual. Active electrodes were placed at the C_4 and C_3 areas and referenced with the Pz and FPz areas. A ground electrode was placed on the left-ear. In this program, the reinforcement band was composed of SMR (12–15 Hz) and beta (15–18 Hz) frequency bands in each protocol, and the suppressed bands were delta (2–5 Hz), theta (5–8 Hz) and high beta (18–30 Hz) frequency bands in both protocols. Thresholds were adjusted such that when subjects maintained the reinforcement band above the threshold for 80 % of the time during at least .5 s, and the suppressed band below the threshold for 20 % of the time, feedback was received. When the subjects were able to maintain the reinforcement band above the threshold for 90 % of the time during two continuous trials, the threshold was changed automatically so that it was closer to the optimal threshold (Scott et al. 2005).

Feedback in the alpha/theta training protocol on the Pz area was only in the audio format. In this protocol, the subjects closed their eyes, and only listened to the sound being played to them. Three pathways connected with this protocol were dedicated to the theta (5–8 Hz), alpha (8–12 Hz), and beta (15–18 Hz) frequency bands, while an additional pathway was used to control the delta (2–5 Hz) frequency band. The initial sessions were used to train patients to decrease alpha levels that were $\geq$12 mV (peak to peak), while augmenting theta levels, until there was "crossover." This was defined as the point at which the alpha amplitude dropped below the theta level. After achieving the first crossover, both alpha and theta frequencies were augmented and the delta frequency range was inhibited. This was intended to discourage the sleep transition during low-arousal states. Each alpha/theta session began with the subject sitting in a chair with eyes closed. The active electrode was placed at the Pz area with a left-ear reference (A1) and right-ear ground (A2). Two distinct tones were employed for alpha and theta reinforcement, with the higher pitched sound used to index the higher-frequency alpha band. At the start of each session, the therapist spent 3–5 min reading a script of guided imagery to the experimental subject that dealt with identified essential elements of maintaining abstinence. After the guided imagery, the subjects were clearly informed that the objective of the training did not involve explicit rehearsal of the script during the NFB. Subjects reporting previous meditative practices were asked not to use them during the training, because meditation has been observed to override the alpha/theta reinforcement effects (Scott et al. 2005). Following alpha/theta training, the subjects were given the opportunity to process their experience. When it appeared that subjects' delta activity began to increase and that sleep might occur during training, those subjects were told prior to their next session to move a limb if they heard the therapist say for example "left hand." Subsequently, during sessions where delta was increasing toward no responsiveness levels, the feedback sounds were inhibited in order to discourage the sleep transition (Peniston and Saxby 1995; Scott et al. 2005).

Instruments

The addiction severity index (ASI; McLellan et al. 1980), Symptoms Check List 90 version (SCL-90; Derogatis et al. 1973), and world health organization quality of life (WHOQOL; Skevington et al. 2004) questionnaires were used to evaluate the subjects on addiction severity, psychological health, and quality of life, respectively, before and after treatment.

ASI is the most widely used instrument in clinical and research situations that assess the intensity of addiction in individuals with all types of SDDs. It is a semi-structured instrument used in face-to-face interviews conducted by clinicians, researchers or trained technicians. The

instrument covers 7 areas of a SDD patient's life: medical condition, employment/support, drug, alcohol, legal, family/social, and psychiatric problems. Each area has the range of .000–1.000 possible scores in which higher scores indicate more intensive problem in that area. The ASI obtains lifetime information about problems, as well as problems within the previous 30 days (Cacciola et al. 2011). Studies have shown its high reliability and validity (Feelemyer et al. 2014; McLellan et al. 1980; McMahon 2008; Zemore 2012).

