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Der Pharmacia Lettre, 2017, 9 [4]:179-185
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**The Effects of Transcranial Direct Current Stimulation (TDCS) on Reducing
the Desire for Methadone among Addicts under Treatment in Taleghani
Hospital of Ilam, Iran 2016**

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ABSTRACT

Introduction: At the moment, abusing illicit drugs and addiction is considered as one of great challenges all over the world. The desire stage in the addiction cycle is assumed to be a key element in abuse relapse. The main objective of the current study is to investigate the effects of tDCS (Transcranial Direct Current Stimulation) on addicts under treatment in Taleghani Hospital of Ilam 2016.

Materials and Methods: The current study is a semi-experimental study. 40 people are divided into two groups, an experimental group of 20 individuals and a control group of 20 participants in order to investigate them. The experimental group will go through 20 sessions of Frontal 3 Anodal electrode stimulus and cathodal right shoulder electrode stimulus with a 48-hour distance between the sessions. Moreover, the control group will go through a

fictional transcranial electric stimulus on the skull. In order to analyze the obtained data, SPSS software application version 16 is used.

Results: *The results of the study show that the highest frequency is seen among people under 35 years of age and the most common used illicit substance is opium. Moreover, assessing the induced desire in pre-test and post-test groups indicates that the highest average difference is related to the effects of tDCS in Anodal Frontal 3 stimulus. (P=0.0001)*

Conclusion: *The results show that Anodal Frontal 3 stimulus will reduce methadone craving significantly compared to cathodal right shoulder stimulus. It is recommended that the tDCS method be used as a complementary treatment method for reducing drug cravings.*

Keywords: *Transcranial Direct Current Stimulation (tDCS), Methadone Addicts, Iran, Ilam.*

INTRODUCTION

Addiction means depending on drugs. These drugs include all the substances that change the functionality of the brain in the form of excitement, depression, abnormal behavior, weakness and lethargy, anger, false energy, and disruptions of judgment and understanding. Addiction is a phenomenon that destroys the individual, the family, and the society and it is considered as one of the most damaging illnesses and social complications. Accordingly, after nuclear crisis, population increase, and environmental pollution, it is considered the fourth crisis in the world [1]. Addiction is a complex illness which is characterized by compulsions, irresistible temptation, substance searching behaviors, and continuous abuse even when it has many negative consequences for the individual. Continuous drug abuse over time and the long-term poisonous effects of its usage on the functionality of the brain will lead to a wide range of negative behavioral, psychological, social, and physiological symptoms, which prevent normal behavior and natural functionality of addicts in the family, in working environment, and on the broader social stage. The trend of drug abuse has changed in three main aspects compared to the past. On the one hand, nowadays, the average age of drug addicts has decreased significantly compared to previous years. On the other hand, the abuse pattern of using opium in the form of smoking is shifting towards injection of heroin. Statistics indicate the increasing number of addicts in our society. Nowadays, drug abuse is considered one of the main social complications in a way that it not only endangers the health of the individual and the society, it also paves the way or psychological and ethical degeneration [2, 3].

This is while the addiction age is decreased and women are exposed to higher levels of danger. Moreover, the health problems related to addiction, particularly contracting HIV, are also of great concern [4]. Unfortunately, the increase in the level of drug abuse in today's society has even got people with higher education and higher status involved [5]. Treatment of addiction can be carried out through clinical treatments or outpatient treatments. Due to utilizing fewer numbers of equipment and requiring lesser investment as well as better and easier acceptance on the behalf of patients, outpatient treatments can be more cost-effective and

useful, particularly when many studies indicate their effectiveness [6]. In European countries and the USA, the outpatient treatment of drug abuse is done through three methods of abstinence, methadone maintenance, and harm reduction [7]. Usually, people who stop abusing drugs will relapse in a few years. The core of this relapse is the phenomenon of craving or the desire to abuse, which can continue for years after stopping substance abuse. Therefore, reducing cravings can have a significant importance in controlling the problem of drug abuse. Methadone is used as a drug to treat addicts; however, it is itself an addictive drug which can create complications for the addicts. Among the most common complications of using methadone we can mention skin irritation, headaches, depression, paleness, sweating, palpitations and delays in normal urination patterns, constipation, and respiratory problems [4, 9].

Transcranial direct current stimulation (tDCS) is considered one of the secure treatments methods with the lowest number of side effects in a way that there hasn't been any side effects reported so far. Mild side effects which are rarely reported include very mild irritation at the electrode site, fatigue, and insomnia, which are resolved after 48 hours. Transcranial direct current stimulation (tDCS) can adjust the perception of substance cravings among drug addicts by changing the cortical excitability in the posterior-frontal lobe in the forehead. In this study, the effects of tDCS methods in the brain on reducing substance cravings among methadone addicted individuals visiting Taleghani Hospital in Ilam in 2016 are investigated.

