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ABSTRACT

Neurofeedback (NF) training has been employed as a therapeutic method in substance-dependence disorder over the last three decades. The purpose of the present study was to examine the effectiveness of this method on improvement of comorbid neuro-psychological syndromes in opioid-dependence disorder. Psychopathological and craving dimensions and brain activity signals of 20 opioid dependent patients were measured using Symptom Checklist-90-Revised (SCL-90-R), Heroin Craving Questionnaire (HCQ), and Quantitative Electroencephalography (QEEG). All the patients were undergoing pharmacotherapy. They were assigned to two groups that were matched based on SCL-90-R scores, education and age. The experimental group received 30 sessions of NF training in addition to their medicine. The control group received only the usual pharmacotherapy. The probable changes were monitored by reappraisal of all the patients after the treatment. We hypothesized that patients in the experimental group would show more reduction in their comorbid syndromes.

The Multivariate Analysis of Covariance (MANCOVA) showed that the experimental group, in comparison with control group, showed significantly more improvement in all three outcome measures. In the SCL-90-R, improvement was noted with the hypochondriacs, obsession, interpersonal sensitivity, aggression, psychosis, and general symptomatic indexes. In the HCQ, improvement was found in the anticipation of positive outcome, desire to use substance, and total average score. Finally, the QEEG showed positive changes in frontal, central and parietal delta, frontal and central theta, parietal alpha and frontal and central Sensory Motor Rhythm (SMR) amplitudes.

This study suggests that NF can be used as a therapeutic method to ameliorate abnormalities related to opioid-dependence disorders. The results emphasize the importance of neuropsychological interventions in treatment of substance-dependence disorders.

INTRODUCTION

Drug and alcohol abuse is an enormous biopsychosocial problem associated with disruption of social situation and communities, mental and medical disorders and healthcare costs. The relationship between substance-related disorders and other psychiatric disorders or general medical illnesses is accordingly of significant interest. Until recently, substance abuse and comorbid psychiatric/medical problems were typically treated independently. But current trends promote coordinated treatment of comorbid substance abuse, psychiatric, and general medical problems in order to optimize patient care and reduce cost.[1] In recent years neurophysiological dimensions of substance disorders also have attracted more scientific attention too. Studies have shown that substance dependence disturbs the normal function of the brain and can create abnormalities in the neural system.[2] Therefore, because of the complex interaction between mind and body in this disorder, therapeutic approaches should ideally address all mental and physical dimensions in order to provide a comprehensive treatment.[2]

During the last 30 years, a powerful scientific movement has developed to explore the connection between the brain and the mind. Many studies have discovered the ways in which psychological states affect brain function, or are affected by it.[3] In this field, neurophysiological examinations have clarified the relationship between the surface electroencephalography (EEG), underlying thalamocortical mechanisms and psychological temperaments. These studies have shown that optimum modulations in rhythms and frequency of the electrophysiological brain activities can make positive changes in psychological states.[4,5]

In the early 1960s Joe Karmiya,[5] a psychologist at the University of Chicago, discovered that when patients were provided with information about their brain's activity, they could learn how to alter the power and speed of the brainwaves. He showed that this subsequently can change and improve their psychological states.[5] This examination provided the basic principles of brainwave feedback training. Afterward the efficacy of NF changing brain activity has been studied in many investigations.

NF is based on this accepted scientific idea that the mind and the body are interconnected. This is a treatment method that trains the brain to act in a more optimal way in order to improve emotional, cognitive, physical, and behavioral experiences.[6] NF is a technique that trains patients to alter their brainwave patterns as they receive information about those patterns. As studies have shown, many neurological, psychological and medical disorders are accompanied by abnormal patterns of the cortical activity.[5-9] In NF training abnormal patterns of brain activity can be identified through an EEG baseline or sometimes with QEEG. Furthermore, clinical training with EEG feedback or neurofeedback enables the individual to modify those patterns and normalize or optimize brain activity.[7]

NF has been used as a therapeutic method to help ameliorate different types of disorders, for example, Attention Deficit Activity Disorder (ADHD),[8,9] epilepsy,[10] depression,[11] anxiety and affect