SCL-90-R is a widely used instrument composed of 90 items describing psychiatric and medical symptoms. Patients are asked to rate the severity of their experiences with 90 items over the past week on a 5-point scale ranging from 0 "not at all" to 4 "extremely". It consists of 9 symptom dimensions including somatization, obsessive–compulsive, interpersonal sensitivity, depression, anxiety, hostility, phobic anxiety, paranoid ideation, and psychoticism. Each dimension has the range of 0–4 possible scores that the higher scores indicate greater psychopathology (Derogatis et al. 1973; Prinz et al. 2013). This instrument has been normed on four groups: adult psychiatric outpatients, adult nonpatients, adult psychiatric inpatients, and adolescent nonpatients and studies have shown its significant validity and reliability (Bergly et al. 2014; Derogatis 1994; Prinz et al. 2013; Urbán et al. 2014).

WHOQOL has been developed by WHO group as a self-appraise instrument for evaluating quality of life. The brief version of this measure includes 26 items, encompassing four major domains of quality of life: physical health (7 items), mental health (6 items), social relation, (3 items) and environmental health (8 items), in addition of 2 items from the general facet (Skevington et al. 2004). Each domain is made up of questions for which according to a Likert scale, the scores vary between 1 "very poor" to 5 "very good". The mean score in each domain indicates the individual's perception of their satisfaction with each aspect of their life, relating it with quality of life. Higher scores show better perceived quality of life. The brief version of WHOQOL is commonly used for academic research, clinical evaluations, and cross-cultural comparisons (Hsiao et al. 2014). This instrument has been validated on a wide range of conditions and its scores are sensitive to changes in clinical condition. Furthermore, studies have showed its excellent psychometric properties (Feelemyer et al. 2014; Skevington et al. 2014; Skevington and McCrate 2012; Tracy et al. 2012).

Results

The results obtained in the pre and post-treatment phases for the experimental and control groups were analyzed using the SPSS.16 tool. To determine whether NFB plus pharmacotherapy was more effective than pharmacotherapy alone, the scores of the experimental and the control groups in pre- and post-treatment stages were compared using Multivariate Analysis of Covariance (MANCOVA). A separate MANCOVA was performed for each of the three major dependent variables (i.e. addiction severity, mental health, and quality of life):

Addiction Severity

For the first MANCOVA, the scores of the post-treatment indexes of ASI served as the dependent variables, the intervention (NFB in two experimental and control group levels) as the independent variable, and the scores of pre-treatment indexes of ASI as the covariates. After examining the hypothesis of normality, linearity, univariate and multivariate outliers, homogeneity of variance–covariance matrices, and multicollinearity, with no serious violation noted, the effect of intervention with the indexes of ASI was studied. This analysis yielded a significant multivariate groups main effect [$W = .34$; $F(6, 49) = 7.62$, $\rho = .001$] which showed that there was a significant difference between the groups on the combined dependent variables (indexes of ASI), and the group variable (intervention) could establish 47 % of this difference ($\eta^2 = .47$). These primary findings justified separate examination of each indexes of ASI effects.

Descriptive statistics for the experimental and control groups, the pre- and post-test scores of indexes of ASI are shown in Table 2 and graphically displayed in Fig. 1. MANCOVA results are presented in Table 3, where it is apparent that the intervention produced significant change in the medical condition [$F(1, 99) = 3.77$; $p = .04$], employment [$F(1, 99) = 5.92$; $p = .01$], drug use [$F(1, 99) = 17.14$; $p = .0001$], legal problems [$F(1, 99) = 13.31$; $p = .0001$], and psychiatric problems [$F(1, 99) = 17.75$; $p = .0001$]. It can be argued that the independent variable caused a significant difference between

Table 2 Descriptive indexes for the ASI prior to and following treatment

Variables	Experimental				Control			
	Mean		SD		Mean		SD	
	Pre	Post	Pre	Post	Pre	Post	Pre	Post
Medical	.25	.04	.22	.13	.26	.12	.23	.22
Employment	.51	.48	.32	.31	.51	.55	.3	.35
Drug use	.10	.02	.08	.04	.11	.06	.07	.08
Alcohol use	.04	.01	.09	.04	.04	.03	.08	.08
Legal	.09	0	.12	0	.09	.06	.12	.11
Family	.33	.1	.24	.11	.34	.27	.23	.23
Psychiatric	.44	.11	.21	.09	.43	.28	.21	.2

