Research Paper

The Effects of Transcranial Direct Current Stimulation on Anxiety and Neural Oscillations in Generalized Anxiety Disorder: A Clinical Investigation

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ABSTRACT

Introduction: Generalized anxiety disorder (GAD) is a chronic psychiatric condition characterized by persistent, excessive, and uncontrollable worry, leading to significant impairments in cognitive and emotional functioning. Previous research has established a strong association between heightened anxiety and deficits in attention and concentration. Neurophysiological evidence suggests that theta wave activity plays a crucial role in attention regulation, while both alpha and theta waves are implicated in the modulation of anxiety-related neural processes.

Methods: Given these findings, the present study aims to evaluate the effectiveness of transcranial direct current stimulation (tDCS) in modulating the absolute power of alpha and theta brain waves and enhancing visual and auditory attention in individuals diagnosed with GAD. This single-blind, randomized controlled study was conducted in Tabriz City, Iran, between 2023 and 2024 and involved 24 patients diagnosed with GAD. Participants, aged 18 to 40 years, were randomly assigned to either the experimental group (n=12) or the control group (n=12) following a comprehensive psychiatric evaluation and screening using the GAD 7-item (GAD-7) scale, which assesses the impact of GAD on personal, social, familial, and occupational functioning.

Results: The findings revealed significant modulation of alpha and theta wave activity, along with improvements in visual and auditory attention in individuals with GAD. Specifically, in the experimental group, theta wave power decreased from 5.26 to 2.80 μV^2, and alpha wave power increased from 9.66 to 5.06 μV^2. Concurrently, visual attention scores improved from 120.13 to 190.86, and auditory attention scores increased from 118.73 to 150.33 following the tDCS intervention. These improvements were accompanied by statistically significant P-values and large effect sizes.

Conclusion: This study suggests that tDCS effectively modulates alpha and theta brain wave activity, thereby enhancing attentional and auditory performance in individuals with GAD. These findings provide further support for the potential therapeutic benefits of tDCS in managing anxiety-related cognitive deficits. Future research should focus on optimizing stimulation protocols and investigating the long-term efficacy and sustainability of tDCS effects in clinical settings.

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Highlights

- Orbitofrontal tDCS modulated alpha and theta activity in patients with GAD.
- Active tDCS improved visual and auditory attention compared with sham.
- Fifteen tDCS sessions produced large neurocognitive effect sizes.
- Greater baseline anxiety was associated with larger attention improvements.

Plain Language Summary

Generalized anxiety disorder (GAD) involves persistent and excessive worry and can make it difficult to concentrate. This study examined whether transcranial direct current stimulation (tDCS), a non-invasive technique that applies a weak electrical current to the scalp, could improve attention and alter brain activity in people with GAD. Twenty-four adults were randomly assigned to receive either active or sham stimulation. The active group completed 15 sessions over five weeks, targeting the orbitofrontal areas involved in emotional and attentional regulation. Brainwave activity and visual and auditory attention were assessed before and after treatment. Compared with sham stimulation, active tDCS was associated with changes in alpha and theta brainwaves and improvements in several aspects of attention. Participants with more severe anxiety at baseline appeared to show greater improvements. However, because the study included few participants and no long-term follow-up, larger studies are needed before tDCS can be recommended as a routine treatment for GAD.