MATERIALS AND METHODS

This study is a semi-experimental study where the frequency distribution of participants' answers to the visual Desires for Drug Questionnaire (DDQ) are analyzed based on psychometric measures. The statistical population of this study includes individuals addicted to methadone in Ilam City who visited Taleghani Hospital of Ilam for treating methadone abuse and who are under treatment at the moment. These individuals have been treated for at least one week, and during this week, they haven't used any effective drugs related to the side effects of stopping methadone abuse or any other illicit drug. In order to select the sample of the study, 40 male patients visiting the Therapeutic Center of Ilam City were selected randomly and their consent and demographic information were obtained. The conditions for entering the study included methadone abuse or dependency on methadone based on the diagnostic criteria of Diagnostic Statistical Manual (DSM-V), diagnosed by a physician, at least for 12 months, along with avoiding the consumption of any effective drugs for at least one week, and responsiveness to induced consumption symptoms. Moreover, the patients shouldn't fit any criteria for being omitted from the study, which included any history of epilepsy, brain surgery, tumors, and any effective blow to the head which resulted in unconsciousness. In this study the Active dose Iontophoresis device of Active Tek Company was used. At the first stage of the treatments, direct current is obtained from a battery-based electric current generation device (tDCS) and transferred to a pair of 5×7 electrodes (35 square centimeters). The electrodes are made of carbon and they were wrapped inside a sponge cover with 10% NaCl solution. The anodal electrode would be placed on the posterior-lateral area above the left eye and the cathodal electrode would be placed on

the right shoulder, then, a 2mA current is passed through the brain in 20 minutes during 20 sessions [7]. In the next stage, the control group received a fake brain electric stimulation on the skull. In order to carry out the fake stimulations, the placements of anodal and cathodal electrodes were real. During 30 seconds, the current generator increases the current to 2 mA and then, it gradually decreases it to 0 mA in 30 seconds and the device will turn off at that point. However, the electrodes are attached to the participant's head for 20 minutes during 20 sessions, while they are not aware of the fact that the device has turned off. In order to increase the accuracy level of research findings, the computerized cue-induced craving consumption (CCIC) test with a reliability of 0.85 to 0.88 with the Cronbach's Alpha value of 0.92 as well as the Desires for Drug Questionnaire (DDQ) for methadone with the reliability of 0.73 to 0.77, with the Cronbach's Alpha value of 0.71, were also used. In both sessions, before and after brain stimulation, cue-induced craving consumption was measured. After the required data were obtained, they were analyzed in SPSS software application version 16.

RESULTS

The results obtained from demographic information show that the highest frequency is related to the age range of lower than 35 years of age with 35 percent of the participants, and the lowest frequency is related to people with an age higher than 50 years with 11 percent (Table 1).

Table-1: Age Distribution of Participants

| Age Mean | Frequency | percent |
|------------------------|-----------|---------|
| below 35 years | 7 | 35 |
| between 35 to 40 years | 3.2 | 16 |
| between 40 to 45 years | 4 | 20 |
| between 45 to 50 years | 3.6 | 18 |
| More 50 years | 2.2 | 11 |
| Total | 20 | 100 |

The information related to the educational level of participants show that the highest frequency of participants has a primary education degree with 35 percent and the lowest frequency of participants have a secondary school education level with 5 percent. The frequency of marital status shows that 70 percent of the participants are single and only 30 percent of the participants are married. The results show that the most common drug used by the participants is opium which is used by 85 percent of the participants, while 15 percent of the participants use heroin. The information for the amount of consumption shows that the highest frequency, 50 percent, of the participants use more than 2 grams on a daily basis, while the lowest frequency, 20 percent, of the participants use less than 1 gram of drugs on a daily basis (Table 2). Moreover, among the participants, 80 percent

had a history of quitting drugs. Pre-test and post-test data of cue-induced cravings in Anodal Frontal 3 stimulations and Cathodal Right Shoulder stimulations show that the highest level of average difference between pre-test and post-test for cue-induced craving measurements is for the Anodal Frontal 3 stimulations ($P < 0.0001$) (Table 3).