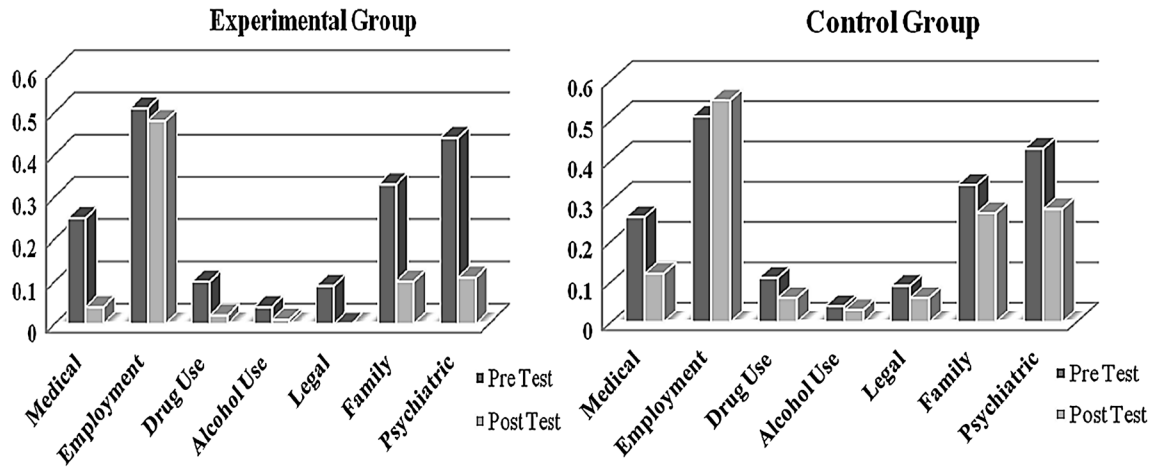

Fig. 1 Pre and post test results of ASI subscales in experimental and control groups

Table 3 Results of MANCOVA for ASI subscales in the experimental and control groups

Variable	F	Sig.	η^2
Medical	3.77	.04*	.04
Employment	5.92	.01**	.06
Drug	17.14	.0001***	.15
Alcohol	.46	.49	0
Legal	13.31	.0001***	.12
Family/social	3.15	.07	.03
Psychiatric	17.75	.0001***	.16

$df = (1, 99)$; * $p < .05$; ** $p < .01$; *** $p < .001$

the experimental and control groups in these dimensions of addiction severity. Pre- and post-test means' comparison in these dimensions say that their changes were reduction of their intensity. No differences in alcohol use and family problems were observed between the groups. On the other hand, Etta coefficients show that the effect size of independent variable (grouping) is small in Medical and Employment variables, but also average in Drug use, Legal and Psychiatric. So it could be concluded that the group factor (NFB intervention) has had just a small or average role on changes occurred in these areas of addiction severity, but it had been still a significant effect.

Psychological Symptoms

In second MANCOVA, the scores of the post-treatment indexes of SCL-90 served as the dependent variables, the intervention (in two levels) as the independent variable, and the scores of pre-treatment SCL-90 indexes as the covariates. After examining the hypothesis of normality, linearity, univariate and multivariate outliers, homogeneity of variance–covariance matrices, and multicollinearity, with no serious violation noted, the effect of intervention with the indexes of ASI was studied. This analysis yielded a significant multivariate groups main effect [$W = .27$; $F(8, 49) = 14.01$, $\rho = .001$] which showed that there was a significant difference between the groups on the combined dependent variables (indexes of SCL-90), and the group variable (intervention) could establish 83 % of this difference ($\eta^2 = .83$). These primary findings justified separate examination of each indexes of SCL-90 effects.

Descriptive results in means and standard deviations of the experimental and control groups in the pre- and post-test scores of SCL-90 are shown in Table 4.

