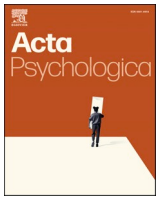
Acta Psychologica 255 (2025) 104939

Contents lists available at ScienceDirect

Acta Psychologica

journal homepage: www.elsevier.com/locate/actpsy



Effectiveness of transcranial alternating current stimulation (tACS) and cognitive bias modification (CBM) in treating anxiety, depression, attentional bias, and drug craving in opioid-dependent patients

Kiyanoosh Papi [a,*], Masoud Nosratabadi [a], Farhad Taremian [a], Nikzad Ghanbari [b], Maryam Ebrahimi Varkiyani [a]

[a] Department of Clinical Psychology, University of Social Welfare and Rehabilitation Sciences, Tehran, Iran
[b] Department of Clinical Psychology, Faculty of Psychology and Educational Sciences, Shahid Beheshti University, Tehran, Iran

ARTICLE INFO

Keywords:
Transcranial alternating current stimulation
tACS
Cognitive bias modification
CBM
Anxiety
Depression
Craving
Attention bias
Substance use disorders
Opioid use disorders

ABSTRACT

Introduction: Substance Use Disorders (SUDs) pose significant challenges globally, with opiate addiction being particularly prevalent. This study investigates the impact of transcranial alternating current stimulation (tACS) at 10 Hz and individual alpha frequencies (IAF), along with cognitive bias modification (CBM), on drug craving, anxiety, depression, and attention bias in individuals with SUDs.

Methods: Participants ($N = 72$) were allocated to control, tACS 10 Hz, tACS IAF, Sham, CBM, and CBM + tACS groups ($n = 12$ each). Measures included demographic questionnaires, dot probe tasks, Desires for Drug Questionnaires (DDQ), DASS-21 assessments, and Visual Analog Scale (VAS) for craving. Mixed repeated measures ANOVA were conducted, revealing significant interactions (TIME*GROUP), indicating differential treatment effects over time.

Findings: The study involved 72 substance abusers divided into six groups: control, tACS.10 Hz, tACS Real, Sham, CBM, and CBM + tACS. Demographic variables were similar among groups. Mixed ANOVA showed significant TIME*GROUP interactions for all assessments. Significant differences were found in anxiety, drug dependence, and visual analog scale measures.

Conclusion: In brief, although using tACS and CBM separately didn't lead to significant decreases in substance-related issues, employing them together demonstrated potential. This research underscores how the brain can adapt to electrical stimulation and emphasizes the importance of delving deeper into treating SUDs. However, limitations such as limited participant availability and the reliance on verbal craving induction indicate the necessity for more comprehensive study designs and varied assessment methods in future investigations.

1. Introduction

Substance use disorders (SUDs) pose enduring and severe challenges in modern societies, yielding significant repercussions (Ouzir & Errami, 2016). Conceptually, SUDs represent chronic neurological conditions influenced by genetic, physiological, and societal factors. They manifest as diminished self-regulation and an urge to engage in specific behaviors despite awareness of their adverse effects (Gipson & Beckmann, 2023; Sripada, 2022). Opioid SUDs, such as heroin and opium abuse, are notably widespread in countries like Iran, significantly affecting cognitive functions such as learning, memory, and attention (Rezapour et al., 2021). Those grappling with SUDs commonly confront cognitive and psychological repercussions, including depression and anxiety during withdrawal. Furthermore, cognitive challenges like cravings and attentional biases can complicate clinical presentations and contribute to relapse (Marissen et al., 2006).

Anxiety and depression represent significant psychological conditions linked with SUDs. They may prompt individuals to turn to substance use as a means of coping with symptoms and the social challenges associated with opiates, anxiety, and depression. Also heightened negative emotional states in individuals experiencing mood and anxiety disorders could elevate the probability of experiencing craving episodes and relapsing into drug use (Preston & Epstein, 2011). Anxiety and depression are prevalent throughout the various phases of SUDs, and research indicates a

* Corresponding author.
E-mail address: Kiyanooshpapi92@gmail.com (K. Papi).

https://doi.org/10.1016/j.actpsy.2025.104939
Received 16 April 2024; Received in revised form 5 March 2025; Accepted 25 March 2025
Available online 1 April 2025

correlation between negative mood and substance use (Buckner et al., 2015). Depressive symptoms induced by withdrawal can endure for extended periods, heightening the risk of suicidal tendencies (Swan & Chang, 2003). Depressive disorders and SUDs frequently co-occur, posing significant challenges and highlighting the need for innovative treatment approaches (Kelly & Daley, 2013). Neuroimaging research indicates shared neurological pathways between depressive disorders and SUDs (Dunlop et al., 2017). The involvement of the anterior cingulate cortex and cognitive control impairments are suggested as neural connections between depression, anxiety, and SUDs (Riesel et al., 2019).

As noted, prolonged substance use can result in cognitive impairments that impact attention, learning, memory, and reasoning abilities. Executive functions such as working memory, cognitive flexibility, and inhibition control are especially susceptible to these effects (Gupta et al., 2018). Distinct cognitive deficits linked with drug use encompass impaired cognitive flexibility and attention (Lyvers & Yakimoff, 2003). Attentional bias, characterized by a modified allocation of attention towards certain stimuli, holds considerable importance in SUDs and could contribute to the difficulty in managing substance abuse behaviors (MacLean et al., 2018). This bias is observable in anxiety disorders, depression, and addiction (Field et al., 2016; Suslow et al., 2020; Thomas et al., 2013; Wieser & Keil, 2020). This bias is notably pronounced during craving episodes, wherein individuals concentrate on stimuli reminiscent of their substance use patterns (Bollen et al., 2024). Craving stands as a pivotal aspect of substance abuse and relapse, holding substantial ramifications for treatment approaches (Culbertson et al., 2010; Hormes & Rozin, 2010; Vafaie & Kober, 2022). Conventional methods for addressing craving and managing substance withdrawal have demonstrated limited effectiveness (Hone-Blanchet et al., 2015). Several treatments, including cognitive behavioral therapy (CBT), third-wave therapies, and psychoanalytical therapies, are available for addressing anxiety, depression, and psychological concerns in SUDs (Leichsenring & Rabung, 2008; McHugh et al., 2010). CBT has emerged as a prevalent non-pharmacological intervention for SUDs, demonstrating higher effectiveness in comparison to the twelve-step program and group counseling (Dutra et al., 2008). However, despite its widespread use, CBT may not consistently yield positive outcomes, with certain studies suggesting that patients may encounter difficulties in altering their cognitive patterns (Baker et al., 2014). Recent progress in neuroscience has sparked growing enthusiasm for noninvasive brain stimulation as a viable treatment approach. Cognitive bias modification (CBM) and transcranial electrical stimulation with alternating current (tACS) have emerged as notable focuses of interest in recent years (Paulus, 2011). Stimulation methods such as transcranial electrical stimulation (TES) and cognitive bias modification (CBM) hold potential in elucidating neuropsychological processes and reshaping cognitive biases (Bocci et al., 2019; Wells & Beevers, 2010). Transcranial direct current electrical stimulation (tDCS) has the capacity to impact decision-making mechanisms associated with impulsivity in addictive disorders (Boggio et al., 2010). Employing tDCS to target particular brain areas has demonstrated potential in mitigating cravings (Hone-Blanchet et al., 2015). Transcranial electrical stimulation with alternating current (tACS) stands out as a promising method for regulating brain waves through alternating electrical currents (Papi et al., 2024; Wu et al., 2021). As far as the authors are aware, unlike tDCS, there hasn't been concentrated research on the impact of tACS on substance use disorders. Numerous investigations have revealed the influence of tDCS on conditions such as depression, craving, attentional bias, and impulsivity (Tavakoli & Yun, 2017). tACS and tDCS share notable similarities, but their distinction lies in the manner of current application. Unlike tDCS, which typically delivers current throughout a complete cycle, tACS is designed to engage with natural brain oscillations instead of administering direct electrical current (Tavakoli & Yun, 2017).

As previously discussed, tACS stimulation involves alternating brain wave frequencies, with particular emphasis on alpha waves (8 to 12 Hz) due to their significance in regulating anxiety levels and mood states. The 10 Hz frequency predominates in the recording of alpha brain waves during periods of rest. Consequently, given the interest in comprehending brain processes during rest, which serves as the foundation of brain activities, this frequency serves as the standard (classical frequency) for quantitative analysis. It stands as one of the foremost physiological markers of brain function (Singh & Sharma, 2015). These inherent brain activities exhibit considerable intra-individual stability, yet they demonstrate notable variations among individuals (Posthuma et al., 2001) and also undergo alterations with age and psychological conditions (Scally et al., 2018). The individual alpha frequency (IAF) has been associated with cognitive functions and intelligence levels (Corcoran et al., 2018).

Transcranial Alternating Current Stimulation (tACS) is a form of non-invasive brain stimulation that applies an oscillating electrical current through electrodes placed on the scalp. This method aims to modulate brain oscillations, which are rhythmic activities of neural circuits responsible for various cognitive functions (Wischnewski et al., 2019).

tACS is designed to interact with and influence the brain's natural oscillatory rhythms, such as alpha waves (8–12 Hz), which are linked to functions like attention, memory, and mood regulation. By applying alternating currents at specific frequencies, tACS can enhance or reduce the synchronization of neurons, potentially altering the brain's functional connectivity. This modulation is believed to affect cognitive and behavioral performance by either enhancing communication between brain areas involved in specific tasks or by disrupting maladaptive patterns of activity associated with conditions like addiction, depression, or anxiety.

The after-effects of tACS, which are observed after stimulation, rather than during, are considered significant for understanding its potential therapeutic impact. These effects can last from several minutes to hours and are thought to be due to mechanisms such as spike-timing-dependent plasticity (STDP). STDP involves changes in synaptic strength based on the timing of neuronal activity, which can lead to lasting modifications in brain networks. Several Studies have shown that tACS can induce after-effects on brain oscillations, suggesting potential for sustained changes in cognitive and emotional states, which are crucial for addressing issues like drug craving and addiction (Wischnewski et al., 2019).

