Basic and Clinical NEUROSCIENCE

November & December 2022 Volume 13, Number 6

Research Paper

Impact of Transcranial Direct Current Stimulation on Ultra-Rapid Opioid Detoxification Outcome

Hamid Mirhosseini[1], Masoud Kargar[2*], Michael Nitsche[3], Mohammad Ali Sheikhi Abarghouei[4], Mohammad Ali Nazari[5], Ghasem Dastjerdi[1]

1. Department of Psychiatry, Research Center of Addiction and Behavioral Sciences, Shahid Sadoughi University of Medical Sciences, Yazd, Iran.
2. Department of Anesthesia, Faculty of Allied Medical Sciences, Shahid Sadoughi University of Medical Sciences, Yazd, Iran.
3. Department of Neurology, University Medical Hospital Bergmannsheil, Bochum, Germany. Leibniz Research Centre for Working Environment and Human Factors, Dortmund, Germany.
4. Department of Neuroscience, Faculty of Advanced Technologies in Medicine, Iran University of Medical Sciences, Tehran, Iran
5. Department of Psychology, Neuroscience laboratory, University of Tabriz, Tabriz, Iran.

Use your device to scan and read the article online

Citation Mirhosseini, H., Kargar, M., Nitsche, M., Sheikhi Abarghouei, M. A., Nazari, M. A., and Dastjerdi, G. (2022). Impact of Transcranial Direct Current Stimulation on Ultra-Rapid Opioid Detoxification Outcome. *Basic and Clinical Neuroscience*, *13*(6), 799-806. http://dx.doi.org/10.32598/bcn.2021.1573.1

http://dx.doi.org/10.32598/bcn.2021.1573.1

Article info:
Received: 03 Nov 2018
First Revision: 18 Jul 2020
Accepted: 25 Aug 2020
Available Online: 01 Nov 2022

Keywords:
Craving, Transcranial direct current stimulation, Substance withdrawal syndrome, Opioid-related disorders

ABSTRACT

Introduction: The persistence of post-detoxification problems in drug addiction is one of the disadvantages of the ultra-rapid opioid detoxification (UROD) method. Transcranial direct current stimulation (tDCS) has been introduced in experimental addiction treatment for some years. Results of pilot studies suggest that it might be a promising method for addiction treatment. This study explores the adjunctive application of tDCS during treating opiate addiction with the UROD approach.

Methods: This double-blind, sham-controlled clinical trial was carried out on patients with substance abuse admitted to the Bahman Clinic of Yazd City in Iran (from March to September 2014). Forty participants were randomly allocated to treatment and control groups. Two sessions of tDCS (real or sham) over dorsolateral prefrontal cortices (DLPFC) were applied, accompanied by UROD. Withdrawal symptoms and craving were assessed by the drug desire questionnaire and objective opiate withdrawal scale before UROD and for the 24-hour interval after.

Results: Transcranial direct current stimulation optimized the opiate addiction treatment through craving and withdrawal syndrome alleviation.

Conclusion: The study results indicate that prefrontal tDCS may promote the efficacy of the UROD method in opioid addiction.

*** Corresponding Author:**
Masoud Kargar, MSc.
Address: *Department of Anesthesia, Faculty of Allied Medical Sciences, Shahid Sadoughi University of Medical Sciences, Yazd, Iran.*
Tel: *+98 (353) 6238626*
E-mail: *masoudkargar1985@gmail.com*

Highlights

- Patients did not report side effects of transcranial direct current stimulation (tDCS) except for a tolerable tingling sensation under the electrodes reported by 5 patients.
- The study's results support the hypothesis that tDCS reduces craving and withdrawal symptoms caused by treating opioid addiction with ultra-rapid opioid detoxification (UROD).
- The results of this study deliver evidence that prefrontal tDCS may promote the tolerability and efficacy of treatment approaches for opioid addiction using UROD.
- tDCS reduced withdrawal symptoms for a relatively short time after anxiety-reducing and a possible dopamine-increasing effect, which have been proposed in other studies.

