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Original Article

Effects of neurofeedback on the short-term memory and continuous attention of patients with moderate traumatic brain injury: A preliminary randomized controlled clinical trial

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ABSTRACT

Purpose: There are some studies which showed neurofeedback therapy (NFT) can be effective in clients with traumatic brain injury (TBI) history. However, randomized controlled clinical trials are still needed for evaluation of this treatment as a standard option. This preliminary study was aimed to evaluate the effect of NFT on continuous attention (CA) and short-term memory (STM) of clients with moderate TBI using a randomized controlled clinical trial (RCT).

Methods: In this preliminary RCT, seventeen eligible patients with moderate TBI were randomly allocated in two intervention and control groups. All the patients were evaluated for CA and STM using the visual continuous attention test and Wechsler memory scale-4th edition (WMS-IV) test, respectively, both at the time of inclusion to the project and four weeks later. The intervention group participated in 20 sessions of NFT through the first four weeks. Conversely, the control group participated in the same NF sessions from the fifth week to eighth week of the project.

Results: Eight subjects in the intervention group and five subjects in the control group completed the study. The mean and standard deviation of participants' age were (26.75 ± 15.16) years and (27.60 ± 8.17) years in experiment and control groups, respectively. All of the subjects were male. No significant improvement was observed in any variables of the visual continuous attention test and WMS-IV test between two groups ($p \geq 0.05$).

Conclusion: Based on our literature review, it seems that our study is the only study performed on the effect of NFT on TBI patients with control group. NFT has no effect on CA and STM in patients with moderate TBI. More RCTs with large sample sizes, more sessions of treatment, longer time of follow-up and different protocols are recommended.

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Introduction

Traumatic brain injury (TBI) means an injury to the brain that is caused by an external physical force. It is well known that TBI is an

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important cause of mortality and morbidity and it is reported that each year about 1.7 million people sustain a TBI in USA. Some of them die (about 50,000) and some other experience long-term disability (80,000 to 90,000).^{1–3} The severity of TBI can be categorized based on the Glasgow coma scale (GCS) at the time of injury as follows: mild (13–15), moderate (9–12) and severe (<9).⁴ TBI usually affect the brain function such as cognitive status, executive function, memory, data processing, language skills and

attention.⁵ It has heterogeneous aspects and based on the injury location and type. It can have different presentations. Hence it is considered as a difficult one to treat.⁶

The brain plasticity could help it in rehabilitation phase to restore its normal function after any trauma or disease. But the amount of this ability is poorly understood. Some studies approved that neurofeedback therapy (NFT) can promote neuroplasticity.⁷ In the method of neurofeedback (NF), as a non-pharmacological intervention, the feedback to brain waves which are representative of subconscious neural activity can be observed by the client and then he/she will be able to control and change them.^{8,9} There are some evidences that show NFT can be useful in some other diseases like Obsessive-compulsive disorder,¹⁰ attention-deficit/hyperactivity disorder¹¹ and also refractory epilepsy.¹² There are also some published studies about the effect of NFT on patients with TBI. Surmeli in 2007 investigated the effect of NFT on 24 patients with mild TBI and reported that NFT can result in significant improvement in test of variables of attention, beck depression inventory and minnesota multiphasic personality inventory.¹³ In a study in 2014, with evaluation of two patients with moderate head injury and without control group, it is reported that electroencephalogram biofeedback can lead to increase the cognitive scores and improve the concussion symptoms and finally concluded that NFT can be effective on the changes in the structural and functional connectivity among patients with moderate TBI.¹⁴

Although these published papers reported a positive effect of NFT on the TBI patients, we have not enough data about the standard treatment protocol with NF, and literature still needs more original studies like randomized controlled clinical trial to suggest NF as a treatment option among patients with TBI regarding the two following functions of cognitive status: short-term memory (STM) and continuous attention (CA).⁵

In this preliminary study, we tried to evaluate the effect of NFT on CA and STM of patients with moderate TBI using a randomized controlled clinical trial.