In tACS, some studies demonstrate the importance of considering individual alpha variability when applying tACS, showing that aftereffects were only observed when stimulation was applied at the individual alpha frequency (Stecher & Herrmann, 2018). Individual differences in alpha frequency can impact perceptual processes (Cecere et al., 2015), supporting the rationale for using IAF in stimulation protocols. Other researchers showed the advantages of tailoring stimulation parameters, including frequency, to individual participants for more effective neuromodulation (Romei et al., 2016). However, further research is necessary to comprehensively grasp the impact of tACS on substance use disorders (SUDs). In conjunction with the aforementioned non-invasive therapies, recent research has explored the application of CBM to address attentional bias in SUDs (Harvey et al., 2004). CBM involves computer-based exercises aimed at reshaping cognitive biases. Cognitive biases encompass a wide range of automatic processes that can occur even without conscious awareness. For instance, the heightened attention of an individual with addiction to drug-related cues may lead to a propensity to react to such stimuli (Wiers et al., 2015).

The current study sought to examine the efficacy of combining tACS at 10 Hz and individual alpha frequencies with CBM in mitigating depression, attentional bias, and craving among individuals with a past of opium use. The primary objective was to explore the effectiveness of these promising interventions in addressing craving and internalizing symptoms (such as depression and anxiety) associated with opioid use disorder. Therefore, the study aimed to address the following questions:

1. Is there a difference between the effectiveness of the 10 Hz tACS and the IAF based tACS method on craving, anxiety, depression and attentional bias in people with a history of opium use?

2. Is there a difference between the effectiveness of the tACS and the CBM on drug craving, anxiety, depression and attention bias in people with a history of opium use?
3. Is the combined intervention of tACS and CBM more effective than tACS and CBM separate interventions in reducing the craving, anxiety, depression, attention bias of people with a history of opium use?

2. Material and methods

2.1. Participants

Seventy-two participants were involved in the study, with 12 individuals assigned to each group. The age of the participants ranged from 18 to 65 years (Mean = 33.83, Standard Deviation = 9.05). All participants were individuals with a background of opium abuse receiving treatment at De-addiction camps in Khorramabad city for addiction rehabilitation.

Also, we want to address the concern about the small sample size in our study (Especially in follow-up groups). It is common for experimental studies involving clinical groups to have a limited number of participants due to difficulties in accessing enough suitable patients. For instance, our target population consists of individuals addicted to opium who are in rehabilitation centers. These individuals must have been abstinent for a week, experiencing minimal physical withdrawal pain, and it must not have been more than one month since the end of their physical withdrawal period.

Additionally, follow-up with some opium addicts was not possible. For example, one participant had passed away, three participants were sentenced to long-term imprisonment, and other individuals were unavailable to the researcher for various reasons. Consequently, the number of participants available for follow-up was reduced.

2.2. Study design

The study employed a randomized controlled design to examine the impacts of various interventions on participants. Initially, participants were randomly divided into two groups: one receiving tACS (10 Hz) and the other receiving IAF tACS (with 12 participants in each group). In the subsequent phase, participants were evenly distributed across four groups: CBM, CBM combined with tACS (10 Hz), tACS (10 Hz) alone, sham intervention, and a control group (each with 12 participants). Two follow-up assessments were conducted at 30-day and 90-day intervals. The study design, depicted in a flowchart, adhered to the

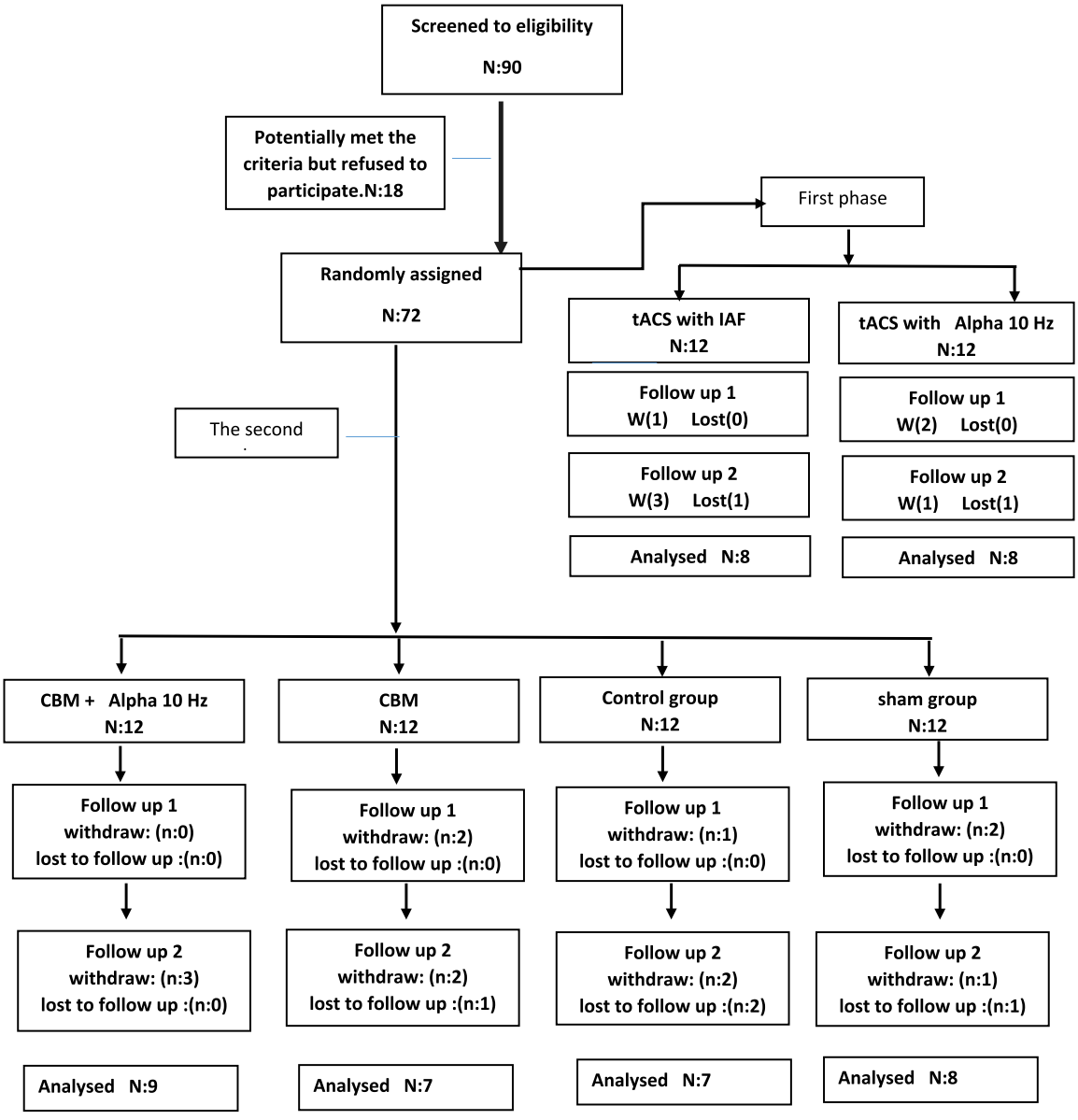


Fig. 1. CONSORT flow diagram to illustrate the study design and trial procedures used in the present study.

recommendations of CONSORT guidelines, as illustrated in Fig. 1.

2.3. Recruitment and criteria

Participants were recruited from addiction treatment clinics, ensuring they met specific inclusion criteria. These criteria included a documented history of opium use disorder for at least 12 months according to DSM-5 criteria, verified abstinence from all substances except smoking for a minimum of one week, a reported craving for drug use of at least 20 %, the absence of certain medical conditions, and fulfillment of specific demographic criteria. Exclusion criteria included ongoing treatment for another psychiatric disorder (excluding substance use disorders), the presence of significant neurological disorders, the commencement of medications affecting the central nervous system, and attendance at fewer than two treatment sessions.

2.4. Group allocation

Participants were allocated into six distinct groups as follows:

Group One: tACS with 10 Hz alpha

This group received transcranial alternating current stimulation (tACS) at a frequency of 10 Hz. This frequency, referred to as "classical alpha," is widely used in research as the basis for alpha band stimulation.

Group Two: tACS with individual alpha

This group received tACS at their individual alpha frequency, tailored to each participant. This approach is known as "real" or "individual alpha" stimulation in this study.

Group Three: Combined tACS and CBM

Participants in this group received both tACS and Cognitive Bias Modification (CBM) simultaneously, combining brain stimulation with cognitive training.

Group Four: CBM only

Participants in this group received only Cognitive Bias Modification without any electrical stimulation.

Group Five: sham

This group received a placebo form of electrical stimulation, with only 30 s of current rise at the beginning and 30 s of fall at the end, mimicking the sensation of tACS without delivering actual stimulation.

Group Six: control

This group did not receive any form of tACS or CBM, serving as a baseline for comparison Intervention.

The electrical stimulation device was programmed by one of the principal investigators to administer either tACS or sham stimulation in a double-blind fashion. The intervention comprised five consecutive sessions, with intervals of at least 24 h between each session, and participants received interventions at consistent times daily. Prior to participation, all individuals provided informed consent, and ethical standards outlined by the Institutional Review Board were rigorously followed throughout the study.

The time table of this research. The duration of each electrical stimulation was 20 min and the duration of bias correction was 40 min.

2.5. Measures

2.5.1. Demographic questionnaire (BDSP)

This form encompassed essential demographic details, substance use history and patterns, received treatments, and related information.

2.5.2. Dot probe task (CBM protocol)

The dot probe test stands as a prevalent method employed to assess attention bias and has been utilized in numerous studies focusing on attention bias. In this assessment, two stimuli, typically words or images, are presented simultaneously, with one being threatening and the other neutral, for a designated duration. Following their disappearance from the screen, a target symbol replaces one of the initial stimuli (Faridi et al., 2022; Lancee et al., 2017).

Instead of words, pictures were employed as stimuli to ensure the project's suitability for addicts with diverse educational backgrounds. To select the opioid craving-related picture, an initial pool of 100 craving-related images was compiled from the International Affective Picture System and the picture collection of the SINA Institute in Tehran. Subsequently, these pictures were presented to 20 non-participant opioid addicts, who rated the images based on the level of craving they induced, enabling the identification of the most stimulating pictures. Subsequently, 40 target pictures were paired with neutral counterparts, ensuring compatibility in composition, size, and color. Each trial commenced with a 500-ms presentation of a black fixation cross (measuring 8 × 8 mm) positioned at the center of a white screen. Following this, two pictures—one neutral and one opioid craving-related—were simultaneously displayed for 1000 ms. The dimensions of each picture were standardized, with a height of 50 mm and a vertical distance of 60 mm. Following the 1000-ms presentation of the picture pair, a target or dot (measuring 3 mm in diameter) randomly appeared on either the right or left side for 250 ms. In 50 % of the trials, the target emerged alongside a neutral picture. Participants were instructed to indicate the direction of the dot by pressing the corresponding button on the computer keyboard. They were verbally informed that the dot would appear either on the right or left side of the two pictures and were instructed to focus on both the pictures and dots while performing the task as swiftly and accurately as possible. Both speed and accuracy were emphasized as crucial aspects. The task engaged participants in a total of 160 dot-probe trials, with each of the 40 picture pairs being displayed four times (4*40). Participants maintained a distance of 50 to 70 cm from the screen throughout the session, which typically lasted approximately 5 to 7 min and was operated following the protocol established by Faridi et al. (2022; see Fig. 2).