MANCOVA of SCL-90 indexes showed the experimental group, compared with the control group, to be changed on the scales of somatization [$F(1, 99) = 37.9$; $p = .01$], obsessive–compulsive [$F(1, 99) = 23.98$; $p = .001$], interpersonal sensitivity [$F(1, 99) = 4.94$; $p = .04$], anxiety [$F(1, 99) = 21.32$; $p = .002$], and hostility [$F(1, 99) = 4.8$; $p = .04$] but not on the scales of depression, phobic anxiety, paranoid ideation, and psychotics (Table 5). Comparison of the pre- and post-test means in scales with significant changes, clarify that they reduced in post stage which means the reduction of symptoms severity. Etta coefficients show that the effect size of independent variable is average and the group factor (NFB intervention) caused 40–75 % of changes occurred in these scales of psychological symptoms.

The results of pre- versus post-test assessments of the symptoms subscales in the experimental and control groups are presented in Fig. 2.

Quality of Life

Finally in the last MANCOVA, the scores of the post-treatment indexes of WHOQOL served as the dependent

Table 4 Descriptive indexes for the SCL-90-R prior to and following treatment

Variables	Experimental				Control			
	Mean		SD		Mean		SD	
	Pre	Post	Pre	Post	Pre	Post	Pre	Post
Somatization	1.33	.57	.67	.41	1.32	1.19	.68	.82
Obsessive–compulsive	1.71	1	.69	.63	1.75	1.75	.64	.82
Interpersonal sensitivity	1.40	.71	.72	.47	1.39	1.14	.73	.79
Depression	1.65	.83	.72	.56	1.65	1.24	.71	.87
Anxiety	1.40	.07	.7	.56	1.4	1.04	.7	.72
Hostility	1.13	.64	.61	.42	1.15	1.16	.59	.69
Phobic anxiety	.6	.37	.32	.36	.6	.4	.31	.36
Paranoid ideation	1.48	.94	.75	.59	1.49	1	.75	.66
Psychotics	1.25	1.11	.63	.34	1.25	.98	.6	.56

Table 5 Results of MANCOVA for SCL-90-R subscales in the experimental and control groups

Variable	F	Sig.	η^2
Somatization	37.9	.01*	.53
Obsessive–compulsive	23.98	.001**	.75
Interpersonal sensitivity	4.94	.04*	.42
Depression	1.56	.24	.16
Anxiety	21.32	.002**	.72
Hostility	4.8	.04*	.4
Phobic anxiety	0	.9	0
Paranoid ideation	.01	.9	.02
Psychotics	1.46	.26	.15

$df = (1, 99)$; * $p < .05$; ** $p < .01$

variables, the intervention (in two levels) as the independent variable, and the scores of pre-treatment indexes of WHOQOL as the covariates. After examining the hypothesis of normality, linearity, univariate and multivariate outliers, homogeneity of variance–covariance matrices, and multicollinearity, with no serious violation noted, the effect of intervention with the indexes of ASI was studied. This analysis yielded a significant multivariate groups main effect [$W = .41$; $F(5, 49) = 5.62$, $\rho = .03$] which showed that there was a significant difference between the groups on the combined dependent variables (indexes of WHOQOL), and the group variable (intervention) could establish 39 % of this difference ($\eta^2 = .39$). These primary findings justified separate examination of each indexes of WHOQOL effects.

The means and standard deviations of WHOQOL pre- and post-test assessments in the experimental and control groups are presented in Table 6.