Plain Language Summary

This study was conducted on drug abuse patients. We introduced an adjunctive treatment for drug abuse. Craving has a critical role in addiction. It is a powerful desire to consume drug. It is a significant factor in relapsing or continuing drug abuse after withdrawal from consuming. Craving is imprecisely defined and is very difficult to measure. Different treatments like transcranial direct current stimulation (tDCS) have been introduced to overcome the craving. It is a method to stimulate the brain using constant and low direct current delivered via electrodes on the head. This study explores the adjunctive application of tDCS during treating opiate addiction with the ultra-rapid opioid detoxification approach. We found that tDCS may promote the tolerability and efficacy of treatment approaches for opioid addiction using ultra-rapid opioid detoxification.

1. Background

Drug abuse highly threatens the health of societies. Addicts are prone to fatal infections and pregnancy complications, as well as other drug-related health problems (Mark, et al., 2001). Different approaches to drug detoxification exist; however, their effectiveness is limited (Amato et al., 2008). One of the methods developed in the 1990s is ultra-rapid opiate detoxification (UROD). This detoxification includes the application of a large dosage of opiate antagonists under general anesthesia. Even though this method has numerous advocates, disadvantages are possible side effects after treatment, which can last 3 to 10 weeks. Besides, a relatively high relapse rate limits the efficacy of this treatment (Safari, Mottaghi, Malek, & Salimi, 2010). Anxiety and mood disorders are relevant for this high relapse rate and further limit the applicability and value of UORD (Amato et al., 2008).

Hypofunction of the dorsolateral prefrontal cortices (DLPFC) with regard to its contribution to the reward system in addiction plays a critical role in craving illicit drugs (Boggio et al., 2008). Stimulation of this area might thus be useful for the enhancement of dopamine-related physiological processes and alleviation of craving (Fregni et al., 2008). Transcranial direct current stimulation (tDCS) is a non-invasive procedure that delivers a weak electrical direct current to the brain for several minutes. Anodal stimulation increases cortical excitability, while cathodal tDCS has antagonistic effects. Stimulation for some minutes results in likewise directed neuroplastic after-effects (Lupi et al.). Indeed, drug craving is reduced by prefrontal tDCS in methamphetamine abuse, but also other drug addictions (Dastjerdi & Mohammadi, 2015; Sauvaget et al., 2015; Martinotti et al., 2019; Taremian et al., 2019).

Besides its presumed effect on craving, anodal stimulation of the prefrontal cortex might be useful in reducing mood and anxiety problems (Borckardt et al., 2013). tDCS might furthermore be useful for the reduction of detoxification-related pain symptoms. It has been used as an additional treatment for reducing post-operative pain and, indeed, reduced opioid consumption in these patients (Bashir & Yoo, 2016). Improving cognitive performance due to tDCS may be another useful aspect of treating these patients (Conti & Nakamura-Palacios). Because of these features of tDCS, we aimed to explore its putative effect on treating opioid addiction via the UROD method.

2. Materials and Methods

Study participants

This double-blinded, sham-controlled clinical trial was conducted on 40 opiate-dependent male patients, as defined by the Diagnostic and Statistical Manual of Mental Disorders (4th edition). The sample size was determined based on similar previously conducted studies (Gandiga, Hummel, & Cohen, 2006).

The inclusion criteria were male subjects aged between 18 and 40 years, the first attempt for treatment, the abuse of heroin, opium, opium extract (shire in Persian), or opium and shire combination via inhalation. Subjects with a history of current or past physical, neurological, or psychiatric disorders or contra-indications for tDCS or anesthesia were excluded from the study. Patients were randomly allocated to the experimental or control group (20 subjects in each group, Mean±SD age were 25±2.11 and 26±1.71 years, and the Mean±SD with a mean history of abuse were 8.37±2.4 and 7.37±2.2 years in the experimental and control groups, respectively). Subjects were required to refrain from opiate abuse for at least 12 h before UROD.