Group	Pre test One day before the intervention.	Intervention 5 consecutive days with an interval of 24 h	Post test One day after the intervention	Follow up 1	Follow up 2
Group One	DAAS21, DDQ, VAS, BDSP, Dot probe task	Electrical stimulation with alpha frequency of 10 Hz	DAAS21, DDQ, VAS, BDSP, Dot probe task	One month after the post test	three month after the post test
Group two	DAAS21, DDQ, VAS, BDSP, Dot probe task	Electrical stimulation with individual alpha frequency	DAAS21, DDQ, VAS, BDSP, Dot probe task	One month after the post test	three month after the post test
Group Three	DAAS21, DDQ, VAS, BDSP, Dot probe task	Combined tACS and Cognitive Bias Modification	DAAS21, DDQ, VAS, BDSP, Dot probe task	One month after the post test	three month after the post test
Group Four	DAAS21, DDQ, VAS, BDSP, Dot probe task	Cognitive Bias Modification	DAAS21, DDQ, VAS, BDSP, Dot probe task	One month after the post test	three month after the post test
Group Five	DAAS21, DDQ, VAS, BDSP, Dot probe task	tACS with only 30-s rise and 30-s fall	DAAS21, DDQ, VAS, BDSP, Dot probe task	One month after the post test	three month after the post test
Group six	DAAS21, DDQ, VAS, BDSP, Dot probe task	We did not do any intervention	DAAS21, DDQ, VAS, BDSP, Dot probe task	One month after the post test	three month after the post test

2.5.3. Desires for Drug Questionnaire (DDQ)

This questionnaire is widely acknowledged for its effectiveness in evaluating current drug cravings. Originally developed and standardized by Franken et al. (2002) for German-speaking heroin users, the questionnaire has been adapted for Persian-speaking methamphetamine users. The Persian version comprises 14 questions organized into three subscales: 'tendency to use drugs and negative reinforcement,' 'desire to use drugs,' and 'control and pleasure.' Hassani-Abharian et al. (2016) assessed the questionnaire's validity using the Cronbach's alpha method, yielding a general score of 0.63 and subscale scores of 0.78, 0.65, and 0.81 for the mentioned subscales, respectively. Participants rate their agreement with each item on a scale ranging from 1 (completely disagree) to 7 (completely agree).

2.5.4. DASS-21

The Depression, Anxiety, and Stress Scales (DASS) questionnaire consists of 21 statements designed to evaluate a range of negative emotions, encompassing depression, anxiety, and stress symptoms (Lovibond & Lovibond, 1995). However, for the current study, only the depression and anxiety subscales were utilized to assess internalizing symptoms associated with these psychopathologies. The depression subscale evaluates feelings related to a melancholic mood, diminished self-esteem, hopelessness, feelings of insignificance, loss of interest in activities, joylessness, and fatigue (Lovibond & Lovibond, 1995). On the other hand, the anxiety subscale assesses physiological hyperactivity, apprehensions, and situational anxieties (Lovibond & Lovibond, 1995).

Participants indicate the intensity of each symptom they have experienced over the past week using a 4-point scale, ranging from 0 to 3. Each subscale comprises 7 questions, and scores are determined by totaling the responses within each subscale. A notable advantage of the DASS questionnaire is its capacity to distinguish between depression and anxiety, thus mitigating the risk of overestimating depression within various patient cohorts (Lovibond & Lovibond, 1995).

The psychometric properties of the DASS have been extensively examined. In non-clinical populations, internal consistency coefficients for the depression, anxiety, and stress subscales were reported as 0.91, 0.84, and 0.90, respectively (Lovibond & Lovibond, 1995). In clinical populations, these coefficients were 0.96, 0.89, and 0.93, respectively (Brown et al., 1997). Moreover, retest coefficients for the DASS subscales ranged from 0.71 to 0.81 over a two-week interval in a sample of 20 patients (Brown et al., 1997). The factorial structure of the DASS questionnaire has garnered support from various studies, and its psychometric properties have been affirmed across diverse populations. For instance, a study involving 227 Iranian chronic pain patients utilized confirmatory factor analysis, demonstrating the validity of the questionnaire's three-factor structure (Asghari et al., 2008). In this study, the internal consistency coefficients (Cronbach's alpha) for the depression, anxiety, and stress scales were reported as 0.87, 0.81, and 0.87, respectively (Asghari et al., 2008). Furthermore, the concurrent validity of the DASS-21 scales was established by correlating them with scores from the Beck Depression Inventory and the Multidimensional Pain Inventory (Moghaddam et al., 2008). Scores on the depression subscale of the DASS questionnaire can range from 0 to 63, with higher scores reflecting more pronounced depression symptoms. In the present study, the Cronbach's alpha values for the depression and anxiety subscales were 0.75 and 0.70, respectively. These results indicate that the DASS questionnaire is a valid and reliable instrument for assessing negative emotional states.

2.5.5. Induced craving (VAS)

To evaluate induced craving, each participant was asked to recall three past instances that triggered drug cravings and led to drug use, with these statements being recorded simultaneously. Subsequently, participants review these situations and are prompted to visualize them, rating their craving for opium on a Visual Analog Scale (VAS). The VAS utilized in this study is a 100 mm linear scale, ranging from 0 (indicating no desire at all) to 100 (indicating the most intense desire). Participants' highest level of craving is determined from these scenarios, and their response is documented. During the post-test phase, the same scenarios are revisited to elicit craving (Sinha et al., 2011).

2.5.6. tACS (classic 10 Hz and Individual alpha frequency stimulation)

The tACS application utilized a battery-powered electrical stimulator along with a pair of electrodes (5 × 7 cm) at an intensity of 2 mA (peak-to-peak). To target the DLPFC, one electrode was positioned over the F4 region, while the other electrode was placed over the F3 region,

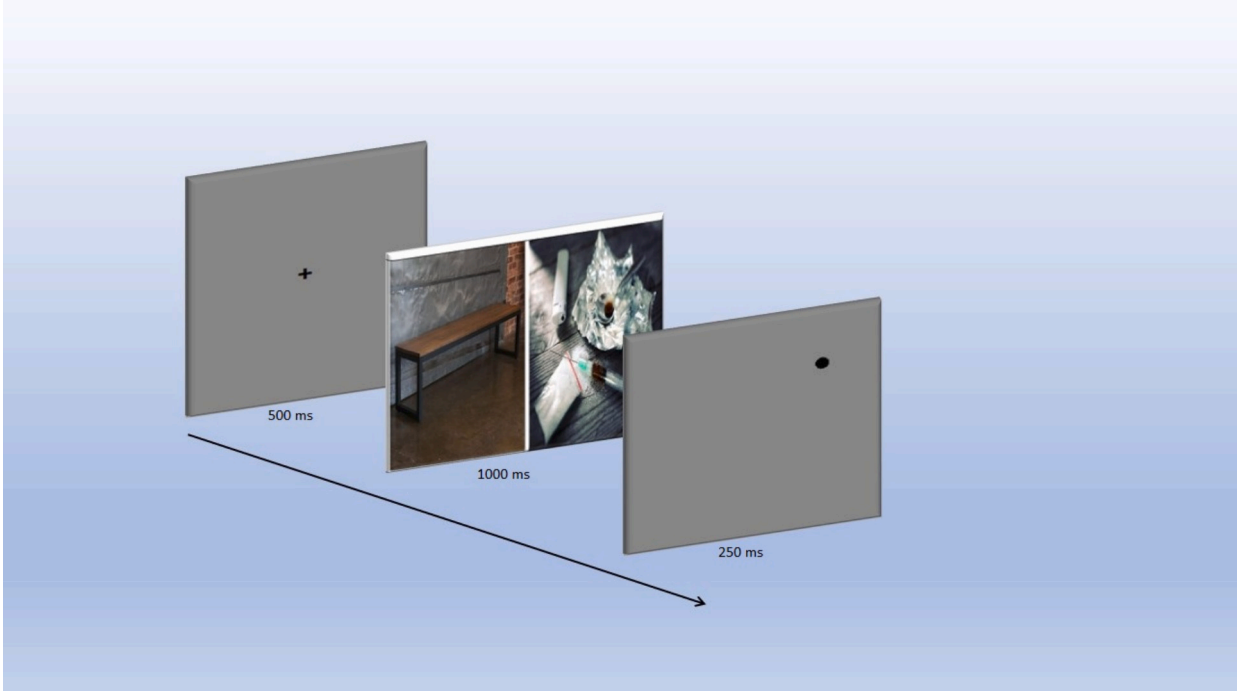


Fig. 2. Picture of the images and time intervals used in CBM protocol.

determined according to the 10–20 System of electrode placement. Stimulation was administered for 20 min with a 30-s rise and fall time using the Neurostim2 device, provided by Medinateb company (www.medinateb.com). The tACS (real or sham) was administered via an electric stimulator (Neurostim-2, Medinateb, Tehran), with 10 Hz stimulation selected as the standard frequency. In the IAF group, a 12-channel BioLine device (manufactured by Medinateb, Iran) was employed to compute the Individual Alpha Frequency (IAF). We employ a method that capitalizes on the characteristic modulation of alpha activity between eyes-closed and eyes-open states. We begin by recording EEG data from three occipital sites: O1, O2, and Pz. The recording consists of two 2-min resting-state conditions: eyes-open (EO) and eyes-closed (EC). Following data collection, we perform spectral analysis on the EEG data from each electrode site and condition, focusing on the alpha frequency range of 7–14 Hz. We then calculate the difference in spectral power between the EC and EO conditions across this frequency range for each electrode site. This difference spectrum highlights the frequencies that exhibit the greatest modulation between eyes-closed and eyes-open states, which is a hallmark of alpha activity. Within each electrode's difference spectrum, we identify the frequency that shows the maximum amplitude difference between EC and EO conditions. This frequency represents the site-specific peak alpha frequency. Finally, we calculate the mean of these peak frequencies identified for O1, O2, and Oz, and use this average value as the Individual Alpha Frequency (IAF).