Table-2: The Distribution of Consumption Amount among Participants

| Dosage | Frequency | percent |
|----------------------|-----------|---------|
| Under 1 gram | 4 | 20 |
| Between 1 to 2 grams | 6 | 30 |
| More than 2 grams | 10 | 50 |
| Total | 20 | 100 |

Table-3: Descriptive Data for Cue-Induced Craving Pre-Test and Post-Test in Cathodal and Anodal Frontal 3 Stimulations for the Pre-Test Experimental and Control Groups.

| | Variable | Average | Standard deviation | Minimum | Maximum |
|-----------|-------------------------|---------|--------------------|---------|---------|
| Pre-Test | Cathodal right shoulder | 24/55 | 21/648 | 5 | 100 |
| | Frontal 3 Anodal | 25/70 | 9/453 | 13 | 45 |
| Post-Test | Cathodal right shoulder | 20/40 | 23/120 | 0 | 100 |
| | Frontal 3 Anodal | 17/70 | 8/034 | 7 | 32 |

DISCUSSION

The current study is a semi-experimental study. The statistical population of this study includes individuals with a history of methadone abuse, among which 20 participants were selected as the control group and 20 participants were selected as an experimental group. In order to gather the required data for the study, visual and computerized questionnaires for measuring the levels of desire and craving were utilized. tDCS is a non-invasive and safe treatment method where the brain is stimulated using electrodes placed on certain areas of the subject's head. A very weak continuous and direct electrical current is sent to the target calls. In this way, the flexibility of brain neurons is stimulated. One of the most important characteristics of tDCS can be considered its ability for creating cortical changes after the stimulations are stopped. The effects of the stimulation and the continuous nature of these changes depend on the duration of the stimulation, the intensity of the stimulation, as well as the

number of the sessions and the brain damage location [10, 11]. tDCS can be effective in improving sensory disorders, memory disorders, speech impairments, various headaches, and migraines [12]. In fact, the movement of the current through brain areas responsible for controlling heart rate or breathing in the brain stem can be theoretically dangerous. For instance, in a study carried out by Monai et al. (2016) where the reference electrode was placed on the legs of the patient and other electrodes were placed on the prefrontal cortex, one case of nausea and respiratory complications was reported, which was alleviated after the current was stopped [13]. In recent years, there have been many studies on the effectiveness of tDCS on controlling the desire to consume drugs among addicts, opening great opportunities for resolving this problem for addiction therapists. Nevertheless, the best way to treat drug abuse patients seems to be a combinatory method.

In this study, the effects of tDCS on reducing the desire to consume methadone among addicts visiting the treatment centers in Ilam City were evaluated and investigated. While the findings of the study show that twenty minutes of anodal stimulation for the posterior-lateral left area of the forehead can reduce the desire to abuse methadone, reducing the average desire in the experimental group from 25/70 to 17/70 after the stimulation ($P=0.0001$), it should be noted that this reduction can be temporary. Therefore, repeating the stimulation can have a more long-term effect. Considering the fact that no single method can be completely effective in treating drug abuse and drug dependence, the best approach is the one which influences various aspects simultaneously and one that doesn't have the complications of previous methods such as relapse, superficiality, and side effects. In fact, the results obtained in this study show that there is a significant relationship between utilizing the tDCS method and the cognitive brain functions of individuals who are dependent on methadone ($P=0.0001$), which is confirmed by other studies [14]. It seems that despite various significant complications related to drug abuse, people still continue to consume these illicit drugs. Moreover, it is suggested that drug abuse in people with intense disorders will create a fundamental change in brain connections, which can stay with the person even after the detoxification [15]. Based on the clinical observations, it is suggested that intense and chronic abuse of psychoactive drugs can interfere with the cognitive functions and capability of individuals [16].

In fact, various studies have shown that long-term drug abuse is related to high levels of neuropsychological complications [17]. Darke et al. (2000) compare cognitive impairments between two groups, a group of addicts under treatment with methadone maintenance and a group of ordinary individuals. It is reported that individuals under treatment with methadone had a weaker performance in Wisconsin Card Sorting Test, compared to ordinary individuals [18]. Yan et al. (2013) argue that heroin-addicted individuals have a lower performance regarding working memory tasks compared to individuals in the control group [19]. So far, there have been various studies on the effects of tDCS on brain functionality. For instance, Borgheresi et al. (2013) evaluated the effects of short-term physiotherapy along with tDCS on walking difficulties in Parkinson's patients and reported that compared to the control group, patients receiving tDCS had a more significant improvement [20]. Furthermore, in other studies, the positive effects of tDCS on various chronic pains and the improvement of skillful functionalities have been proven [21, 22].

CONCLUSION

The results obtained from this study show that Anodal Frontal 3 stimulations significantly reduce the desire to abuse methadone in methadone-addicted individuals. It is recommended that this method be used as a complementary treatment method for reducing the desire to abuse illicit drugs in rehabilitation centers.