Introduction

Generalized anxiety disorder (GAD) is a debilitating psychological condition marked by persistent, excessive, and uncontrollable worry that significantly impairs daily functioning. According to the diagnostic and statistical manual of mental disorders, fifth edition (DSM-5), its core symptoms include pervasive anxiety, restlessness, fatigue, irritability, nervousness, and heightened reactivity (APA, 2022). In many cases, muscle tension and increased muscle tone are also observed. For a formal diagnosis, these symptoms must persist for at least 6 months (Courtney et al., 2020). GAD is a prevalent and complex disorder, with a 12-month prevalence rate ranging from 1.2% to 2.8% (Abernathy et al., 2010). It is associated with a higher risk of comorbid medical and psychiatric conditions, particularly depression and substance abuse. From a behavioral and cognitive perspective, anxiety represents an exaggerated form of a normal adaptive response to perceived threats, a mechanism that prepares the individual for action. However, in individuals with GAD, this response becomes dysregulated, leading to chronic and generalized worry about a wide range of situations (Denny et al., 2012). One of the cognitive domains critically affected in GAD is attention. As attention serves as the gateway to perceptual and cognitive processing, impairments in this domain can amplify the severity and persistence of anxiety symptoms. Attention allows individuals to prioritize relevant sensory input while filtering out irrelevant information, a function that is particularly sensitive to emotional and cognitive states (Breitenwischer, 2015). Electrophysiologically, GAD has been associated with characteristic alterations in brain oscillatory activity. Previous studies have highlighted increased theta and decreased alpha activity, especially in prefrontal and limbic regions, as neural signatures of anxiety. These oscillations are believed to underlie attentional and emotional regulation deficits commonly observed in GAD (Jafari Asl et al., 2024).

In recent years, transcranial direct current stimulation (tDCS) has emerged as a promising neuromodulatory technique for targeting neural networks implicated in psychiatric disorders (Antal et al., 2022; Qi et al., 2024; Xie et al., 2024; Zheng et al., 2024). Specifically, anodal tDCS over the prefrontal cortex has been shown to enhance cortical excitability and modulate functional connectivity with limbic regions such as the amygdala and anterior cingulate cortex (Antal et al., 2022; Wu et al., 2022). These regions play a pivotal role in regulating emotional and attentional processes (Palmisano et al., 2021; Wu et al., 2022). Empirical evidence suggests that tDCS may increase alpha activity and reduce pathological theta activity, potentially alleviating cognitive and affective symptoms in individuals with GAD (Jafari Asl et al., 2024).

Numerous studies have examined the process of attention (Shiozawa et al., 2013). Many patients with GAD experience difficulties in concentration, which can significantly impact their daily functioning (Gholipour Fallahy et al., 2025). Cognitive dysfunction has been recognized as a diagnostic criterion for GAD, described as a "diminished ability to think or concentrate." These cognitive impairments may affect executive functions, learning and memory, information processing speed, focus, and attention (Gholipour Fallahy et al., 2025; Kane et al., 2007). Furthermore, these deficits can have profound negative effects on an individual's early psychological, social, and occupational adaptation. In particular, attentional impairments can disrupt daily functioning and significantly reduce quality of life (Badre et al., 2010).

Two key brain regions, the intraparietal sulcus (IPS) and the frontal eye field (FEF), are integral components of the dorsal attention system, an anatomical network of interconnected regions. Additionally, measurements are taken when individuals are resting within a scanner, a process referred to as resting-state covariance (Andrews et al. 2011). Within the dorsal attention system, the IPS and FEF are spatially mapped, meaning that when individuals engage in covert attention, activation in these regions increases upon scanning. The pathway most influential in visual and auditory attention is the fusiform face area (FFA), which plays a critical role in facial processing. Studies have employed motion-based point stimuli to assess how faces are processed in the FFA and further investigate the hypothesis regarding facial representation (Andrews et al., 2011).

One of these tests involves gender recognition of faces, while another assesses the direction of motion of dots when attention is directed toward a face. Stimulation of the prefrontal cortex increases activation in the FFA, a region of the inferior temporal cortex that is critically involved in facial recognition. Additionally, when attention is directed toward the motion of the dots rather than the face, prefrontal stimulation increases activation in higher-order sensory regions. Therefore, the prefrontal cortex plays a fundamental role in both visual and auditory attention, acting as a key initiator of ascending neural signals (Andrews et al., 2011).