The occipital region typically shows the strongest alpha oscillations, especially during eyes-closed resting state. This makes it easier to reliably measure IAF. There is evidence suggesting that alpha oscillations share similar frequency characteristics across different cortical regions, supporting the use of occipital IAF for other areas like DLPFC (Haegens et al., 2014; Nunez et al., 2001).

2.6. Data analysis

Data analysis encompassed descriptive statistics such as frequency, mean, and standard deviation, alongside inferential statistics including analysis of covariance and *t*-tests to compare the six groups. SPSS version 22 served as the tool for data analysis. Mixed repeated measures ANOVAs were employed to compare groups based on each outcome variable.

3. Results

The study comprised 72 substance abusers, distributed across the control group ($n = 12$), tACS at 10 Hz (n = 12), real tACS (n = 12), sham tACS (n = 12), CBM (n = 12), and CBM combined with tACS (n = 12). The average age of all participants was 33.83 years (Standard Deviation = 9.05, range of 20–49 years). Chi-square and Analysis of Variance (ANOVA) tests were conducted to detect potential differences in demographic variables among the groups. No significant between-group differences were observed for demographic variables, including marital status, onset and duration of substance use, number of addicts, and duration of abstinence from substances. Detailed demographic variables are presented in Table 1.

Mixed Repeated Measures ANOVA were conducted to examine differences between the groups on the study variables. Group (tACS at 10 Hz, real tACS, control, sham tACS, CBM, and CBM combined with tACS) served as the between-subject factor, while assessment time (pre-test, post-test, follow-up1, and follow-up2) was the within-subject factor. Similarities were observed between the six groups at the pretest phase (refer to Table 2). An interaction effect between-subject and within-subject (TIME*GROUP) was observed. However, this interaction effect was not statistically significant [F(15, 123) = 1.65, $p = 0.069$, $\eta^2 = 0.17$]. Subsequently, one-way ANOVA tests were conducted for comparisons among groups at pre-test, post-test, follow-up1, and follow-up2 to assess group differences before and after the intervention.

Mixed Repeated Measures ANOVA were performed to examine differences among the groups on depression scores. Group (tACS at 10 Hz, real tACS, control, sham tACS, CBM, and CBM combined with tACS) served as the between-subject factor, while assessment time (pre-intervention, post-intervention, follow-up1, and follow-up2) was the within-subject factor. Similarities were observed between the groups at the pretest phase, with no significant differences found [F(5, 41) = 1.10, $p = 0.37$, $\eta^2 = 0.12$]. No significant interaction effect between Time and Group was found [F(15, 123) = 1.65, p = 0.069, $\eta^2 = 0.17$]. However, the within-subject effect of TIME was significant [F(3,123) = 17.87, $p < 0.001$, $\eta^2 = 0.30$] (refer to Table 2 & Fig. 3).

Mixed repeated measures ANOVA were employed to assess differences among the groups regarding anxiety levels. Group (tACS classic, real tACS, control, sham, CBM, and CBM combined with tACS) served as the between-subject factor, while assessment time (pre-intervention, post-intervention, follow-up1, and follow-up2) was the within-subject factor. Similarities were observed between the groups at the pretest phase, with no significant differences detected [F (5, 41) = 1.26, $P = 0.29$, η2 = 0.13]. However, significant differences emerged in the between-subject by within-subject interaction effect (TIME*GROUP) [F (15, 123) = 2.05, $P < 0.05$, η2 = 0.20] and the within-subject effect (TIME) [F (3, 123) = 13.31, $P < 0.001$, η2 = 0.24] (refer to Table 2 & Fig. 4).

Mixed repeated measures ANOVA were conducted to evaluate differences among the groups regarding drug dependence (DDQ). Group (tACS at 10 Hz, real tACS, control, sham tACS, CBM, and CBM combined with tACS) served as the between-subject factor, while assessment time (pre-intervention, post-intervention, follow-up1, and follow-up2) was the within-subject factor. Similarities were noted between the groups at the pretest phase, yet significant differences were observed among the groups [F (5, 41) = 1.99, P < 0.05, η2 = 0.20]. Additionally, significant effects were found for the between-subject by within-subject interaction (TIME*GROUP) [F (15, 123) = 2.78, P < 0.001, η2 = 0.25] and the within-subject effect (TIME) [F (3, 123) = 18.43, P < 0.001, η2 = 0.31] (refer to Table 2 & Fig. 5).

Mixed repeated measures ANOVA was conducted to assess differences among the groups on the Visual Analog Scale (VAS). Group (tACS at 10 Hz, real tACS, control, sham tACS, CBM, and CBM combined with tACS) served as the between-subject factor, while assessment time (pre-intervention, post-intervention, follow-up1, and follow-up2) was the within-subject factor. Similarities were observed between the groups at the pretest phase. However, significant differences were found among the groups [F (5, 41) = 1.99, $P = 0.05$, η2 = 0.20], as well as for the between-subject by within-subject interaction effect (TIME*GROUP) [F (15, 123) = 2.78, P < 0.001, η2 = 0.25], and the within-subject effect (TIME) [F (3, 123) = 18.43, P < 0.001, η2 = 0.31]. (Refer to Table 2 & Fig. 6). To clarify, we conducted separate ANOVA tests for each variable at the pre-test, post-test, follow-up 1, and follow-up 2 stages. The significant differences identified are marked with asterisks in the figures. For instance, in the DDQ, the CBM + tACS group showed a significant decrease compared to the Sham group after the post-test, and this difference remained significant in the follow-up. Additionally, VAS scores decreased in the CBM + tACS group compared to the control group in the post-test, and this significant difference persisted into follow-up 2 (Refer to Table 3).

4. Discussion

The current research examined the effects of five sessions of 10 Hz transcranial alternating current stimulation (tACS) and five sessions of tACS targeting the individual alpha frequency (IAF) on the bilateral dorsolateral prefrontal cortex (DLPFC). The stimulation involved anodal stimulation of the right hemisphere and cathodal stimulation of the left hemisphere. The study aimed to assess alterations in drug craving, anxiety, depression, and attention bias among individuals diagnosed with substance use disorders. The main objective was to evaluate the

Table 1
Demographic characteristics based on groups.

tACS ($n = 8$)	tACSr (n = 8)	Control ($n = 7$)	Sham (n = 8)		CBM (n = 7)	CBM + tACS ($n = 9$)	Statistical analyses
Marital status (single/married)	(5/3)	(6/2)	(5/2)	(5/3)	(3/4)	(5/4)	$\chi2(5) = 13.6$, $P = 0.56$
Prison (yes/no)	(2/6)	(5/3)	(4/3)	(3/5)	(3/5)	(5/4)	$\chi2(5) = 4.05$, $P = 0.54$
Selling dug (yes/no/no answere)	(0/6/1)	(2/4/2)	(2/4/1)	(3/5/0)	(0/6/1)	(4/5/0)	$\chi2(10) = 10.55$, $\boldsymbol{P} = 0.39$
Unset (S·D)	25.88 (5.27)	19.88 (5.35)	23.43 (5.88)	20.50 (3.70)	23.57 (6.32)	19.78 (3.73)	$F(5,41) = 1.98$, $P = 0.107$
Duration of addiction-years	9.50 (4.27)	6.63 (4.50)	7.43 (3.82)	7.38 (1.92)	7.14 (4.59)	11.00 (4.71)	$F(5,41) = 1.44$, $P = 0.23$
How many addicts do you know?	14.50 (8.14)	24.88 (31.45)	15.29 (12.25)	11.38 (6.27)	12.43 (8.63)	24.67 (28.95)	$F(5,41) = 0.77$, $P = 0.57$
Abstinance from substances-days	29.00 (11.50)	40.25 (27.91)	29.86 (12.72)	30.75 (13.37)	27.43 (14.21)	32.67 (13.51)	$F(5,41) = 0.59$, $P = 0.71$

Table 2
Mean and standard deviation of measures in the assessment sessions in the study groups.

Group, M (SD)						
Measures	tACS.10 hz	tACS. real	Control	Sham	CBM	CBM + tACS
Depression						
Pre-test	17.88 (2.74)	18.75 (2.43)	17.86 (5.87)	15.50 (6.02)	17.71 (4.92)	16.56 (5.17)
Post-test	16.38 (2.50)	16.13 (5.03)	16.86 (6.66)	13.88 (5.51)	16.71 (2.69)	11.67 (4.74)
Follow up 1	16.0 (2.33)	15.25 (2.71)	16.86 (5.01)	14.37 (5.50)	16.14 (3.43)	12.44 (3.39)
Follow up 2	15.75 (2.61)	16.0 (3.54)	17.29 (4.34)	15.0 (5.63)	15.86 (2.85)	12.56 (3.87)
Anxiety						
Pre-test	15.0 (2.77)	15.25 (3.01)	14.57 (3.73)	14.63 (4.74)	16.86 (2.79)	15.89 (4.25)
Post-test	12.75 (2.12)	14.63 (2.72)	13.86 (4.06)	13.13 (3.68)	16.14 (3.48)	11.33 (4.12)
Follow up 1	13.00 (1.85)	14.00 (1.85)	13.43 (4.11)	13.00 (2.4)	16.14 (2.61)	12.00 (3.27)
Follow up 2	12.13 (1.35)	13.63 (2.44)	15.00 (3.46)	13.75 (1.67	14.43 (2.23)	11.67 (2.44)
DDQ						
Pre-test	67.13 (10.69)	68.88 (6.81)	63.00 (7.87)	69.25 (10.74)	65.43 (8.79)	66.11 (7.20)
Post-test	61.0 (11.04)	60.50 (11.26)	64.29 (6.89)	66.13 (16.36)	55.86 (9.28)	49.89 (7.18)
Follow up 1	64.13 (9.17)	61.63 (8.45)	65.71 (5.64)	68.63 (9.11)	59.29 (12.07)	52.78 (8.41)
Follow up 2	63.50 (10.73)	62.38 (11.57)	63.14 (6.25)	65.75 (5.17)	59.86 (10.35)	52.56 (9.55)
VAS						
Pre-test	62.50 (24.92)	67.50 (13.62)	66.14 (20.75)	60.0 (14.88)	65.71 (13.67)	64.44 (15.29)
Post-test	64.38 (18.79)	50.63 (22.74)	71.43 (23.57)	61.88 (18.69)	47.14 (10.35)	41.11 (11.11)
Follow up 1	60.00 (15.11)	48.13 (16.46)	62.14 (14.96)	58.13 (15.33)	49.29 (23.17)	45.56 (13.09)
Follow up 2	59.38 (11.78)	50.63 (11.47)	67.14 (18.89)	61.88 (10.67)	52.14 (19.76)	46.44 (9.48)

Note: M: mean, SD: standard deviation, DDQ: Drug Dependence Questionar.

effectiveness of the two tACS techniques. However, no notable distinctions were detected between the two methods, and neither approach proved effective in alleviating cravings, anxiety, depression, or attention bias in individuals with substance use disorders.