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Table 1

Demographic data associated with experimental and control groups

		Age			Education (years)			Abstinence (month)		
Group	N	Mean	SD	Range	Mean	SD	Range	Mean	SD	Range
Experimental	10	30.3	7.01	21-45	14.5	1.8	12-16	3.2	1.93	1-6
Control	10	29.1	6.5	21-40	14	1.9	12-17	3.6	2	1-7
Total	20	29.7	6.64	21-45	14.25	1.86	12-17	3.2	1.9	1-7

disorders,[12,13] fibromyalgia,[14] and obsessive compulsive disorder.[15] NF also has been used to enhance attention and memory performance in healthy subjects.[16-19]

Substance dependence is another disorder which recently has caught neurologists' attention. It has been suggested that the effective treatment for substance abuse always requires a combination of neurophysiological and psychological approaches.[20] This fact, and also the limitations of pharmacotherapy and behavioral therapy, increase the need for alternative and/or complementary therapies with long-lasting effects and minimal side effects.[21] NF appears to be a very promising alternative, as reduced dependence symptoms and improved psychological variables have been consistently reported in the literature after NF treatment.[22-24]

Substance dependence includes a complex series of disorders with frequent psychopathological comorbidities and EEG abnormalities of several types.[25] Acute and chronic drug abuse may be associated with some other mental disorders like anxiety, depression and personality disorders [20,21] and also a significant alteration and abnormality of the brain's activity.[25-28] These brain function abnormalities may commonly be detected with a QEEG evaluation.[24] With the advent of NF, many researchers have used this technique as a therapeutic method for correcting brainwave abnormalities in substance or alcohol dependent patients. The results have corroborated the efficacy of NF training on neuropsychological consequences of drug/alcohol dependency.[23,24,29,30] Early research in this field was conducted in 1989 and 1990 by Peniston and showed positive changes in alcoholic patients.[31] Since then the Peniston's protocol in alpha-theta training has been used for substance abuse patients in different studies.[24,32,33]

Earlier studies assessed the effects of the alpha conditioning on the habits of substance-dependant patients were assessed. Most positive outcomes were associated with reduced drug-seeking, improved coping with everyday problem situations, decreased illicit drug usage and also increased feeling of self-control.[34,35]

In other experimental studies, it has been reported that participants who have received NF treatment (alpha-theta training) showed significant improvement in Minnesota Multiphase Personality Inventory-2 (MMPI-2) personality scales. They also experienced a decrease in stress-related, blood-based Beta-endorphins and a significant decrease in craving.[32,33,36] Follow-up studies presented the constancy of treatment outcomes in substance-dependant patients who had completed an alpha/theta NF training program.[37]

In the latest study done by a behavioral research team, opioid and stimulant addicts were given feedback on their brain's electrical activity in conjunction with conventional treatment for drug abuse. NF protocols included Beta training and SMR training to address attention variables, and alpha/theta training to improve mood and personality abnormalities. The authors reported that NF treatment had doubled the recovery rate for drug dependant patients. The experimental group showed normalization of attention variables following the SMR-Beta portion of the NF, whereas the control group showed no improvement. Experimental participants demonstrated significant changes ($p < .05$) in comparison with control participants on 5 of the 10 scales of the MMPI-2. Participants in the experimental group were also more likely to stay longer in the treatment and were more likely to complete treatment as compared to the control group. Finally, the 1-year follow up indicated that abstinence levels were significantly higher for the experimental group as compared to the control group. In addition, the study documented significant improvements in the ability of the experimental group patients to focus their thinking and process information.[24]

Recently, as different studies have confirmed, NF has shown to be successful in treating some aspects of substance dependence disorders.[23-31] However at present the results concerning the effectiveness of this method on psychological and neural functioning in opioid-dependence disorder are still narrow and almost scant.

The purpose of the present study was to examine if NF training can improve neurological and psychological consequences of substance abuse in opioid-dependant patients and decrease their desire to use opioids. Therefore, an SMR NF training program was combined with an alpha-theta protocol to train opioid-dependent patients who were undergoing Methadone or Buprenorphine maintenance therapy for substance-dependence disorder. The control group did not receive any NF.

Referring to studies on the effects of NF on substance-dependence disorders,[23] we hypothesized that NF in comparison with pharmacotherapy will make more improvement on psychopathological symptoms, craving and brain activity in opioid-dependent patients in the experimental group.