Materials and methods

Study design and subjects

All the subjects with the history of TBI were included in our RCT if they met following criteria: the patients' GCS should be nine through thirteen at the time of admitting in the emergency department; the patients' age should be between 15 and 60 years and there should be no history of co-morbid disease, psychiatric or mental disorders or substance abuse which shows patients' state of health. 22 patients with moderate TBI who were admitted at the two university hospitals of Sina or Shariati Hospitals (Tehran, IR Iran) were assessed for eligibility by the neurosurgeons participating in this project. Patients with trauma event more than six weeks and patients with Afghani nationality were excluded. Considering current Afghani immigrants' unstable situation in our country so that we were not sure that they could continue their participation in our prospective study, we excluded them. Seventeen patients enrolled randomly to intervention or control group. All patients were injured through traumatic events in Tehran City and had traumatic injury to their head with GCS between nine and thirteen. Due to lost to follow-up, finally eight subjects in intervention group and five in control group were analyzed. The clients paid nothing for NFT and some of the costs related to their transportation were paid.

Intervention

The patients in the intervention group participated in 20 sessions of NFT through the first four weeks, five sessions in each

week. Conversely, the patients in the control group participated in the same NF sessions from the fifth week to eighth week of the project. For considering ethical issues, we did not prevent patients from getting routine cares and medicines for traumatic injury and patients in both groups (experiment and control) were getting related medicine based on prescription of their physicians.

The NFT was performed at the Atieh Clinical Neuroscience Center in Tehran, Iran. Subjects seated in front of a monitor with open eyes and performed the task determined by neurofeedback biograph software which was produced by Thought Technology Company. Our NFT protocols were beta and alpha coherence methods (two-channel). In coherence of beta band, electrodes were positioned on the left hemisphere, pre-frontal and temporal regions (FP1-T3) and the purpose of increasing beta waves was improving the concentration while keeping calm. In coherence of alpha band, electrodes were positioned on the central and occipital regions (Cz-Oz) and the purpose of increasing alpha waves was preparing feeling of relaxation for subjects while performing their alpha task. Each protocol was performed in 25 min and the total time for each session was 50 min. If a participant used any medicine prescribed by their physicians, we would not change them during study.

Measurements

Wechsler memory scale-4th edition

We used the Wechsler memory scale-4th edition (WMS-IV) for evaluation of short-term memory. This scale consists of eight subtests including general information, memory quotient, orientation, mind control, learning associations, logical memory, visual memory and repeat numbers.

DAUF

We used the DAUF test, a continuous attention computer based test, for measuring the long-term attention and concentration performance. In this test, the participants watch rows of triangles on the computer screen that are presented under time-critical conditions. The tips of each triangle can point either up or down. The participant should press the reaction button when a previously determined triangles points down. There are three main items in this test that are evaluated: the number of correct and incorrect responses and the mean reaction time.

Outcome assessment

The patients in both intervention and control groups were evaluated for CA using DAUF and short-term memory using WMS, respectively. The DAUF and WMS were administered at the baseline time and then four weeks after the beginning of the study. Accordingly, the subjects in the experiment group were evaluated before and after 20 sessions of NF while the patients in control group were evaluated at the baseline and the fourth week of inclusion without any intervention. A questionnaire was designed to record related data to each participant. We also calculated the mean difference for aforementioned variables at the baseline and the fourth week of inclusion and compared them between control and experiment groups.

Statistical analysis

Quantitative and qualitative variables were presented as mean \pm standard deviation (SD) and frequency (percentage), respectively. Independent *t*-test and paired *t*-test were used for comparison of each variable between two groups of the study and also before and after the intervention. Categorical variables also

were analyzed by Chi square test. *p* values less than 0.05 were considered statistically significant.

Ethics and consent

The project was approved by the Iranian Registry of Clinical Trials and was assigned as IRCT201111085024N2 serial number. After explaining the protocol of study for each participant, all of them or their parent (for patents with age of between 15 and 18) signed their written informed consent for participation to this project.