The individual alpha frequency (IAF) tends to decline with age, which may have implications for cognitive functions in adulthood (Cesnaite et al., 2023). Garn et al. (2012) highlighted the dynamic nature of individual alpha frequencies, noting that they can fluctuate over time and in response to cognitive states. Similarly, Fresnoza et al. (2018) explored the impact of transcranial alternating current stimulation (tACS) on cortical excitability among both young and older individuals. Their findings indicated that tACS, personalized to each person's unique alpha frequency, enhanced cortical excitability in both age groups. Interestingly, while the study revealed changes in intracortical inhibition for both groups, the underlying mechanisms differed. Nonetheless, the overall positive effects of tACS were comparable across age groups, with no significant performance differences based on age.

Moreover, Fresnoza et al. (2018) noted a rise in GABA levels among the elderly participants and a decline in the younger group post-stimulation. This observation implies that adults may find motor sequence learning advantageous through diminished GABA-mediated inhibition in the sensory-motor cortex. In essence, the study underscored the potential of tACS as a valuable instrument for manipulating oscillatory activity to achieve therapeutic outcomes and cognitive enhancement.

In essence, the studies conducted by Grandy et al. (2013) and Fresnoza et al. (2018) present divergent views regarding the stability and adaptability of individual alpha frequency (IAF) and its response to cognitive interventions. While Grandy et al. (2013) suggest that IAF remains relatively unchanged, Fresnoza et al. (2018) offer evidence supporting the idea that IAF can be modified through techniques like tACS, thereby showcasing its potential for cognitive enhancement. Nevertheless, further investigation is warranted to reconcile these disparate findings and gain a comprehensive understanding of the implications for cognitive interventions aimed at manipulating individual alpha frequency.

Transcranial electrical stimulation (tACS) has shown promise in enhancing mood and cognition among individuals with major depression, as indicated by a study conducted by Haller et al. (2020). In this research, six participants diagnosed with severe depression were divided into two groups. The first group received two sessions of 10-min stimulation, while the second group underwent ten consecutive days of 20-min stimulation.

The findings indicated a notable decrease in Hamilton depression and Beck depression rating scale scores for both groups. The first group exhibited reductions of 85 % and 78 %, respectively, while the second group showed reductions of 62 % and 24 %, signifying an amelioration of depressive symptoms throughout the treatment duration. Furthermore, enhancements in cognitive function were evident based on the N-Back test results, implying a favorable influence of tACS on cognitive performance.

The results imply that tACS might facilitate the synchronization of disrupted frequency bands within the frontal and prefrontal cortex regions of the brain (Vossen et al., 2015). This synchronization possibly accounts for the observed enhancements in mood and cognitive function, underscoring the therapeutic promise of tACS for individuals grappling with major depression (Chander et al., 2016). Nevertheless, further investigation employing larger sample sizes and controlled experimental designs is imperative to validate these findings and elucidate the mechanisms driving the observed effects (Ruffini et al., 2014).

Basanovic et al. (2019) implemented Cognitive Bias Modification (CBM) as a preventive strategy for depression in mid- to late-life individuals. The study comprised twenty Australian adults diagnosed with depression and utilized a controlled trial design. The intervention, delivered via computer-based methods, spanned a duration of 52 weeks.

The secondary findings of the study revealed modifications in

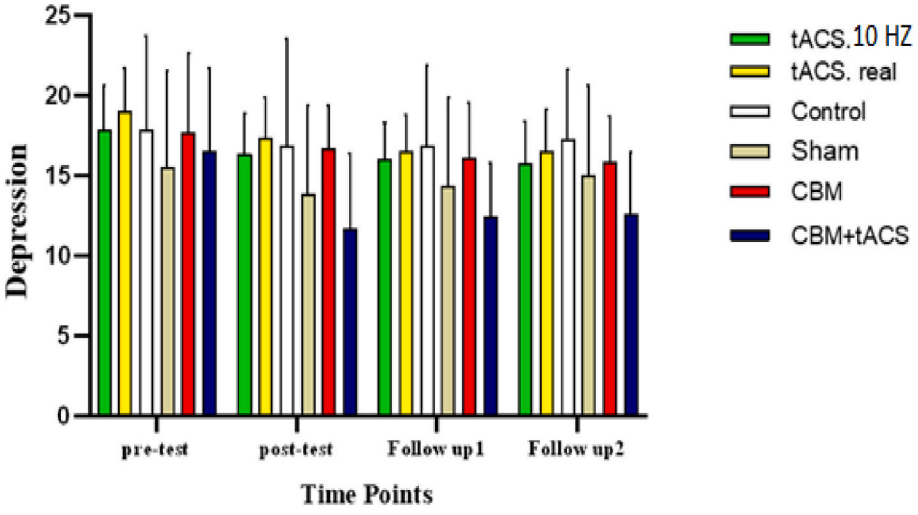


Fig. 3. Time points(depression) This figure presents the Depression scores at different time points (pre-test, post-test, follow-up 1, and follow-up 2) for various intervention groups: tACS 10 Hz, tACS real, Control, Sham, CBM, and CBM + tACS. The graph illustrates the changes in depression levels over time for each group, enabling a comparison of the effectiveness of the treatments.

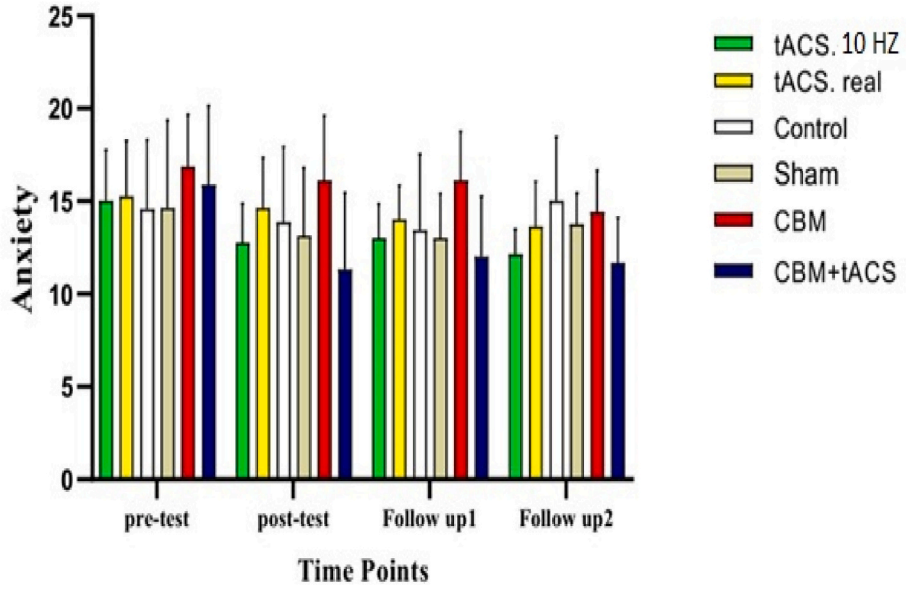


Fig. 4. Time points(Anxiety). This figure shows the Depression and Anxiety scores across different time points (pre-test, post-test, follow-up 1, and follow-up 2) for various groups: tACS 10 Hz, tACS real, Control, Sham, CBM, and CBM + tACS. The data indicates trends in the levels of depression and anxiety over time across the different intervention groups, allowing for comparison of the efficacy of each treatment.

depression severity alongside alterations in attention and interpretation biases. However, the primary outcomes indicated the incidence of major depression according to DSM-IV-TR criteria. Interestingly, by the sixth week of the intervention, a statistically significant contrast in depression symptoms emerged between the active CBM group and the control group (Basanovic et al., 2019).

Additionally, Fodor et al. (2020) conducted a systematic review and network meta-analysis to evaluate the efficacy of CBM in treating depression and anxiety disorders. The review indicated that although CBM shows a sustainable effect, its effectiveness magnitude is modest. These results highlight the potential of CBM as a depression intervention; nevertheless, further research is necessary to thoroughly assess its long-term efficacy and clinical applicability (Fodor et al., 2020).

The results of the present study unveiled a notable discrepancy in the decrease of anxiety, depression, and attentional bias among individuals with a background of opium use when comparing the combined application of tACS and CBM techniques to their individual usage. However, the findings indicated no significant variation in craving reduction among individuals with a history of opioid use when contrasting the combined tACS and CBM approaches to their separate utilization. Consistent with these findings, Mondino et al. (2020) delved into the concurrent application of attention bias modification (ABM) and transcranial alternating current stimulation (tACS) in smokers to mitigate cravings and impulsive decision-making. The study featured two cohorts: one subjected to ABM alongside active tACS stimulation, while the other underwent sham ABM stimulation. ABM was employed to gauge attentional bias towards smoking cues using eye-tracking technology and reaction time assessments via a visual-probe task during passive exposure to smoking and neutral cues. Craving was evaluated through a questionnaire gauging the urge to smoke and impulsive decision-making while anticipating a reward. Results revealed that when coupled with ABM, active tACS reduced the duration of viewing

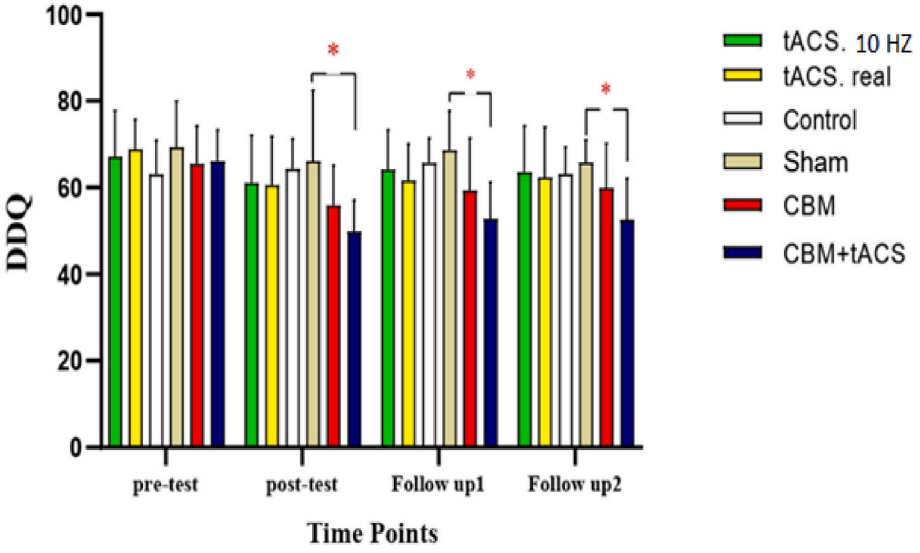


Fig. 5. Time points DDQ. This figure illustrates the DDQ scores across different time points (pre-test, post-test, follow-up 1, and follow-up 2) for various groups: tACS 10 Hz, tACS real, Control, Sham, CBM, and CBM + tACS. The asterisks (*) indicate significant differences between groups. Specifically, the CBM + tACS group showed a significant decrease in DDQ scores compared to the Sham group in the post-test and follow-up phases, indicating a persistent reduction in symptoms.