Transcranial direct current stimulation

The participants received three consecutive sessions of anodal tDCS over the right DLPFC combined with cathodal tDCS over the left DLPFC with a 24-h intersession interval. This montage was successful for addiction treatment in previous trials (Lupi et al.). Two sessions of tDCS were performed before UROD, and the third one was conducted one day after UROD therapy. The electrode locations (F3 and F4) were identified according to the 10/20 international system for EEG electrode placement. tDCS was delivered by a battery-driven stimulator (Activa Dose II, Taiwan) with two rubber electrodes covered by 5×7 cm saline-soaked sponges. tDCS intensity was 2 mA, and stimulation duration was 20 minutes in the experimental tDCS group. In the control group, the electrodes were placed at exact locations, but the current flow was ramped down after 30 s stimulation (Kaye et al., 2003).

The evaluation of symptoms was conducted by a researcher who was blinded with regard to the stimulation protocol. Participants were ignorant of the tDCS condition. The UROD lasted for 4 h. In UROD, a large dosage of an opiate antagonist (Naloxone 0.01 mg/kg) is applied under general anesthesia to detoxify the patients from opioid addiction. Anesthesia was initiated with a short-acting intravenous agent (propofol 1.5 mg/kg) and a muscle relaxant (atracurium 0.5 mg/kg) followed by a maintenance dose of the anesthetic propofol and the muscle relaxant (Shahbabaie et al., 2014).

Evaluations

Craving and withdrawal symptoms were assessed before and after each tDCS session. The results were analyzed via SPSS software, version 16. Additional assessments were selected for further evaluation, as shown in Tables 1 and 2.

Craving

Craving is a main psychological withdrawal symptom in drug addicts, which enhances the probability relevantly for relapse (Boggio et al., 2008). In this study, the craving was monitored via the 14-item Desire for Drugs Questionnaire (DDQ). This questionnaire assesses instantaneous craving at the time of assessment. Each scale comprises three subdivisions: desire and intention, negative reinforcement, and inhibition (Ekhtiari et al., 2008).

Withdrawal syndrome

Abstinence from opioid consumption results in physically observable withdrawal symptoms in drug addicts. These symptoms may vary in their intensity depending on the previous level of opioid consumption as well as other factors, such as context and environment (Segrave, et al., 2014). The objective opiate withdrawal scale is an interview and observation tool for assessing opioid withdrawal signs and symptoms. It contains 13 physically observable signs, rated as present or absent, based on observation of the patient by a rater for 5 minutes (Safari et al., 2010). The validity and reliability of this questionnaire have been demonstrated in Iran and other countries (Ekhtiari et al., 2008).

3. Results

Demographic factors

Four subjects from the real tDCS and two from the control group left the study within one month after the treatment due to unknown reasons. For statistical analyses, we treated missing values by the missing completely at random mechanism followed by mean imputation of missing data. The demographic characteristics in the study groups did not show any significant discrepancies between groups (Table 3).

Table 1. Results of t-tests comparing average craving between the two groups

Stages	Evaluation Period	Mean±SD		P
		Control	Experimental	
1	Before the first intervention	34.05±15.16	32.3±16.55	0.72
2	After the first intervention	24.35±13.40	22.6±15.24	0.702
3	Night	61.15±10.55	41.5±8.29	0.0001
4	Before the second intervention	48.05±14.74	32.9±9.23	0.0001
5	After the second intervention	30.95±11.67	22.2±9.48	0.013
6	After awakening	39.8±12.14	26.05±10.26	0.0001
7	Before the third intervention	33.45±11.33	21.05±9.57	0.001
8	After the third intervention	27.0±11.02	11.45±7.32	0.001
9	Two weeks after treatment	29.36±16.81	29.72±5.30	0.947
10	One month after treatment	13.37±3.40	14.7±4.90	0.347
11	Three months after treatment	15.8±9.73	20.0±20.01	0.481

NEUROSCIENCE

Craving

We used a 2-factorial ANOVA model to analyze variance and test for group and time effects of the intervention on each primary outcome measure. For craving, the interaction of time and group was significant (P=0.0001), and both main effects of group and time were significant (P=0.0001 and P=0.0001, respectively).