Results

Demographic data

The mean and SD of participants' age in experiment and control groups were (26.75 ± 15.16) years and (27.60 ± 8.17) years, respectively (*p* = 0.91). All participants were male.

WMS-IV

Each variable of WMS-IV was evaluated at the baseline and the fourth week of inclusion based on the each groups of study (Table 1).

Also, the mean differences at the baseline and the fourth week of inclusion for each variable were calculated and then compared between two groups (Table 2). Based on these two tables, none of the mean differences were statistically significant (*p* < 0.05).

DAUF

The mean number of correct answers, incorrect answers and mean reaction time were compared at the baseline and the fourth week of inclusion based on each group of the study (Figs. 1–3). Only mean number of correct answers in control group (*p* = 0.04) and mean number of incorrect answers in experiment group (*p* = 0.04) increased significantly at the fourth week. The mean difference (SD) for the number of correct answers for control and experiment groups were 10 (7.74) and –1.14 (9.15), respectively, which showed no significant difference (*p* = 0.052). Also the mean difference (SD) for number of incorrect answers for control and experiment groups were 36.8 (25.4) and –15.28 (139.15), respectively, which showed no significant difference (*p* = 0.30). Furthermore, the mean

Table 1
Comparison of the WMS-IV variables at the baseline and the fourth week of inclusion between the two groups.

Variable	Group	Mean (SD) at the baseline	Mean (SD) at the fourth week	<i>p</i> value
Memory quotient	Experiment	84.83 (23.02)	87.66 (16.64)	0.57
	Control	79.40 (13.42)	88.60 (23.07)	0.13
General information	Experiment	3.75 (1.38)	4.50 (1.30)	0.11
	Control	4.20 (1.78)	4.80 (2.16)	0.52
Orientation	Experiment	3.75 (1.58)	4.25 (0.88)	0.22
	Control	4.0 (1.22)	4.20 (1.78)	0.62
Learning association	Experiment	12.75 (5.46)	15 (4.65)	0.06
	Control	11.60 (3.59)	15.60 (4.56)	0.01
Mind control	Experiment	3.87 (3.31)	3.75 (2.60)	0.85
	Control	4.80 (2.28)	4.80 (2.04)	1
Logical memory	Experiment	6.68 (2.75)	2.75 (0.97)	0.48
	Control	6.0 (2.97)	4.18 (1.87)	1
Repeat numbers	Experiment	8.62 (1.92)	8.50 (1.51)	0.80
	Control	8.20 (0.44)	8.0 (2.00)	0.86
Visual memory	Experiment	7.12 (3.64)	3.58 (1.26)	0.31
	Control	9.60 (1.51)	2.16 (0.96)	0.46

Table 2

Comparison of the improvement in the WMS-IV variables at the baseline and the fourth week of inclusion between the two groups.

Variable	Group	Mean difference (SD) at the baseline and the fourth week	<i>p</i> value
Memory quotient	Experiment	2.83 (11.50)	0.38
	Control	9.20 (11.08)	
General information	Experiment	0.75 (1.16)	0.86
	Control	0.6 (1.94)	
Orientation	Experiment	0.50 (1.06)	0.60
	Control	0.20 (0.83)	
Learning association	Experiment	2.25 (2.95)	0.28
	Control	4 (2.26)	
Mind control	Experiment	–012 (1.88)	0.90
	Control	0 (1.87)	
Logical memory	Experiment	0.56 (2.14)	0.61
	Control	0 (1.45)	
Repeat numbers	Experiment	–0.12 (1.35)	0.94
	Control	–0.20 (2.38)	
Visual memory	Experiment	1.37 (3.62)	0.61
	Control	0.60 (1.67)	

difference (SD) for reaction time in control and experiment groups were 11.2 (12.19) and 1.85 (16.05), respectively (*p* = 0.43, Table 3).