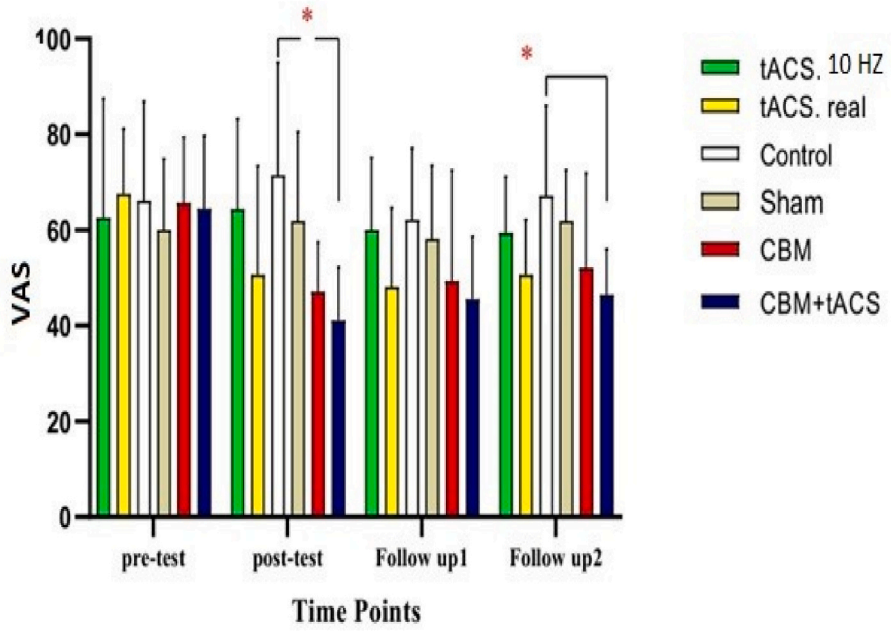


Fig. 6. Time points(VAS) This figure depicts the VAS scores across the same time points (pre-test, post-test, follow-up 1, and follow-up 2) for the groups mentioned above. Significant differences between groups are marked with asterisks (*). Notably, the CBM + tACS group demonstrated a significant reduction in VAS scores compared to the Control group in the post-test, and this significant difference was maintained in follow-up 2, suggesting sustained improvements.

smoking images ($p = 0.03$), arrested the rise in spontaneous urge to smoke ($p = 0.026$), and diminished the proportion of impulsive choices ($P = 0.049$) compared to sham and ABM alone. However, no statistically significant distinctions were noted in other facets of craving based on reaction time in this investigation.

Kroczek et al. (2016) explored the effects of transcranial direct current stimulation (tDCS) on craving, heart rate variability, and prefrontal brain hemodynamics when exposed to cigarette cues. The study involved twenty-nine participants randomly allocated to three groups: control (placebo), randomized, and double-blind, with a mean age of 25 years and a standard deviation of 5. During the tDCS procedure, the anode was positioned over the dorsal prefrontal cortex, while the cathode was placed over the orbitofrontal region, administering a current intensity of 2 mA. Results revealed that exposure to cigarette cues heightened subjective craving and induced changes in heart rate among smokers. Additionally, stronger connectivity between the orbitofrontal and dorsolateral prefrontal cortices was observed in the group receiving active stimulation compared to the placebo group. However, tDCS did not yield a significant difference in craving levels or heart rate variability during exposure to cigarette cues.

Salemink et al. (2014) utilized Cognitive Bias Modification (CBM) as a treatment for anxiety in patients. The experimental group ($n = 18$) received positive interpretations of ambiguous social situations online for eight days, whereas the control group (n = 18) received a combination of 50 % positive and 50 % negative interpretations. Results showed that participants in the experimental group exhibited a stronger

Table 3
The result of mixed repeated ANOVAs for effect of group and time on mental distress and drug dependance.

Task	Source	df	F	*P*-Value	Partial eta
Depression	Time	3–123	17.873	0.001	0.304
	Group	5–41	1.104	0.373	0.119
	Time*Group	15–123	1.653	0.069	0.168
Anxiety	Time	3–123	13.314	0.001	0.245
	Group	5–41	1.261	0.299	0.133
	Time*Group	15–123	2.057	0.028	0.201
DDQ	Time	3–123	18.43	0.001	0.31
	Group	5–41	1.99	0.049	0.20
	Time*Group	15–123	2.78	0.001	0.25
VAS	Time	3–123	7.17	0.001	0.16
	Group	5–41	1.76	0.142	0.177
	Time*Group	15–123	1.86	0.034	0.18

inclination towards positive interpretations compared to those in the control group. Furthermore, both groups reported reductions in anxiety, depression, and psychological tension.

In Fodor et al.'s (2020) systematic review on cognitive bias modification (CBM) interventions targeting anxiety and depression disorders in individuals aged 18 years and older, studies were selected based on the inclusion of subjects with clinical or subclinical levels of anxiety or depression. The review uncovered consistent yet modest benefits associated with CBM interventions. However, it's worth noting that the presence of heterogeneity and potential bias in the reviewed studies could impact the reliability of these findings.

The lack of significant differences at the pre-test stage across all variables suggests that the randomization process was successful, ensuring comparable baseline characteristics among the groups. This consistency is crucial as it strengthens the validity of the subsequent findings.

The significant within-subject effects over time across most variables indicate that the interventions had a meaningful impact on the participants, regardless of the group. This highlights the overall effectiveness of the treatment protocols in influencing outcomes such as anxiety, depression, drug dependence, and VAS scores.

The significant interaction effects between time and group in some variables, such as anxiety and drug dependence, suggest that certain interventions may have been more effective than others over time. For example, the combination of CBM and tACS appeared to be particularly effective, resulting in significant improvements that persisted through the follow-up stages. This could be due to the synergistic effects of combining cognitive-behavioral approaches with neuromodulation, which may enhance the overall therapeutic impact.

In terms of the non-significant interaction effects observed in some variables, it is possible that the sample size limited the power to detect more subtle differences. Alternatively, the effects of certain interventions may take longer to manifest or may be more sensitive to individual differences in response to treatment. These findings could inform future research by highlighting the need for larger sample sizes or longer follow-up periods to capture the full extent of the interventions' effects.

Overall, these results contribute to the growing body of evidence on the effectiveness of tACS and CBM in treating substance use disorders. They suggest that while both interventions are effective, their combination may offer enhanced benefits, particularly in reducing drug dependence and improving psychological well-being. This aligns with previous research suggesting that multimodal approaches can be more effective than single interventions, particularly in complex conditions like substance use disorders.

4.1. Limitations

The present study has several limitations that warrant consideration when interpreting the results. Firstly, the implementation of randomization was hindered by restricted participant access, leading to a less rigorous randomization process than desired. This challenge was compounded by the small sample size ($N = 72$, with 12 participants per group), which is a common constraint in experimental studies involving clinical populations, such as individuals with opium use disorder in rehabilitation settings. Recruiting participants who met our strict inclusion criteria—abstinent for at least one week but not more than one month post-withdrawal, with minimal physical pain—proved difficult, and follow-up was further complicated by external factors (e.g., participant mortality, incarceration, or unavailability). While small sample sizes are typical in such trials, they reduce statistical power and limit the generalizability of findings.

Secondly, our reliance on mixed repeated measures ANOVA as the primary statistical method may introduce additional limitations, particularly given the small sample size. ANOVA assumes normality of data distribution and relies on the central limit theorem, which may not hold robustly with small samples. As a result, non-normal distributions could potentially skew the results, reducing the reliability of the test. Alternative approaches, such as non-parametric tests (e.g., Kruskal-Wallis or Friedman tests) or Bayesian statistical methods, might have been more suitable for handling non-normality and providing greater robustness in this context. However, we chose to retain ANOVA due to its suitability for analyzing the study's repeated measures design and its widespread use in similar clinical research, which facilitates comparison with existing literature. To address this concern, we acknowledge that the statistical tests employed may not be optimal under these conditions, and this limitation could affect the interpretation of our findings.

Thirdly, the reliance on verbal induction of drug craving, which required researcher presence for measurement, coupled with challenges in coordinating participant attendance at treatment centers, resulted in unsuccessful follow-up attempts for some participants. This methodological constraint may have introduced bias into the craving assessments. Additionally, the study utilized a single measure (the dot probe task) to assess and modify cognitive bias. Incorporating multiple measures of attention bias could have provided a more comprehensive evaluation of its role in craving-related outcomes.

Further limitations include the restricted number of tACS sessions (five), which may not have been sufficient to elicit significant and lasting effects, as prior studies suggest that extended stimulation periods enhance efficacy (Kuo et al., 2014). Technical constraints also affected the precision of individual alpha frequency (IAF) stimulation; the tACS device required whole-number frequency inputs, necessitating rounding of IAF values (e.g., from 10.6 Hz to 11 Hz), which may have reduced the effectiveness of tailored stimulation (Zaehle et al., 2010). Finally, the heterogeneity of opium use among participants—such as variations in type, amount, duration, and cessation attempts—could not be fully assessed or controlled, potentially influencing baseline cognitive and emotional states and, consequently, treatment outcomes (Rounsaville et al., 2003).