Before and immediately after the first tDCS session, the craving was identical between groups. Craving was, however, reduced in the experimental group, compared to the control group, from the night after the first intervention up to the craving measure after the third intervention (respective one-tailed P<0.05, Table 1). However, this inter-group difference was not present two weeks after therapy (post hoc t test, P=0.947), which indicates a limited duration of tDCS effects on craving.

According to the results of the t test, craving increased for both groups at night before detoxification and after waking up from anesthesia, which was more intense in the control group (stages 3 & 6).

We also assessed the ratio of mean changes of craving by the R=E-B/B formula (E indicates craving after tDCS and B craving before tDCS). The values of R comparing craving before the first tDCS and 1 month after treatment were -0.4 in the sham and -0.5 in the real group; thus, the craving was more prominently reduced after intervention in the real tDCS group.

An additional assessment for craving was accomplished 3 months after the treatment. R values for craving before and after the first tDCS session were -0.3 in the sham and -0.33 in the real stimulation group. Also, R values before and after the second tDCS were -0.33 in the sham and -0.35 in the real stimulation group. Finally, R values before and after the third tDCS session were -0.21 in the sham and -0.49 in the real stimulation group.

Withdrawal syndrome

The results of the 2-factorial ANOVA showed a significant interaction between time and group (P=0.0001). Both main effects of group and time were significant (P=0.0001 and P=0.0001, respectively). Withdrawal symptoms were identical for both groups before the first tDCS session but differed significantly between groups after the first intervention and the night before UROD. Before and after the second tDCS session, withdrawal symptoms were identical in both groups. However, after UROD, withdrawal symptoms were significantly lower in the real compared to the sham tDCS group up to the third tDCS session, as shown by the respective post hoc tests (Table 2).

Table 2. Results of the t-tests comparing withdrawal symptoms between the two groups

Stage	Evaluation Period	Mean±SD		P
		Control	Experimental	
1	Before the first intervention	1.3±1.03	1.25±107	0.88
2	After the first intervention	1.15±0.88	0.3±0.47	0.0001
3	Night	5.6±1.60	4.55±1.23	0.026
4	Before the second intervention	2.6±0.94	3.15±1.35	.143
5	After the second intervention	2.5±0.83	1.15±0.75	0.283
6	One hour after the operation	5.1±1.71	2.55±1.10	0.0001
7	Three hours after the operation	2.95±1.61	1.45±1.0	0.001
8	Twelve hours after the operation	2.2±1.06	0.7±0.80	0.0001
9	Before the third intervention	2.8±1.40	0.8±0.77	0.0001
10	After the third intervention	2.5±1.40	0.15±0.37	0.0001

NEUROSCIENCE

In addition, the night before and 1 h after UROD, the intensity of withdrawal symptoms increased in both groups, especially one hour after UROD (P =0.026 and P=0.0001, respectively). This increase was related to baseline values.