Table 7 shows the results of MANCOVA of WHOQOL. These results suggested that changes were significant in the scales of mental health [$F(1, 99) = 5.5$; $p = .02$], social relation [$F(1, 99) = 3.96$; $p = .04$], general health status [$F(1, 99) = 5.15$; $p = .02$], and general quality of life

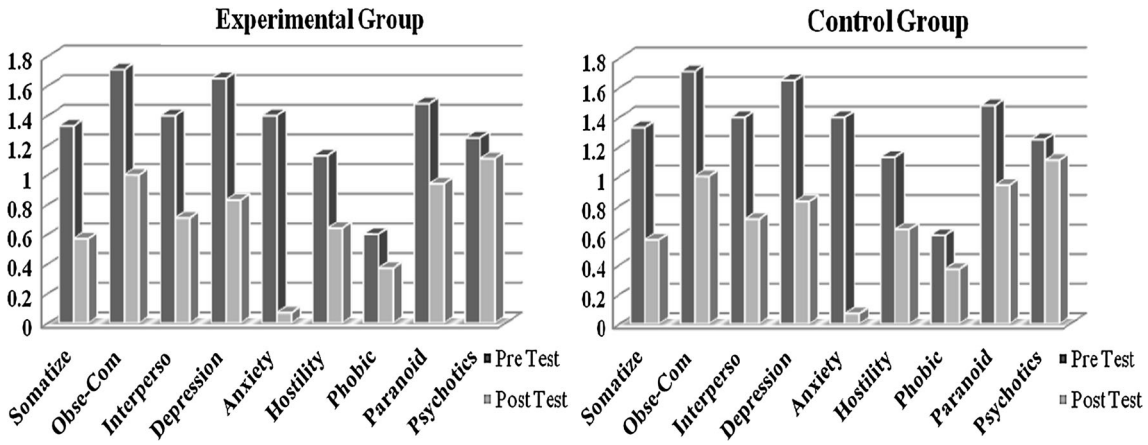

Fig. 2 Pre and post test results of SCL-90-R subscales in experimental and control groups

Table 6 Descriptive indexes for the WHOQOL prior to and following treatment

Variables	Experimental				Control			
	Mean		SD		Mean		SD	
	Pre	Post	Pre	Post	Pre	Post	Pre	Post
Physical health	18.2	18.9	4.1	4	18.28	18.88	4	4.12
Mental health	16.22	17.48	4.09	3.07	16.3	16.21	3.98	3.89
Social relation	7.58	9.05	2.88	2.2	7.28	7.82	2.68	2.89
Environmental health	23	23.62	5.55	1.4	23.02	23.12	5.42	5.4
General quality of life	2.94	3.95	1.89	1.07	2.84	2.76	1.92	1.96
General health status	3.26	4.17	1.24	1.11	3.26	4.15	1.21	1.14

Table 7 Results of MANCOVA for WHOQOL subscales in the experimental and control groups

Variable	F	Sig.	η^2
Physical health	1.58	.21	.03
Mental health	5.5	.02*	.13
Social relation	3.96	.04*	.09
Environmental health	1.3	.26	.03
General quality of life	4.39	.03*	.12
General health status	5.15	.02*	.11

$df = (1, 99)$; * $p < .05$

$[F(1, 99) = 4.39; p = .03]$. By comparing the pre- and post-test means it can be seen that the changes were enhancement of these QOL scales. However, no changes were observed in the scales of physical health and environmental health. Etta coefficients show a small effect size for independent variable. According to these findings, although the group effect was significant, but it has had just a small role on changes occurred in scales of QOL.

Figure 3 shows the pre- and post-test results of WHOQOL for the experimental and control groups.

Discussion

The results of present study showed that NFB plus pharmachotherapy, in comparison with pharmachotherapy alone, generate more improvement in severity of addiction, mental health, and quality of life in CMD patients. Earlier studies on alcoholic patients (Passini et al. 1977; Bodehnamer and Callaway 2004; Burkett et al. 2005; Raymond et al. 2005) demonstrated improvement similar to that observed in our study in which the experimental group that received NFB showed greater improvement than the control group. Our study also provides support for the study by Scott et al. (2005) that showed an increase in psychological health in patients with mixed SDD receiving NFB and for the studies by Passini et al. (1977) and Peniston and Kulkosky (1989) that found significant differences in anxiety signs. Prior to present study Unterrainer et al. (2014) also had found significant results confirming the efficacy of NFB in a case of adolescent with substance misuse. The most important finding subscribe to all these studies, as could be concluded in present study too, is that in SDD treatment, a combination of different treatment approaches including pharmachotherapy, psychotherapy,