In the field of neuropsychology, brain magnetic and electrical stimulation methods have gained attention as innovative solutions (Antal et al., 2022; Qi et al., 2024). Additionally, psychological therapies such as psychoanalysis, behavioral therapies, and cognitive therapies can be implemented individually or in groups. In some cases, combined therapies that include multiple treatment approaches are utilized. Furthermore, pharmacological interventions are effective, although they may be associated with side effects such as gastrointestinal problems, weight gain, sexual dysfunction, and sleep disturbances. These side effects typically decrease after a few weeks, but in some cases, they may persist in the long term (Kane et al., 2007).

Research has shown that increased anxiety levels can reduce attention and concentration abilities. The ability to accurately recognize others' facial expressions is fundamental to social interactions. Among the brain regions, the left dorsolateral prefrontal cortex (L-dlPFC) is a pivotal node in the neural network involved in processing emotional faces, playing a key role in recognizing and interpreting emotional states (Alvarez, 2006).

In 2018, Frings and colleagues conducted a study to investigate the effects of a single session of tDCS on cognitive functions in healthy individuals (Fings et al., 2021). The study introduced an alternative approach for measuring the effects of a single-session tDCS on cognitive processes using the Stroop test. In the previous design, the L-dlPFC region was stimulated with a 9 cm^2 electrode, whereas in the new protocol, a 35 cm^2 electrode was placed over the lateral occipital cortex. Anodal stimulation was compared with cathodal stimulation, and the Stroop test was used to assess the effects of tDCS on participants. In a sample of 32 healthy students, the study found a significant effect of a single-session tDCS on Stroop interference in error data. These findings support previous studies indicating that L-DLPFC neuroplasticity influences cognitive processing.

In another study, Wu et al. (2022) suggested that cathodal stimulation over the right dorsolateral prefrontal cortex (R-dlPFC) reduces neuronal activity. Additionally, this stimulation may also affect cortical and subcortical regions, such as the amygdala and insula. Longitudinal studies have indicated that anxiety in patients can be effectively reduced with repetitive transcranial magnetic stimulation (rTMS) over the same dlPFC region, highlighting the role of this region in controlling anxiety. Moreover, Qi et al. (2021) found that individuals with GAD experience dysfunction in brain activities, with overactivation of the amygdala interfering with fear processing. Furthermore, anxiety responses can be alleviated through tDCS, leading to better emotional regulation.

Abdian and colleagues reported significant differences between tDCS stimulation at two different locations, namely the posterior lateral prefrontal cortex and the temporo-parietal junction, within a control group. They found that the posterior lateral prefrontal cortex had a greater impact on cognitive components in children with ADHD compared to the temporo-parietal junction (Abdian et al., 2022).

In another study, Colazato et al. suggested that cathodal stimulation over the R-dlPFC reduces neuronal activity in this brain area, thereby directly influencing cognitive processes such as response inhibition, emotional regulation, and attention processing. This reduction in R-dlPFC activity may lead to increased impulsivity, reduced ability to inhibit automatic responses, and changes in emotional processing. These findings confirm the essential role of this area in regulating behavior, emotions, attention, and concentration (Colzato et al., 2012).

Further studies by Nobusako et al. have shown that tDCS over the R-dlPFC can significantly affect emotional regulation and reduce anxiety. This technique not only alters the activity in this brain region but may also influence cortical and subcortical regions involved in emotional processing, such as the amygdala and insula. Additionally, investigations have shown that tDCS over the R-dlPFC effectively reduces anxiety in patients, highlighting the importance of this region in controlling anxiety and regulating emotional responses. As a result, novel technologies like tDCS have gained attention as a complementary treatment for GAD, potentially offering benefits alongside pharmacological and cognitive-behavioral therapies in addressing psychological issues such as anxiety, depression, and cognitive regulation of emotions (Nobusako et al., 2017).