Despite these limitations, we proceeded with the current methodology to maintain consistency with the study's original design and to align with established practices in the field. The findings still offer valuable insights into the application of tACS and CBM for substance use disorders, though future research should address these shortcomings by employing larger samples, more precise frequency matching, additional bias measures, and alternative statistical approaches to enhance robustness and validity.

5. Conclusion

In conclusion, the study investigated the impact of two transcranial alternating current stimulation (tACS) methods—10 Hz and individual alpha frequency (IAF)—on individuals with substance use disorders, focusing on outcomes such as drug craving, anxiety, depression, and attention bias. Despite the application of both tACS methods, no significant differences were observed in alleviating these issues, nor did

either method prove more effective than the other. The combined use of tACS with cognitive bias modification (CBM) did show some promise, particularly in reducing attention bias, but did not significantly improve craving reduction compared to using tACS or CBM alone.

The research also highlighted limitations, including a small sample size, technical constraints with frequency matching, and variability in opium use among participants. These limitations may have impacted the study's findings and suggest the need for further research with larger samples, more precise frequency matching, and more detailed assessments of substance use history.

Overall, while the current study did not find significant improvements in the targeted outcomes, it underscores the potential for tACS and CBM interventions and emphasizes the necessity for more refined methodologies and extended treatment durations in future research. Addressing these factors could provide a clearer understanding of the efficacy and mechanisms of these interventions, ultimately contributing to more effective treatments for substance use disorders.

CRediT authorship contribution statement

Kiyanoosh Papi: Methodology, Investigation, Conceptualization. **Masoud Nosratabadi:** Supervision, Conceptualization. **Farhad Taremian:** Visualization. **Nikzad Ghanbari:** Writing – original draft, Formal analysis. **Maryam Ebrahimi Varkiyani:** Resources, Project administration.

Declaration of Generative AI and AI-assisted technologies in the writing process

During the preparation of this work, the authors used ChatGPT in order to improve language and readability. After using this tool, the authors reviewed and edited the content as needed and takes full responsibility for the content of the publication.

Declaration of competing interest

The authors whose names are listed immediately below certify that they have NO affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

Acknowledgments

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Data availability

The data that supports the findings of this study are available from the corresponding author, upon request.

References

Asghari, A., Saed, F., & Dibajnia, P. (2008). Psychometric properties of the depression anxiety stress Scales-21 (DASS-21) in a non-clinical Iranian sample. *International Journal of Psychology, 2*(2), 82–102.

Baker, A. L., Kavanagh, D. J., Kay-Lambkin, F. J., Hunt, S. A., Lewin, T. J., Carr, V. J., & McElduff, P. (2014). Randomized controlled trial of MICBT for co-existing alcohol misuse and depression: Outcomes to 36-months. *Journal of Substance Abuse Treatment, 46*(3), 281–290.

Basanovic, J., Grafton, B., Ford, A., Hirani, V., Glance, D., MacLeod, C., & Almeida, O. (2019). Cognitive bias modification to prevent depression (COPE): Results of a randomised controlled trial. *Psychological Medicine, 50*, 1–12. https://doi.org/10.1017/S0033291719002599

Bocci, T., De Carolis, G., Ferrucci, R., Paroli, M., Mansani, F., Priori, A., & Sartucci, F. (2019). Cerebellar transcranial direct current stimulation (ctDCS) ameliorates phantom limb pain and non-painful phantom limb sensations. *The Cerebellum, 18*, 527–535.

Boggio, P. S., Zaghi, S., Villani, A. B., Fecteau, S., Pascual-Leone, A., & Fregni, F. (2010). Modulation of risk-taking in marijuana users by transcranial direct current stimulation (tDCS) of the dorsolateral prefrontal cortex (DLPFC). *Drug and Alcohol Dependence, 112*(3), 220–225.

Bollen, Z., Pabst, A., Masson, N., Wiers, R. W., Field, M., & Maurage, P. (2024). Craving modulates attentional bias towards alcohol in severe alcohol use disorder: An eye-tracking study. *Addiction, 119*(1), 102–112.

Brown, T. A., Chorpita, B. F., Korotitsch, W., & Barlow, D. H. (1997). Psychometric properties of the depression anxiety stress scales (DASS) in clinical samples. *Behaviour Research and Therapy, 35*(1), 79–89.

Buckner, J. D., Zvolensky, M. J., Crosby, R. D., Wonderlich, S. A., Ecker, A. H., & Richter, A. (2015). Antecedents and consequences of cannabis use among racially diverse cannabis users: An analysis from ecological momentary assessment. *Drug and Alcohol Dependence, 147*, 20–25.

Cecere, R., Rees, G., & Romei, V. (2015). Individual differences in alpha frequency drive cross modal illusory perception. *Current Biology, 25*(2), 231–235.

Cesnaite, E., Steinfath, P., Idaji, M. J., Stephani, T., Kumral, D., Haufe, S., & Riedel-Heller, S. (2023). Alterations in rhythmic and non-rhythmic resting-state EEG activity and their link to cognition in older age. *Neuroimage, 268*, Article 119810.

Chander, B. S., Witkowski, M., Braun, C., Robinson, S. E., Born, J., Cohen, L. G., & Soekadar, S. R. (2016). tACS phase locking of frontal midline theta oscillations disrupts working memory performance. *Frontiers in Cellular Neuroscience, 10*, 120.

Corcoran, A. W., Alday, P. M., Schlesewsky, M., & Bornkessel-Schlesewsky, I. (2018). Toward a reliable, automated method of individual alpha frequency (IAF) quantification. *Psychophysiology, 55*(7), Article e13064.

Culbertson, C., Nicolas, S., Zaharovits, I., London, E. D., Richard De La Garza, I., Brody, A. L., & Newton, T. F. (2010). Methamphetamine craving induced in an online virtual reality environment. *Pharmacology Biochemistry and Behavior, 96*(4), 454–460.

Dunlop, K., Hanlon, C. A., & Downar, J. (2017). Noninvasive brain stimulation treatments for addiction and major depression. *Annals of the New York Academy of Sciences, 1394*(1), 31–54.

Dutra, L., Stathopoulou, G., Basden, S. L., Leyro, T. M., Powers, M. B., & Otto, M. W. (2008). A meta-analytic review of psychosocial interventions for substance use disorders. *American Journal of Psychiatry, 165*(2), 179–187.

Faridi, A., Taremian, F., Thatcher, R. W., Dadashi, M., & Moloodi, R. (2022). Comparing LORETA Z score neurofeedback and cognitive rehabilitation regarding their effectiveness in reducing craving in opioid addicts. *Basic and Clinical Neuroscience, 13*(1), 81.

Field, M., Werthmann, J., Franken, I., Hofmann, W., Hogarth, L., & Roefs, A. (2016). *The role of attentional bias in obesity and addiction* (Vol. 35). American Psychological Association.

Fodor, L. A., Georgescu, R., Cuijpers, P., Szamoskozi, Ş., David, D., Furukawa, T. A., & Cristea, I. A. (2020). Efficacy of cognitive bias modification interventions in anxiety and depressive disorders: A systematic review and network meta-analysis. *The Lancet Psychiatry, 7*(6), 506–514.

Franken, I. H., Hendriks, V. M., & van den Brink, W. (2002). Initial validation of two opiate craving questionnaires: The obsessive compulsive drug use scale and the desires for drug questionnaire. *Addictive Behaviors, 27*(5), 675–685.

Fresnoza, S., Christova, M., Feil, T., Gallasch, E., Körner, C., Zimmer, U., & Ischebeck, A. (2018). The effects of transcranial alternating current stimulation (tACS) at individual alpha peak frequency (iAPF) on motor cortex excitability in young and elderly adults. *Experimental Brain Research, 236*(10), 2573–2588. https://doi.org/10.1007/s00221-018-5314-3

Garn, H., Waser, M., Lechner, M., Dorfer, M., & Grossegger, D. (2012). *Robust, automatic real-time monitoring of the time course of the individual alpha frequency in the time and frequency domain, 2012*.

Gipson, C. D., & Beckmann, J. S. (2023). Compulsion and substance use disorder: Potential importance of boundary conditions. *Neuropsychopharmacology, 48*(3), 432–433.

Grandy, T. H., Werkle-Bergner, M., Chicherio, C., Lövdén, M., Schmiedek, F., & Lindenberger, U. (2013). Individual alpha peak frequency is related to latent factors of general cognitive abilities. *Neuroimage, 79*, 10–18. https://doi.org/10.1016/j.neuroimage.2013.04.059

Gupta, A., Murthy, P., & Rao, S. (2018). Brief screening for cognitive impairment in addictive disorders. *Indian Journal of Psychiatry, 60*(Suppl. 4), S451–S456.

Haegens, S., Cousijn, H., Wallis, G., Harrison, P. J., & Nobre, A. C. (2014). Inter-and intra-individual variability in alpha peak frequency. *NeuroImage, 92*, 46–55.

Haller, N., Senner, F., Brunoni, A. R., Padberg, F., & Palm, U. (2020). Gamma transcranial alternating current stimulation improves mood and cognition in patients with major depression. *Journal of Psychiatric Research, 130*, 31–34.

Harvey, A. G., Watkins, E., & Mansell, W. (2004). *Cognitive behavioural processes across psychological disorders: A transdiagnostic approach to research and treatment*. USA: Oxford University Press.

Hassani-Abharian, P., Mokri, A., Ganjgahi, H., Oghabian, M. A., & Ekhtiari, H. (2016). Validation for Persian versions of "desire for drug questionnaire" and "obsessive compulsive drug use scale" in heroin dependents. *Archives of Iranian Medicine, 19*(9).

Hone-Blanchet, A., Ciraulo, D. A., Pascual-Leone, A., & Fecteau, S. (2015). Noninvasive brain stimulation to suppress craving in substance use disorders: Review of human evidence and methodological considerations for future work. *Neuroscience & Biobehavioral Reviews, 59*, 184–200.