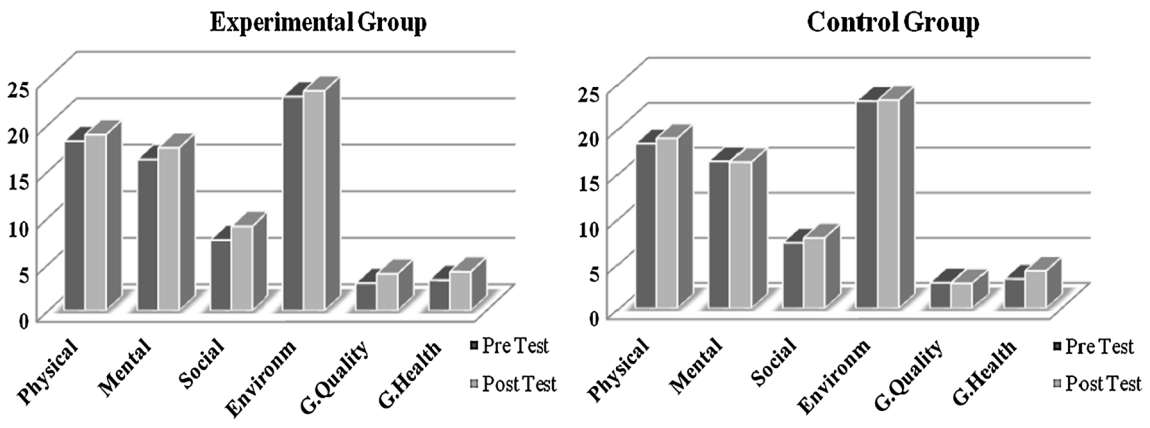

Fig. 3 Pre and post test results of WHOQOL subscales in experimental and control groups

and neurotherapeutic methods such as NFB is highly more effective than using a one-dimensional method. It is more vital in more complex SDDs such as CMD.

Although pharmacotherapy or psychotherapy approaches alone can lead to some improvement in CMD patients, they come with weak points that include side effects and the high risk of relapse (Simkin et al. 2014; Gossop et al. 2002). Because NFB, on the other hand, deals with the fundamental operational functions of the brain and acts as a mechanism for the brain to self-regulate, it has the ability to correct irregular brain functions and consequently improve psychological abnormalities. Furthermore, researches confirmed the stability of NFB effects and its prevention of negative side effects (Hammond 2011; Unterrainer et al. 2014). Thus, pharmacotherapy can be used to maintain the initial balance between physiological and psychological health in SDD and then NFB training can be used to guide the patient toward longer lasting health and balance (Trudeau et al. 2009).

Nowadays, several theoretical opinions exist on the fundamental mechanisms of effectiveness of NFB as a therapeutic method for SDD. Most of these opinions concentrated on the Pension's alpha-theta protocol. McPeak et al. (1991), Rosenfeld (1992), and Taub et al. (1994) introduced this protocol as a kind of meditation technique and suggested that self-induced altered states found in various forms of meditation can sometimes replace the self-destructive pursuit of alcohol and drugs. Cowan (1994) suggested that the effectiveness of such training may be due to the enhanced imprinting of positive temperance suggestions and the feeling of inner empowerment that the alpha/theta state seems to encourage. In a more detailed view, Ochs (1992) has suggested that the most active (and apparently transformational) properties of NFB protocols in SDD treatment may involve teaching the subjects to intentionally increase the amplitude and coherent interaction of both their alpha and theta brainwave frequencies in either of the brain locations. Complementing this finding Simkin et al. (2014) explained that the alpha-theta NFB protocol trains SDD patients to promote stress reduction and achieve profoundly relaxed states by increasing alpha and theta brainwaves and decreasing fast beta brainwaves. In Scott et al. (2005) viewpoint, the efficacy of alpha/theta NFB may lie in its ability to allow subjects to better tolerate stress, anxiety, and anxiety-eliciting situations, which are particularly evident during the initial phases of recovery. On the other side, White and Richards (2009) mentioned that alpha-theta protocol can induct higher states of consciousness and insight, helping to alter one's relationship to self and the world as a result of what is seen and understood in those higher states. They concluded that the effectiveness of this protocol may be explained in large part by a neuroplasticity concept known as the malleability of memory, which means that revisiting and re-evaluating early experiences via alpha–theta protocol allows the neurological rewriting of one's memory and consequently modify affective reactions, and alter the nature of memories. Furthermore, in alpha–theta protocol subconscious (emotional) memories become more available to conscious (episodic) process and traumatic memories are often released and appear as flashbacks from the past. As these flashbacks are relived in the context of current adult resources and perceptions, the subconscious memories may become more readily available for healing and alteration.