The ratios of the mean change of withdrawal symptoms comparing withdrawal before and 1 month after treatment was 0.71 in the sham and -0.64 in the real tDCS group. Withdrawal symptoms decreased after each intervention only in the real tDCS group. R val-

Table 3. Demographic characteristics of the study

Demographic Characteristics		No. (%) / Mean±SD		P
		Real tDCS	Sham tDCS	
Age (y)		25.3±1.29	26.25±1.04	0.571
Marital status	Married	19(47.5)	17(42.5)	0.29
	Single	1(2.5)	3(7.5)	
Level of education	Lower than diploma	15(37.5)	15(37.5)	0.57
	Bachelor	4(10.0)	5(12.5)	
	Upper than bachelor	1(2.5)	0(0)	
Duration of drug dependency (y)	Below 5	7(17.5)	8(20.0)	0.87
	5-10	6(15.0)	7(17.5)	
	Over 10	7(17.5)	5(12.5)	
Amount of drug usage (g)	<2	8(40)	12(60)	0.44
	2–5	8(40)	5(25)	
	>5	4(20)	3(12)	

NEUROSCIENCE

ues for withdrawal symptoms before and after the first tDCS session was -0.058 in the sham and -0.57 in the real stimulation group; before and after the second tDCS, R values were 4.92 in the sham and -0.66 in the real stimulation group, and finally R before and after the third tDCS session, R values were -0.16 in the sham and -0.5 in the real stimulation group.

4. Discussion

Patients did not report any side effects of tDCS except for a tolerable tingling sensation under the electrodes reported by 5 patients (three patients from the real tDCS and 2 from the sham stimulation group). This result is comparable with other studies in the field (Pedron, et al., 2014).

The study's results support the hypothesis that tDCS reduces craving and withdrawal symptoms caused by treating opioid addiction with UROD. Lower levels of craving were observed in the real tDCS group from the night after the first session to the end of the third session, in agreement with the results of other tDCS studies in addiction (Lupi et al.), in further agreement with the role of the prefrontal cortex in urging and control of craving in humans (Fregni et al., 2008), and animal models of addiction (Goldstein & Volkow, 2011). In addition to deep brain structures involved in addiction, recent studies have revealed a relevant contribution to the prefrontal cortex (Fowler, et al., 2007). In accordance, prefrontal cortex and anterior cingulate activation are relevant for cognitive processes, especially drug craving, in cocaine addicts (Boggio et al., 2009).

The positive effect of tDCS on craving is in accordance with similar effects of this intervention on nicotine, marijuana, and alcohol withdrawal, but this is the first study that showed such an effect on opioid addiction. However, the effects were relatively short-lived. This might be caused by minor cumulative effects following three sessions of tDCS (Klauss et al., 2014). Interestingly, we saw slightly enhanced craving in the real stimulation group at the last time point obtained. This event may be related to improved attention caused by tDCS, as described by previous anodal tDCS studies with the electrodes placed over the prefrontal cortices (Borckardt et al., 2013).

Most studies on UROD describe a manifest withdrawal syndrome during and in the weeks after treatment (Rostami, et al., 2013). In one study, symptoms of the drug withdrawal syndrome increased during UROD and 24 hours later (Safari et al., 2010). Other studies indicate sustained withdrawal symptoms for up to 10 weeks (Rostami et al., 2013). In the present study, tDCS reduced withdrawal symptoms for a relatively short time after anxiety-reducing and a possible dopamine-increasing effect, which were proposed in other studies (Klauss et al., 2014). One reason for the positive effects of tDCS on withdrawal may relate to more intensive protocols has to be explored in future studies. The results of this study deliver the first evidence that prefrontal tDCS may promote the tolerability and efficacy of treatment approaches for opioid addiction using UROD.

Ethical Considerations

Compliance with ethical guidelines

The study was approved by the Ethics Committee of Yazd Shahid Sadoughi University of Medical Sciences and registered at the Iranian registry of clinical trials (IRCT ID: 2015022821273N1).

Funding

The paper was extracted from the PhD Thesis of the first author, Department of Psychology Faculty of Neuroscience, University of Tabriz, Iran. MAN was supported by a grant from the German Federal Ministry of Education and Research (GCBS Grant: 01EE1403C).

Authors' contributions

All authors equally contributed to preparing this article.

Conflict of interest

The authors declare no conflict of interest.