Discussion

Our results showed that 20 sessions of NFT cannot be effective in rehabilitation of brain function among patients with TBI regarding CA and STM. Although reaction time in CA test (DAUF) was reduced after NFT, the number of correct answers was reduced. On the other hand, considering WMS-IV test in both groups, memory quotient, general information, orientation and learning control were increased and logical memory, repeat numbers and visual memory were reduced. Mind control in experiment group was reduced and no change in control group. However, all of these changes in DAUF and WMS-IV tests were nonsignificant. Based on WMS-IV test, only learning association in control group was increased from baseline to fourth week of inclusion (*p* = 0.01). However, when we compared the improvement between the two groups, it was nonsignificant (*p* = 0.28, Table 2).

TBI is considered as a silent epidemic and major public health concern. It is an important treat for quality of life, disability and death.¹⁵ The annual incidence rate of TBI in Tehran, Capital of Iran, is 15.3–144/100,000 population.^{16,17} On the other hand head injury in 30% of cases can lead to skull fractures.¹⁸ It is reported that among urban population of Iran, the most common mechanism of skull fracture is related to motor vehicle crash.¹⁹ Head injury also can be associated with decreasing intelligence quotient several months after the injury.^{20,21}

Brain damages due to TBI produces changes in cognitive state, memory and data processing need combination methods of management.²² Furthermore, there is a report indicating useful effects of electromagnetic energy stimulation of brainwave activity on reducing post-traumatic headache among persons in a military service.²³

There are some case studies that evaluate the effect of NFT on the brain functions of patients with TBI. In contrast with our results, Reddy et al in 2009 in a single case study evaluated the effect of 20 sessions of NFT on a patient with mild head injury. They compared neuropsychological profile of this patient pre- and post-NFT. Finally they showed that NFT was effective in improvement of both verbal and visual learning memory and suggested NFT as a method for rehabilitation of patients with TBI.²⁴ Furthermore NFT has been reported as a method for minimal to significant enhancement of

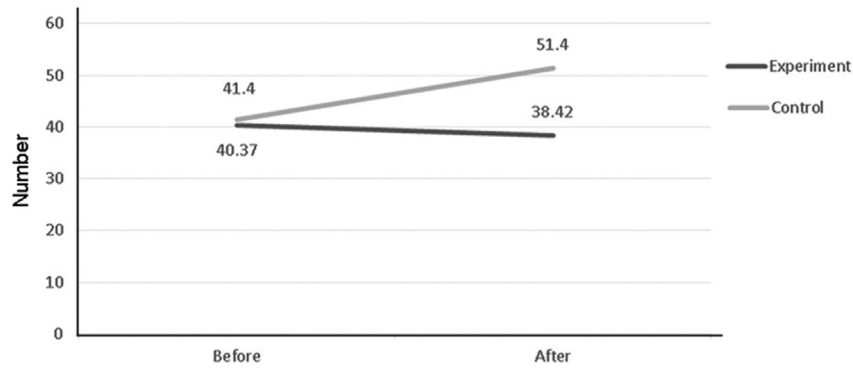


Fig. 1. Comparing the mean number of correct answers of DAUF test at the baseline and the fourth week of inclusion in the two groups.

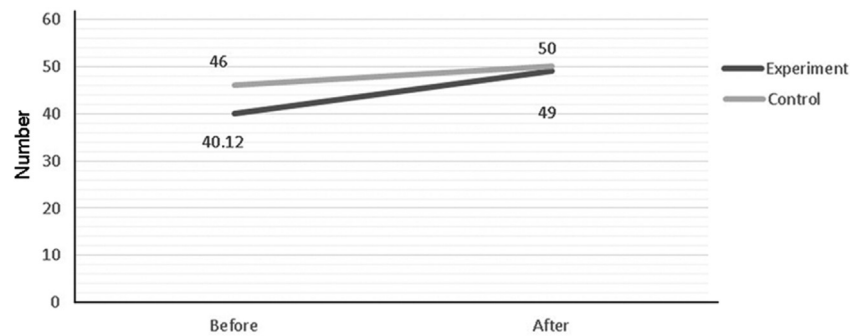


Fig. 2. Comparing the mean number of incorrect answers of DAUF test at the baseline and the fourth week of inclusion in the two groups.