Hormes, J. M., & Rozin, P. (2010). Does "craving" carve nature at the joints? Absence of a synonym for craving in many languages. *Addictive Behaviors, 35*(5), 459–463.
Kelly, T. M., & Daley, D. C. (2013). Integrated treatment of substance use and psychiatric disorders. *Social Work in Public Health, 28*(3–4), 388–406.
Kroczek, A., Häußinger, F., Rohe, T., Schneider, S., Plewnia, C., Batra, A., & Ehlis, A.-C. (2016). Effects of transcranial direct current stimulation on craving, heart-rate variability and prefrontal hemodynamics during smoking cue exposure. *Drug and Alcohol Dependence, 168*, 123–127.
Kuo, H. I., Bikson, M., Datta, A., Minhas, P., Paulus, W., Kuo, M. F., & Nitsche, M. A. (2014). Comparing cortical plasticity induced by conventional and high-definition 4× 1 ring tDCS: A neurophysiological study. *Brain Stimulation, 6*(4), 645–648.
Lancee, J., Yasiney, S. L., Brendel, R. S., Boffo, M., Clarke, P. J. F., & Salemink, E. (2017). Attentional bias modification training for insomnia: A double-blind placebo controlled randomized trial. *PLoS One, 12*(4), Article e0174531. https://doi.org/10.1371/journal.pone.0174531
Leichsenring, F., & Rabung, S. (2008). Effectiveness of long-term psychodynamic psychotherapy: A meta-analysis. *Jama, 300*(13), 1551–1565.
Lovibond, S. H., & Lovibond, P. F. (1995). The structure of negative emotional states: Comparison of the Depression Anxiety Stress Scales (DASS) with the Beck Depression and Anxiety Inventories. *Behaviour Research and Therapy, 33*(3), 335–343. https://doi.org/10.1016/0005-7967(94)00075-U
Lyvers, M., & Yakimoff, M. (2003). Neuropsychological correlates of opioid dependence and withdrawal. *Addictive Behaviors, 28*(3), 605–611.
MacLean, R. R., Sofuoglu, M., Brede, E., Robinson, C., & Waters, A. J. (2018). Attentional bias in opioid users: A systematic review and meta-analysis. *Drug and Alcohol Dependence, 191*, 270–278. https://doi.org/10.1016/j.drugalcdep.2018.07.012
Marissen, M. A., Franken, I. H., Waters, A. J., Blanken, P., van den Brink, W., & Hendriks, V. M. (2006). Attentional bias predicts heroin relapse following treatment. *Addiction, 101*(9), 1306–1312. https://doi.org/10.1111/j.1360-0443.2006.01498.x
McHugh, R. K., Hearon, B. A., & Otto, M. W. (2010). Cognitive behavioral therapy for substance use disorders. *Psychiatric Clinics, 33*(3), 511–525.
Moghaddam, A., Saed, F., Dibajnia, P., & Zangeneh, J. (2008). A preliminary validation of the depression, anxiety and stress scales (DASS) in non-clinical sample. *Daneshvar Medicine, 1*, 23–38.
Mondino, M., Lenglos, C., Cinti, A., Renauld, E., & Fecteau, S. (2020). Eye tracking of smoking-related stimuli in tobacco use disorder: A proof-of-concept study combining attention bias modification with alpha-transcranial alternating current stimulation. *Drug and Alcohol Dependence, 214*, Article 108152.
Nunez, P. L., Wingeier, B. M., & Silberstein, R. B. (2001). Spatial-temporal structures of human alpha rhythms: Theory, microcurrent sources, multiscale measurements, and global binding of local networks. *Human Brain Mapping, 13*(3), 125–164.
Ouzir, M., & Errami, M. (2016). Etiological theories of addiction: A comprehensive update on neurobiological, genetic and behavioural vulnerability. *Pharmacology, Biochemistry, and Behavior, 148*, 59–68. https://doi.org/10.1016/j.pbb.2016.06.005
Papi, K., Nosratabadi, M., MohamadDocheshmeh, A., Varkiyani, M. E., Soleimani, A., Ghasemi, S. A., & Karkaragh, F. F. (2024). *Transcranial alternating current stimulation: Impact on attention, memory, and performance in shooting training*.
Paulus, W. (2011). Transcranial electrical stimulation (tES - tDCS; tRNS, tACS) methods. *Neuropsychological Rehabilitation, 21*(5), 602–617. https://doi.org/10.1080/09602011.2011.557292
Posthuma, D., Neale, M., Boomsma, D., & Geus, E. (2001). Are smarter brains running faster? Heritability of alpha peak frequency, IQ, and their interrelation. *Behavior Genetics, 31*, 567–579. https://doi.org/10.1023/A:1013345411774
Preston, K. L., & Epstein, D. H. (2011). Stress in the daily lives of cocaine and heroin users: Relationship to mood, craving, relapse triggers, and cocaine use. *Psychopharmacology, 218*(1), 29–37. https://doi.org/10.1007/s00213-011-2183-x
Rezapour, T., Hatami, J., Farhoudian, A., Noroozi, A., Daneshmand, R., Sofuoglu, M., & Ekhtiari, H. (2021). Baseline executive functions and receiving cognitive rehabilitation can predict treatment response in people with opioid use disorder. *Journal of Substance Abuse Treatment, 131*, Article 108558. https://doi.org/10.1016/j.jsat.2021.108558
Riesel, A., Klawohn, J., Grützmann, R., Kaufmann, C., Heinzel, S., Bey, K., & Kathmann, N. (2019). Error-related brain activity as a transdiagnostic endophenotype for obsessive-compulsive disorder, anxiety and substance use disorder. *Psychological Medicine, 49*(7), 1207–1217. https://doi.org/10.1017/s0033291719000199
Romei, V., Thut, G., & Silvanto, J. (2016). Information-based approaches of noninvasive transcranial brain stimulation. *Trends in Neurosciences, 39*(11), 782–795.
Rounsaville, B. J., Petry, N. M., & Carroll, K. M. (2003). Single versus multiple drug focus in substance abuse clinical trials research. *Drug and Alcohol Dependence, 70*(2), 117–125.
Ruffini, G., Fox, M. D., Ripolles, O., Miranda, P. C., & Pascual-Leone, A. (2014). Optimization of multifocal transcranial current stimulation for weighted cortical pattern targeting from realistic modeling of electric fields. *Neuroimage, 89*, 216–225.
Salemink, E., Kindt, M., Rienties, H., & van den Hout, M. (2014). Internet-based cognitive bias modification of interpretations in patients with anxiety disorders: A randomised controlled trial. *Journal of Behavior Therapy and Experimental Psychiatry, 45*(1), 186–195. https://doi.org/10.1016/j.jbtep.2013.10.005
Scally, B., Burke, M. R., Bunce, D., & Delvenne, J. F. (2018). Resting-state EEG power and connectivity are associated with alpha peak frequency slowing in healthy aging. *Neurobiology of Aging, 71*, 149–155. https://doi.org/10.1016/j.neurobiolaging.2018.07.004
Singh, Y., & Sharma, R. (2015). Individual alpha frequency (IAF) based quantitative EEG correlates of psychological stress. *Indian Journal of Physiology and Pharmacology, 59*(4), 414–421.
Sinha, R., Fox, H. C., Hong, K. I., Hansen, J., Tuit, K., & Kreek, M. J. (2011). Effects of adrenal sensitivity, stress- and cue-induced craving, and anxiety on subsequent alcohol relapse and treatment outcomes. *Archives of General Psychiatry, 68*(9), 942–952. https://doi.org/10.1001/archgenpsychiatry.2011.49
Sripada, C. (2022). Impaired control in addiction involves cognitive distortions and unreliable self-control, not compulsive desires and overwhelmed self-control. *Behavioural Brain Research, 418*, Article 113639. https://doi.org/10.1016/j.bbr.2021.113639
Stecher, H. I., & Herrmann, C. S. (2018). Absence of alpha-tACS aftereffects in darkness reveals importance of taking derivations of stimulation frequency and individual alpha variability into account. *Frontiers in Psychology, 9*, 984.
Suslow, T., Hußlack, A., Kersting, A., & Bodenschatz, C. M. (2020). Attentional biases to emotional information in clinical depression: A systematic and meta-analytic review of eye tracking findings. *Journal of Affective Disorders, 274*, 632–642. https://doi.org/10.1016/j.jad.2020.05.140
Swan, N., & Chang, L. (2003). New imaging technology confirms earlier PET scan evidence: Methamphetamine abuse linked to human brain damage. *NIDA Notes, 18*(2), 6.
Tavakoli, A. V., & Yun, K. (2017). Transcranial alternating current stimulation (tACS) mechanisms and protocols. *Frontiers in Cellular Neuroscience, 11*, 214.
Thomas, C. L., Goegan, L. D., Newman, K. R., Arndt, J. E., & Sears, C. R. (2013). Attention to threat images in individuals with clinical and subthreshold symptoms of post-traumatic stress disorder. *Journal of Anxiety Disorders, 27*(5), 447–455.
Vafaie, N., & Kober, H. (2022). Association of Drug Cues and Craving with Drug use and relapse: A systematic review and Meta-analysis. *JAMA Psychiatry, 79*(7), 641–650. https://doi.org/10.1001/jamapsychiatry.2022.1240
Vossen, A., Gross, J., & Thut, G. (2015). Alpha power increase after transcranial alternating current stimulation at alpha frequency (α-tACS) reflects plastic changes rather than entrainment. *Brain Stimulation, 8*(3), 499–508. https://doi.org/10.1016/j.brs.2014.12.004
Wells, T. T., & Beevers, C. G. (2010). Biased attention and dysphoria: Manipulating selective attention reduces subsequent depressive symptoms. *Cognition and Emotion, 24*(4), 719–728. https://doi.org/10.1080/02699930802652388
Wiers, R. W., Houben, K., Fadardi, J. S., van Beek, P., Rhemtulla, M., & Cox, W. M. (2015). Alcohol cognitive bias modification training for problem drinkers over the web. *Addictive Behaviors, 40*, 21–26. https://doi.org/10.1016/j.addbeh.2014.08.010
Wieser, M. J., & Keil, A. (2020). Attentional threat biases and their role in anxiety: A neurophysiological perspective. *International Journal of Psychophysiology, 153*, 148–158. https://doi.org/10.1016/j.ijpsycho.2020.05.004
Wischnewski, M., Schutter, D. J. L. G., & Nitsche, M. A. (2019). Effects of beta-tACS on corticospinal excitability: A meta-analysis. *Brain Stimulation, 12*(6), 1381–1389. https://doi.org/10.1016/j.brs.2019.07.023
Wu, L., Liu, T., & Wang, J. (2021). Improving the effect of transcranial alternating current stimulation (tACS): A systematic review. *Frontiers in Human Neuroscience, 15*. https://doi.org/10.3389/fnhum.2021.652393
Zaehle, T., Rach, S., & Herrmann, C. S. (2010). Transcranial alternating current stimulation enhances individual alpha activity in human EEG. *PLoS One, 5*(11), Article e13766.