MATERIALS AND METHODS

Subjects

Twenty detoxified male opioid-dependent patients participated in the study, ranging in age from 20 to 50 years. All the patients were on Methadone or Buprenorphine maintenance treatment for substance-dependence disorder. Exclusion criteria were anoxia, head trauma, stroke, encephalitis and HIV. The average duration of abstinence was 3 months. Table 1 shows some demographic information associated with experimental and control participants.

In the pre-treatment phase, all 20 participants were initially evaluated for psychopathological symptoms, craving and brain activity. Then following a standard controlled research design, the patients were organized into experimental ($N = 10$) and control ($N = 10$) groups. The two groups were matched for age (average of about 30), duration of abusing opioid (average of 3 months of abstinence after at least 1 year dependency to crack heroin, heroin, opium, tramadol), education (diploma or bachelor level), psychopathological symptoms and craving subscales, but not in all QEEG subscales. One of the groups was

chosen randomly as the experimental group. Both groups received pharmacotherapy. The experimental group also received 30 sessions of NF directed toward regulating the brain activity. We believed these protocols would help patients to self-regulate their brainwaves and that this brainwave regulation would cause improvement in psychological function and cravings. The research model was a pre-test post-test with a control group design.

Instruments for gathering data

SCL-90-R,[38] HCQ,[39] and QEEG were used to obtain treatment outcomes. The SCL-90-R is a widely used instrument of self-reported psychopathology. The instrument is composed of 90 items describing symptoms most commonly identified by psychiatric and medical patients. The psychometric properties consist of nine symptom dimensions or factors: Somatization, Obsessive-Compulsive, Interpersonal Sensitivity, Depression, Anxiety, Hostility, Phobic Anxiety, Paranoid Ideation, and Psychotics. The instrument was established on a large sample of heterogeneous outpatient adults from four separate psychiatric facilities.[38,40] Significant correlations were found between the SCL-90-R symptom dimensions and several MMPI scales.[41] Studies also have shown its significant convergent validity and correlations.[42]

The HCQ includes 5 sections with a 7 level Likert scoring system. The five main subsections of this questionnaire are: anticipation of positive outcome, relief from withdrawal, intention and plan to use substance, desire to use substance, and lack of control over use. Research has shown the validity and reliability of the subsections of this questionnaire in measuring the severity of craving in patients.[43-45]

QEEG data were obtained using the Ebneuro Company Mizar 40 system and the International10-20 System. The brainwave activity was then fed into a computer with Neuroguide software which performed mathematical calculations to provide numbers and graphs.[46,47] This tool was established to evaluate brain function, and research has shown that it can also be used as a highly valid diagnosing tool in evaluating psychological disorders.[48,49]

Two minutes of artifact-free data were extracted from the eyes-closed EEG record for quantitative analysis. A computerized artifact-detection algorithm combined with visual inspection was used to obtain 48 epochs (2.5 sec each, for a total of 2 min) of artifact-free data from 20 min of continuous EEG. Power spectral analysis was performed using Fast Fourier Transform (FFT). Absolute power of delta (0.5 – 4 Hz), theta (4 – 8 Hz), alpha (8 – 12 Hz), and beta-2 (18 – 30 Hz) at the electrode sites of F3, F4, Fz (their average identified as the frontal areas), C3, C4, Cz (their average identified as the central areas), and P3, P4, Pz (their average identified as the parietal areas) in both pre- and post-treatment stages, were analyzed in both experimental and control groups.

Experimental procedure

The NF program of the experimental group lasted for 2 months (30 one-hour sessions). The control group patients spent this time on the waiting list. The NF training was based on the Cry-Help substance abuse protocols.[24] Thought Technology software and Procomp2 amplifier were used for the NF sessions. The brain's electrical activity was displayed on a computer monitor in the form of an audio-visual exercise. The feedback informed patients about their success in making changes.