Acknowledgments

We would like to offer our gratitude to the participants for their collaboration

References

Amato, L., Minozzi, S., Davoli, M., Vecchi, S., Ferri, M. M., & Mayet, S. (2008). Psychosocial and pharmacological treatments versus pharmacological treatments for opioid detoxification. *The Cochrane Database of Systematic Reviews, (3)*, CD005031.[DOI:10.1002/14651858.CD005031.pub2]

Bashir, S., & Yoo, W. K. (2016). Neuromodulation for addiction by transcranial direct current stimulation: Opportunities and challenges. *Annals of Neurosciences, 23*(4), 241-245. [PMID] [PMCID]

Boggio, P. S., Liguori, P., Sultani, N., Rezende, L., Fecteau, S., & Fregni, F. (2009). Cumulative priming effects of cortical stimulation on smoking cue-induced craving. *Neuroscience Letters, 463*(1), 82-86. [DOI:10.1016/j.neulet.2009.07.041] [PMID]

Boggio, P. S., Sultani, N., Fecteau, S., Merabet, L., Mecca, T., & Pascual-Leone, A., et al. (2008). Prefrontal cortex modulation using transcranial DC stimulation reduces alcohol craving: A double- blind, sham-controlled study. *Drug and Alcohol Dependence, 92*(1-3), 55–60. [DOI:10.1016/j.drugalcdep.2007.06.011] [PMID]

Borckardt, J. J., Reeves, S. T., Robinson, S. M., May, J. T., Epperson, T. I., & Gunselman, R. J., et al. (2013). Transcranial direct current stimulation (tDCS) reduces postsurgical opioid consumption in total knee arthroplasty (TKA). *The Clinical Journal of Pain, 29*(11), 925–928. [DOI:10.1097/AJP.0b013e31827e32be] [PMID]

Conti, C. L., & Nakamura-Palacios, E. M. (2014). Bilateral transcranial direct current stimulation over dorsolateral prefrontal cortex changes the drug-cued reactivity in the anterior cingulate cortex of crack-cocaine addicts. *Brain Stimulation, 7*(1), 130-132. [PMID]

Dastjerdi, G, Mirhoseini, H., & Mohammadi, E. (2015). Investigating the Synergistic effects of transcranial direct current stimulation and cranial electrical stimulation in treatment of major depression in a double blinded controlled trial. *Biomedical and Pharmacology Journal, 8*(2), 1267-1274. [DOI:10.13005/bpj/885]

Sauvaget, A., Trojak, B., Bulteau, S., Jiménez-Murcia, S., & Fernández-Aranda, F., et al. (2015). Transcranial direct current stimulation (tDCS) in behavioral and food addiction: A systematic review of efficacy, technical, and methodological issues. *Frontiers in Neuroscience, 9,* 349. [PMID] [PMCID]

Martinotti, G., Lupi, M., Montemitro, C., Miuli, A., Di Natale, C., & Spano, M. C., et al. (2019). Transcranial direct current stimulation reduces craving in substance use disorders: A double-blind, placebo-controlled study. *The Journal of ECT, 35*(3), 207–211. [PMID]

Taremian, F., Nazari, S., Moradveisi, L., & Moloodi, R. (2019). Transcranial direct current stimulation on opium craving, depression, and anxiety: A preliminary study. *The Journal of ECT, 35*(3), 201–206. [PMID]

Ekhtiari, H., Edalati, H., Behzadi, A., Safaei, H., Noori, M., & Mokri, A. (2008). [Designing and evaluation of reliability and validity of five visual cue-induced craving tasks for different groups of opiate abusers (Persian)]. *Iranian Journal of Psychiatry and Clinical Psychology, 14*(3), 337-349. [Link]

Fowler, J. S., Volkow, N. D., Kassed, C. A., & Chang, L. (2007). Imaging the addicted human brain. *Science & Practice Perspectives, 3*(2), 4-16. [PMID] [PMCID]