From another perspective, explaining effectiveness of NFB protocols in SDD, some neuropsychologists focused on conditional normalization of reinforcement systems in the brain. Blum et al. (2012) were concerned with the Reward Deprivation Syndrome (RDS) as a dysfunction in the Brain Reward Cascade (BRC), which leads to substance craving and being a possible candidate for susceptibility to alcoholism and SDD. Therefore, SDD patients have a neurologically based inability to experience pleasant feelings and calmness from simple stimulation. It has been noticed that dysfunction of this pleasant feeling is the most important factor in forcing patients to feel craving and resort to substance abuse (Kreek et al. 2005). Following this idea, some studies have stated that an apparent neurological "normalization" could be responsible for shifting the trained subject into a physical state of comfortable calmness (Fahrion et al. 1992; Salansky et al. 1998). Studies suggested that NFB training can initiate this neurological normalizing shift (Scott et al. 2005; Sokhadze et al. 2011; Unterrainer et al. 2014).

Recently, mechanisms by which NFB therapy may cause behavioral changes have been suggested by research in neuronal plasticity. A number of investigators (Rosenzweig 2003; VanPraag et al. 2000) are essentially in agreement pointing out that ongoing direct experience that evokes persistent neuronal activation alters brain structure and brain functioning. A possible link is observed between steady-state stimulation, induced neuronal activation, and neuronal plasticity in the increasing body of evidence that the electrical activity of the brain regulates the synthesis, secretion and actions of neurotrophins (Schindler and Poo 2000), which together promote synaptogenesis. In Sokhadze et al. (2011) explanation pre- to post-treatment electrical activity changes are considered to positively affect motor control, cortical inhibition function, general arousal, and alertness level. This can mediates the positive effects of proposed NFB protocol on addictive behaviors. The crucial point about NFB is that it directly acts on the brain oscillations, which are altered in SUD. So, NFB-induced modifications could be manifestations of neural plasticity, which is a phenomenon that has been considered a basic mechanism for behavioral modifications.

Finally, while taking into consideration the complexity of the dimensions of this disorder, the worthwhile program must be able to affect various factors while not being prone to the problems of previous methods, such as relapsing, instability, and other side effects (Trudeau 2000). On this purpose present study showed the strength of NFB in improving treatment results in MCD, as well as its ability to work collaboratively with other methods. But, as a limitation, although we attempted to control different factors in the process of NFB training, our use of a new method of technology in NFB and patients' hope and motivation for the new treatment could have had an uncontrollable effect on our research. It is also noticeable about the NFB clinician contact effect. Despite this, we believe that the use of a placebo group could have strengthened the design of the NFB program and created control over other aspects of the program. However, this was a preliminary study in which, because of the high cost of the technology involved in NFB, it was not possible to use a placebo group. Although we noticed less use of a placebo group in prior studies, that future studies should include a placebo group to control the effects of interfering factors and thereby clearly reveal the benefits of NFB training. In addition, the present study could not be conducted on CMD patients without using pharmacotherapy. Future studies should include one group of patients who would receive NFB without receiving pharmacotherapy to show the effectiveness of the two methods exclusively.

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