In the Cz area, the feedback was audio-visual. In this program thresholds were adjusted in a way that if the participant maintained the reinforcement bands above the threshold in 80% of the time and the suppressed band under the threshold 20% of the time for at least 1 second, feedback was received. Whenever the participant could maintain these conditions in two continuous 5-minute time trials, threshold changes were made by the therapist so that it was closer to the optimal threshold.[24]

Feedback in alpha-theta training protocol at Pz was in audio format only. In this protocol, the participant closed his eyes and only listened to the sound being played for him. Three pass bands connected with this protocol were related to the theta, alpha, and beta waves, while one additional pass band pathway controlled delta. The frequency range for alpha was 8–11 Hz and for theta it was 5–8 Hz. The initial sessions were used to train patients to decrease alpha levels that were above 12 mV (peak to peak), while augmenting theta, until there was "crossover." This was defined as the point at which the alpha amplitude drops below the level of theta. Subsequent to the first achievement of crossover, both alpha and theta frequencies were reinforced and the 2–5 Hz frequency range (delta) also was inhibited. This was intended to discourage sleep transition during low-arousal states.[24,31]

Each alpha-theta session began with the subject sitting in a chair with eyes closed. The active electrode was placed at Pz with a left-ear reference (A1). The right earlobe was connected to circuit ground. 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, following the Peniston protocol model, the therapist spent 3–5 minutes reading a script of guided imagery to the experimental subject that dealt with identified essential elements of maintaining abstinence. After the guided imagery, it was made clear to the subject that the objective of the training did not involve explicit rehearsal of the script during the NF. Subjects reporting previous meditative practices were asked not to use them during the training, since meditation has been observed to override alpha-theta reinforcement effects. Following the alpha-theta training, clients were given the opportunity to process their experience. When it appeared that subject's delta activity (2–5 Hz EEG) started to elevate and sleep might be occurring during training, 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 elevating toward no responsiveness levels, the feedback sounds were inhibited in order to discourage the sleep transition. At the end of the treatment phase, the participants were re-evaluated with the SCL-90-R, HCQ, and QEEG.

Statistical analyses

The results of pre- vs. post-treatment phases in the experimental and control groups were analyzed by the SPSS.16 tool, the two-tailed statistical significance level was set at $p < 0.05$. In order to control the effect of the pre-treatment phase in an effort to find whether NF plus pharmacotherapy is more effective than pharmacotherapy alone, the Multivariate Analysis of Covariance (MANCOVA) was used. For this purpose, the scores in post-treatment subscales of SCL-90-R, HCQ and QEEG data as the dependent variables, the intervention (at two levels) as the independent variable and the score of pre-treatment subscales as the covariate variables were analyzed. After examining the assumptions of linearity, homogeneity of regression lines, and homogeneity of variances, the effect of intervention with the dependent variables was studied.

RESULTS

Table 2 shows some descriptive indexes of SCL-90-R in experimental and control groups both in pre- and post-treatment stages. Afterwards the results of the MANCOVA are displayed in Table 3. It shows that the effect of the intervention factor is statistically significant in the error level of 0.05 regarding six symptoms: Somatization ($F(1, 8)= 9.37$; $p=.01$), Obsession ($F(1, 8)= 23.98$; $p=.001$), Interpersonal

Table 2

Descriptive indexes of SCL-90-R in pre- and post-test in experimental and control groups

	Experimental				Control			
	Mean		Standard Deviations		Mean		Standard Deviations	
Variables	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	1.4	.71	.72	.47	1.39	1.14	.73	.79
Depression	1.65	.83	.72	.56	1.65	1.24	.71	.87
Anxiety	1.4	.77	.7	.56	1.4	1.04	.7	.72
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	.51	.63	.34	1.25	.98	.6	.56
Hostility	1.13	.64	.61	.42	1.15	1.16	.59	.69
Total Score	1.35	.72	.54	.37	1.35	1.1	.36	.39

Table 3

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

Variable	F	Sig.	Eta Squared
Somatization	37.9	.01*	.53
Obsessive Compulsive	23.98	.001***	.75
Interpersonal Sensitivity	4.94	.04*	.42
Depression	1.56	.24	.16
Anxiety	1.46	.26	.15
Phobic Anxiety	.0	.9	.0
Paranoid Ideation	.01	.9	.02
Psychotics	21.32	.002***	.72
Hostility	4.8	.04*	.4
Total Score	4.7	.04*	.4

Note: DF= (1, 13) (DF: Degrees of Freedom)
*P< .05; **P< .01; ***P< .005

Sensitivity (F(1, 8)= 4.94; p=.04), Psychosis (F(1, 8)= 21.32; p=.002), Hostility (F(1, 8)= 4.8; p=.04) and the total score of symptoms (F(1, 8)= 4.7; p=.04). The anxiety, phobic anxiety, depression, and paranoia scales did not reach significance. Figure 1 shows the pre- and post-test results of SCL-90-R for both experimental and control groups.