Fregni, F., Liguori, P., Fecteau, S., Nitsche, M. A., Pascual-Leone, A., & Boggio, P. S. (2008). Cortical stimulation of the prefrontal cortex with transcranial direct current stimulation reduces cue-provoked smoking craving: A randomized, sham-controlled study. *The Journal of Clinical Psychiatry, 69*(1), 32–40. [DOI:10.4088/JCP.v69n0105] [PMID]

Gandiga, P. C., Hummel, F. C., & Cohen, L. G. (2006). Transcranial DC stimulation (tDCS): A tool for double-blind sham-controlled clinical studies in brain stimulation. *Clinical Neurophysiology, 117*(4), 845-850. [PMID]

Goldstein, R. Z., & Volkow, N. D. (2011). Dysfunction of the prefrontal cortex in addiction: Neuroimaging findings and clinical implications. *Nature Reviews. Neuroscience, 12*(11), 652–669.[DOI:10.1038/nrn3119] [PMID] [PMCID]

Kaye, A. D., Gevirtz, C., Bosscher, H. A., Duke, J. B., Frost, E. A., & Richards, T. A., et al. (2003). Ultrarapid opiate detoxification: A review. *Canadian Journal of Anaesthesia, 50*(7), 663-671. [DOI:10.1007/BF03018708] [PMID]

Klauss, J., Penido Pinheiro, L. C., Silva Merlo, B. L., de Almeida Correia Santos, G., Fregni, F., & Nitsche, M. A., et al. (2014). A randomized controlled trial of targeted prefrontal cortex modulation with tDCS in patients with alcohol dependence. *The International Journal of Neuropsychopharmacology, 17*(11), 1793–1803. [DOI:10.1017/S1461145714000984] [PMID]

Lupi, M., Martinotti, G., Santacroce, R., Cinosi, E., Carlucci, M., & Marini, S., et al. Transcranial direct current stimulation in substance use disorders: A systematic review of scientific literature. *The Journal of ECT, 33*(3), 203–209. [PMID]

Mark, T. L., Woody, G. E., Juday, T., & Kleber, H. D. (2001). The economic costs of heroin addiction in the United States. *Drug and Alcohol Dependence, 61*(2), 195–206. [DOI:10.1016/S0376-8716(00)00162-9] [PMID]

Pedron, S., Monnin, J., Haffen, E., Sechter, D., & Van Waes, V. (2014). Repeated transcranial direct current stimulation prevents abnormal behaviors associated with abstinence from chronic nicotine consumption. *Neuropsychopharmacology, 39*(4), 981-988. [PMID] [PMCID]

Rostami, R., Hamidi Kenari, A., Mirzaieyan, B., & Rezaie kochaksaraie, M. (2012). [The efficacy of repeated transcranial magnetic stimulation of the brain on the rate of material craving in addicts of methamphetaime (Persian)]. *Journal of Mazandaran University of Medical Sciences, 21*(1), 164-176. [Link]

Safari, F., Mottaghi, K., Malek, S., & Salimi, A. (2010). Effect of ultra-rapid opiate detoxification on withdrawal syndrome. *Journal of Addictive Diseases, 29*(4), 449–454. [DOI:10.1080/10550887.2010.509278] [PMID]

Segrave, R. A., Arnold, S., Hoy, K., & Fitzgerald, P. B. (2014). Concurrent cognitive control training augments the antidepressant efficacy of tDCS: A pilot study. *Brain Stimulation, 7*(2), 325–331. [PMID]

Shahbabaie, A., Golesorkhi, M., Zamanian, B., Ebrahimpoor, M., Keshvari, F., & Nejati, V., et al. (2014). State dependent effect of transcranial direct current stimulation (tDCS) on methamphetamine craving. *The International Journal of Neuropsychopharmacology, 17*(10), 1591–1598. [DOI:10.1017/S1461145714000686] [PMID]

This Page Intentionally Left Blank