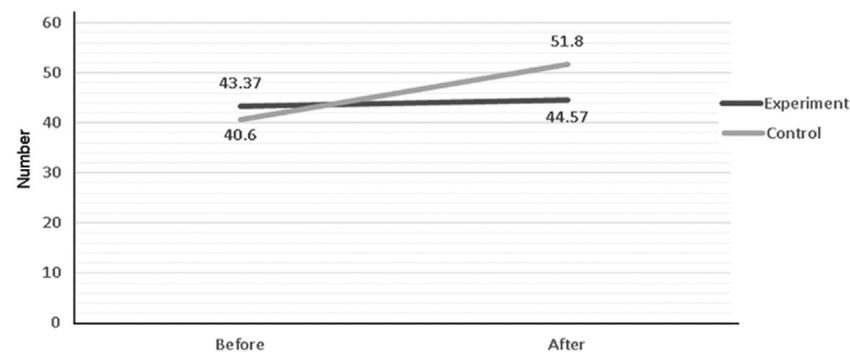


Fig. 3. Comparing the mean reaction time of DAUF test at the baseline and the fourth week of inclusion in the two groups.

Table 3

Comparison of the improvement in the DAUF variables at the baseline and the fourth week of inclusion between the two groups.

Variable	Group	Mean difference (SD) at the baseline and the fourth week	p value
Mean number of correct answers	Experiment	-1.14 (7.74)	0.052
	Control	10 (7.74)	
Mean reaction time	Experiment	1.85 (16.05)	0.430
	Control	11.2 (12.19)	
Mean number of incorrect answer	Experiment	-15.28 (139.15)	0.300
	Control	36.8 (25.4)	

several functional tasks in a brain tumor patient with simultaneous TBI.²⁵ Authors treated the patient with 40 sessions of NFT. Their study suffered from lack of control group.

NFT has also used for management of concussion symptoms and improving quality of life in patients with TBI. It is reported that NFT

can have significant effects on the functional and structural connectivity in young patients with moderate TBI.¹⁴ In an interventional study in 2014, 60 patients with TBI have been evaluated regarding the effect of NFT on improving their quality of life. Patients in intervention group (n = 30) received 20 sessions of NFT during four weeks while there was 30 patients in wait-list group. This project showed that NFT could have significant effect on the improving quality of life in patients with TBI. Therefore authors of this project suggested that NFT can be used in treatment approaches of TBI patients in improving quality of life.¹⁵

Despite these positive points regarding useful effects of NFT on different aspects of patients with TBI, we could not observe any effect of NFT for improving of continuous attention and short-term memory loss in TBI patients. We think that the whole program including its hardware, software and human resources at the Atieh Clinical Neuroscience Center should be re-evaluated. Also our treatment protocol for neurofeedback and the number of its

sessions which was detailed in the method section may need reconsideration for future studies. Moreover, since the effect of NFT can be observed after a relative long period of time (more follow-up of patients), other researchers had better observe the conditions of their patients for a long time.

Limitations

Our main limitation was about the sample size of this study. Other research with adequate sample sizes may conclude significant relationships among the evaluated variables. Second, we were not able to eliminate or change any medicine prescribed to the patients by their physicians and our results might be affected by co-intervention factors.

Conclusion

We concluded that NFT has no effect on CA and STM of the patients with moderate TBI. However, we believe that for making an exact decision about use of NFT in TBI patients, more research projects with adequate sample sizes, longer time of treatment and follow-up and different protocols should be done.

Conflicts of interest

Dr. Reza Rostami, the head of the Atieh Clinical Neuroscience Center, had conflict of interest in this project.

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