Heroin Craving Questionnaire

Descriptive results in mean and standard deviation of experimental and control groups in pre- and post-test of HCQ have been shown in Table 4. Furthermore the MANCOVA analysis of HCQ and its results showed the experimental group, compared to the control group, improved on the following scales: anticipation for a positive outcome (F(1, 13)= 9.32; p=.009), desire to use (F(1, 13)= 10.48; p=.006), and relief from withdrawal (F(1, 13)= 5.97; p=.03). But in the case of the intention and plan to use (F(1, 13)= 0.09; p=.77) and lack of control (F(1, 13)= 0.5; p=.49) the effect of the intervention was not significant (Table 5). The results of pre- vs. post-test assessments in craving subscales in experimental and control groups are shown in Figure 2.

QEEG

Mean and standard deviations of QEEG in pre- and post-test for experimental and control groups are presented in Table 6. Table 7 shows the results of MANCOVA analysis for QEEG. Results indicated that changes are significant in regards to the following variables: over

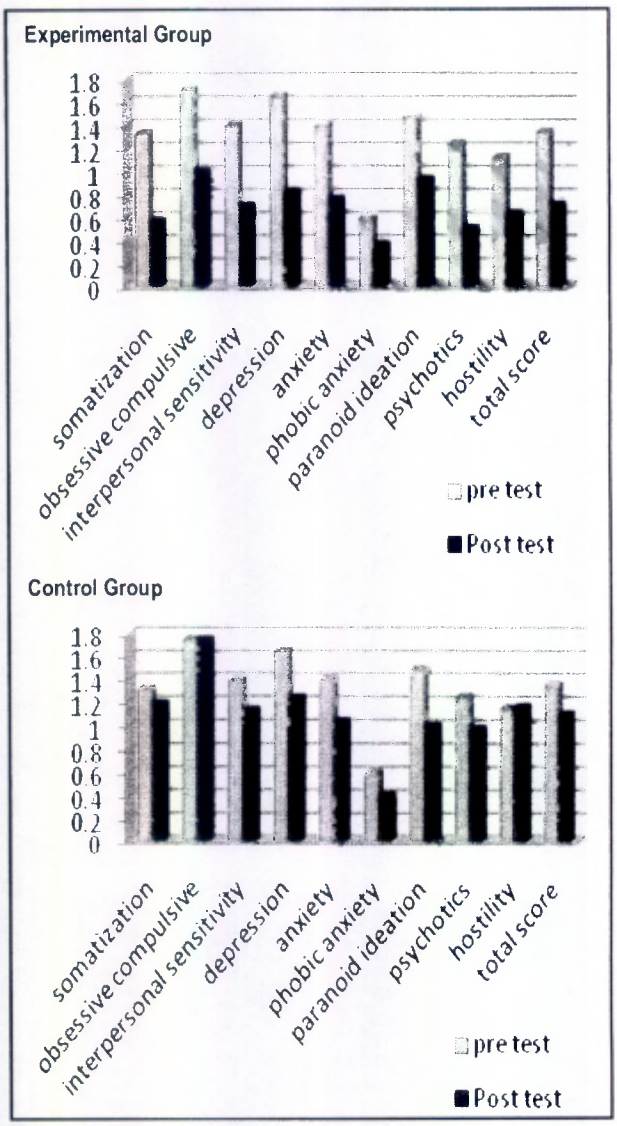

Figure 1.
Pre- and post-test results of SCL-90-R subscales in experimental and control groups.

Table 4

Descriptive indexes of HCQ in pre- and post-test in experimental and control groups

	Experimental				Control			
	Mean		Standard Deviations		Mean		Standard Deviations	
Variables	Pre	Post	Pre	Post	Pre	Post	Pre	Post
Anticipation of Positive Outcome	29.3	19.4	8.65	4.11	29	29.3	8.56	15.82
Intention and Plan to Use	15.53	13.7	5.95	5.63	15.5	16.3	5.96	8.08
Desire to Use	14.5	11.3	5.93	5.37	14.3	16.7	5.93	8.38
Lack of Control over Use	12.8	10.7	5.49	4.9	12.8	12	5.49	8.21
Relief from Withdrawal	18	14.42	4.77	5.27	18.12	19	4.95	9.63

Table 5

Results of MANCOVA of the HCQ subscales in experimental and control groups

Variable	F	Sig.	Eta Squared
Anticipation of Positive Outcome	9.32	.009**	.41
Intention and Plan to Use	.09	.77	0
Desire to Use	10.48	.006**	.45
Lack of Control over Use	.5	.49	.04
Relief from Withdrawal	5.97	.03*	.32

Note:DF= (1, 13)
*P< .05; **P< .01; ***P< .005

the frontal area, delta (F(1, 13)= 10.87, p= .006), alpha (F(1, 13)= 6.35, p= .02), and SMR (F(1, 13) = 5.01, p= .04); over the central area delta (F(1, 13)= 20.67, p= .001), theta (F(1, 13)= 3.22, p= .04) and SMR (F(1, 13)= 4.93, p= .04); and over the parietal area delta (F(1, 13)= 12.45, p= .004) and alpha (F(1, 13)= 7.05, p= .02).

DISCUSSION

In this study we examined the effectiveness of NF training on neuropsychological abnormalities in detoxified patients with opioid dependence disorder. Matched subgroups received either NF training with medicine (methadone/boprenorphin maintenance therapy) or just medicine. The results of MANCOVA showed that the independent variable (NF training) was associated with a significant difference between the experimental and control groups in some neuropsychological scales.

Symptom Checklist-90-Revised

Results show that the patients in the experimental group have shown more improvement in the subscales of somatization, obsession, interpersonal sensitivity, psychosis, hostility and the total score of symptoms after receiving NF, in comparison with the control group which had not received any NF treatment. Research has shown that the treatment of patients with substance abuse disorder by NF may become more complicated when patients present various psychiatric conditions.[23] As this study showed, NF training can improve comorbid syndromes in opioid-dependant patients and decreased craving. These are in line with reports about enhanced cognitive abilities, mood and personality factors in substance-dependent patients who have received NF compared with control groups.[15,24,29,36] But in the case of anxiety, phobic anxiety, depression, paranoia, notwithstanding other studies, the effect of NF was not significant. This may mean that we need more NF sessions to improve anxiety and mood disorders in this population, since there were at least 40 or 50 sessions of alpha-theta training in studies producing change in anxiety.[23]

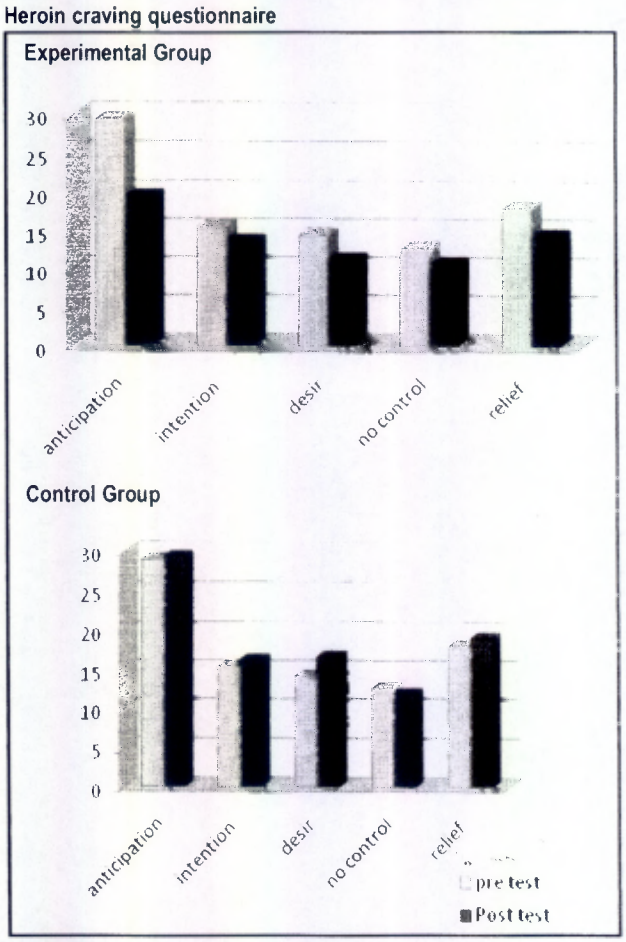

Figure 2.
Pre- and post-test results of HCQ subscales in experimental and control groups

The decrease of craving in the experimental group, compared to patients receiving medication only, was effective in reducing the factors of anticipation positive outcome, desire to use and relief from withdrawal, and was not significant in plan to use and lack of control. The decrease in craving in the NF group is congruent with recent studies that have found a decrease in the rate of abusing and craving and with increased duration of abstinence.[22-24,29,30,37] As studies in substance abuse disorders have shown, the withdrawal state in opium addicts is known to elicit a strong craving for drug, anxiety, nervousness, deficits in inhibitory control, dysphoric motivational state,

Table 6

Descriptive indexes of QEEG in pre- and post-test in experimental and control groups

		Experimental				Control			
		Mean (Amplitude)		Standard Deviations		Mean (Amplitude)		Standard Deviations	
Variables		Pre	Post	Pre	Post	Pre	Post	Pre	Post
Frontal	Delta	17.37	20	9.2	6.9	26.52	37	11.6	17
	Theta	14.16	14.32	17	9	32.5	27.5	25	12
	Alpha	19.2	22.2	16.24	15.8	37.24	31.9	9.6	18.4
	Beta	2.6	2.3	1.68	1.41	2.12	1.63	1.48	.58
	SMR	4.09	5.38	2.03	2.18	5.5	4.27	3.45	1.44
Central	Delta	19.35	16.81	11.39	6.33	36.22	36.53	16.52	13.29
	Theta	14.78	14.88	13.15	8.34	36.67	30.36	23.8	12.26
	Alpha	24.71	24.74	19.5	16.28	6.81	38.21	3.55	19.33
	Beta	4.58	3.72	5.04	4.94	3.44	1.98	3.47	1.04
	SMR	5.62	6.94	2.84	2.93	6.81	4.79	3.5	1.6
Parietal	Delta	19.57	20.85	10.11	13.19	33.91	39.83	20.94	12.49
	Theta	15.89	16.78	12.47	11.55	26.55	34.59	14	17.07
	Alpha	46.59	50.73	38.59	36.82	40	61.79	17	23
	Beta	3.22	2.12	2.02	1.17	2.14	1.93	1.61	1.23
	SMR	6.68	8.17	2.98	5.35	6.98	5.42	3.79	1.95

Note: SMR: Sensory Motor Rhythm

Table 7

Results of MANCOVA of the QEEG subscales in experimental and control groups

Variable		F	Sig.	Eta Squared
Frontal	Delta	10.87	.006**	.38
	Theta	1.92	.18	.12
	Alpha	6.35	.02*	.11
	Beta	5.01	.04*	.27
	SMR	.5	.49	.03
Central	Delta	20.67	.001***	.66
	Theta	3.22	.04*	.09
	Alpha	1.69	.21	.35
	Beta	4.93	.04*	.27
	SMR	1.25	.72	.01
Parietal	Delta	12.45	.004***	.41
	Theta	1.4	.25	.32
	Alpha	7.05	.02*	.18
	Beta	2.85	.11	.18
	SMR	.13	.72	.01

Note: DF= (1, 13)
*P< .05; **P< .01; ***P< .005

and intrusive thoughts related to drugs. [50,51] Also studies have shown the interactions between brain function and the problem of craving in opium addicted patients [52] and the effectiveness of NF to correcting them.[53] NF may decrease craving in two ways: first by improving psychological factors and withdrawal symptoms (as we have seen in the results of this study in SCL-90-R subscales, and second by improving brain function, as reported below.

QEEG Results

Different EEG abnormalities have been described extensively in substance-abuse disorders.[23] In spite of some studies that have shown the persistence of QEEG abnormalities in substance-dependent patient's brain activity, even after abstinence,[54] the present study showed that these abnormalities can be improved by NF treatment. Our results replicate other recent studies.[23,25,29,36]

Studies suggested that the craving and withdrawal syndromes in substance dependence patients are almost all related to abnormalities in alpha and beta, particularly in the parietal and central lobes of the brain [23,52] and also some psychological abnormalities that could be related to delta, theta and SMR functions in frontal, central and parietal area. For example, it has been suggested that delta and theta brainwaves are related to mood and sleep disorders. Also, increased alpha activity may be related to craving especially in the central area along with decreased SMR and beta in frontal and central area that could affect concentration and social function.[23,24] As reported in this study, NF caused a significant increase in beta in central and frontal areas in the experimental group in comparison with the control group, as well as a significant decrease in alpha in parietal and frontal areas.

Researchers and neuropsychologists pose different attitudes toward the mechanisms of action of NF. Cowan[55] suggested that the apparent effectiveness of such training may be due more to the enhanced imprinting of positive awareness suggestions and the feeling of inner empowerment which the Peniston-type script of alpha/theta state seems to encourage. As reviewed by Sterman,[5] variations in alertness and behavioral control following the NF treatment seem to be directly related to specific thalamocortical generator mechanisms. Such variations are evident in distinctive EEG frequency rhythms that emerge over specific topographic regions of the brain. Sterman supposed that neuropathology could alter these rhythms and that EEG feedback training normalized them.

Several researchers suggested that the most efficacious properties of NF may involve teaching the participants to intentionally increase the amplitude and coherent interaction of both their alpha and theta brainwave frequencies in the occipital or the parietal brain locations.[36,56] Fahrion et al.[33] also stated that apparent neurological "normalization" is responsible for shifting the trained client into a physical state of

comfortable awareness. The authors suggested that when chemically dependent persons are aware they often have a neurologically based inability to experience pleasant feelings from simple stimulation.[36] Blum[57] concurred with these ideas and suggested that NF training may activate a neurological-normalizing shift, as explained by his model of the endless quest for neurotransmitter balance.

In more recent approaches, mechanisms by which NF therapy may cause these behavioral changes have been suggested by research in neuronal plasticity.[23] A number of investigators are in essential agreement that ongoing direct experience that evokes persistent neuronal activation alters brain structure and brain functioning.[58-60] A possible linkage between steady-state stimulation induced neuronal activation and neuronal plasticity is the increasing evidence that brain electrical activity regulates the synthesis, secretion and actions of neurotrophins which promote synaptogenesis.[61]

Altogether, based on current and previous studies, NF training acts as a mechanism for the brain to self regulate. In addition, this study showed that this method is more effective than pharmacotherapy alone in promoting mental health. Pharmacotherapy can lead to some improvements in substance-abusing patients, but side effects, instability, and the potential for relapse are some of the main weak-points of using medicine alone with this population.[20] This is in contrast to NF which corrects the brain's function abnormalities and deals with the operational functions of the brain with research confirming the stability of the changes that are facilitated without reports of long-term negative side effects.[22-24] Thus pharmacotherapy can be used to maintain the initial balance between physiological and psychological health in the patient and then NF training can be used to promote longer-lasting health and balance.

The new technological method, hope and motivation were not controlled. An effort was made to keep other factors, such as the connection with the person administering the treatment, from interfering with the process. The use of a placebo group would have strengthened the design of the program.

In future studies, one group should receive NF without pharmacotherapy. A placebo group, receiving sham NF, should be used to control for the effect of therapist contact, as well as the high-technology environment, that is involved in NF treatment. The sham condition will appear identical to the NF in all aspects: equipment, duration, frequency, and videogame choices. The only difference is that the interface module will be pre-programmed to give random feedback rather than contingent on the participant's brainwave power spectrum. By the way it would be possible to control for some variables which can confuse the results. Furthermore, the differences between sham and true NF groups will show the pure effects of NF rather than the effects of prompting, technology and so on. Also, follow-up studies need to assess the stability of changes associated with NF.

In spite of the limitations of the present study, it underlined the efficacy of NF treatment of opioid-dependence. This study showed that neuropsychological treatment can be beneficial.

DISCLOSURE AND CONFLICT OF INTEREST

F. Dehghani Arani, R. Rostami, M. Nostratabadi have no conflicts of interest in relation to this article.

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