Batista and colleagues demonstrated that anodal tDCS over the right dlPFC for 7 sessions significantly improved depression, anxiety, and stress in patients undergoing methadone treatment, compared to a placebo group (Batista et al., 2015). Similarly, Zheng et al. conducted a randomized controlled trial using anodal tDCS over the R-dlPFC in patients with cocaine addiction. They found a significant reduction in anxiety among those receiving tDCS (Zheng et al., 2024). Liu et al. conducted a small randomized study of 20 GAD patients who received either active or sham tDCS, with the R-dlPFC stimulated for 20 minutes over 10 days. Participants who received active stimulation reported an anxiety reduction, indicating a link between the dlPFC and anxiety (Liu et al., 2012). Additionally, a study by Moslemi et al. (2021) on the positive effects of tDCS over the dlPFC for enhancing visual, auditory, and visual memory with theta-wave modulation demonstrated that 15 sessions of 20-minute anodal stimulation at 2 mA significantly improved attention and memory.

By modulating neuronal excitability through changes in the membrane potential of superficial neurons towards depolarization (increased activity) or hyperpolarization (decreased activity), tDCS can impact neuronal activation levels. Although the focal area of tDCS stimulation is somewhat limited, its functional effects are directly observed in the region beneath the electrodes. Early studies in this area were mainly focused on the motor and visual cortices, but recent research has increasingly investigated the effects of tDCS on the dlPFC (Andrews et al., 2011; Antal et al., 2022; Frings et al., 2018). This growing interest stems from the DLPFC's crucial role in cognitive regulation, emotional control, and anxiety reduction (Andrews et al., 2011; Frings et al., 2018; Qi et al., 2024; Shiozawa et al., 2014; Wu et al., 2022).

In general, several questions can be raised. Does tDCS influence cognitive performance, particularly visual and auditory attention, in patients with GAD? Does this effect also apply to Iranian samples? Can this process yield reliable, accurate results to resolve contradictions in previous studies? Based on this, the following hypotheses are proposed: 1) Does tDCS impact theta and alpha waves? 2) Does the targeted stimulation affect visual and auditory attention?

Despite the widespread use of dlPFC stimulation in anxiety research, growing evidence points to the orbitofrontal cortex (OFC) as a key hub in the pathophysiology of GAD, particularly for its roles in affective reactivity, attention allocation, and behavioral inhibition. Therefore, in this study, we targeted the Fp1/Fp2 montage to modulate OFC and related network activity and examine changes in alpha/theta oscillations and cognitive attention in individuals with GAD.

Materials and Methods

Study design

This study used a randomized, controlled, pre-test-post-test design with a pre-test-post-test control group to investigate the effects of tDCS on brainwave patterns and attentional performance in individuals diagnosed with GAD. The design was chosen to allow controlled comparison between a group receiving real stimulation and a matched control group receiving sham stimulation under the same conditions. Before participant recruitment, the research protocol was reviewed and approved by the Ethics Committee of Tabriz University of Medical Sciences. The study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki.

Study participants

The study population consisted of individuals clinically diagnosed with GAD and residing in Tabriz City, Iran, between September 2022 and September 2023. A total of 24 participants were selected through convenience sampling following a clinical assessment conducted by a licensed psychiatrist, using a semi-structured interview based on DSM-5 diagnostic criteria. These participants were then randomly allocated to two equal groups: an experimental group and a control group, each containing 12 participants.

To be eligible for the study, participants were required to meet several inclusion criteria. These included a minimum score of 15 on the GAD 7-item (GAD-7) questionnaire, an age range of 18 to 50 years, and right-handedness, which ensured consistent EEG recording. Additionally, participants needed to have no prior history of substance abuse, neurological disorders, or co-existing psychiatric conditions, as verified by clinical interview and self-report. Individuals currently taking psychoactive medication, those with a history of epilepsy, seizures, or head trauma, and those with implanted electronic medical devices such as pacemakers were excluded from participation. All individuals who met the criteria and agreed to participate in the study signed a written informed consent form. The form detailed the study's purpose and procedures, outlined potential risks and benefits, and assured participants of their right to confidentiality and to withdraw at any time. Participants also completed a demographic questionnaire that collected data on age, gender, education level, handedness, and relevant personal or family medical history.

Study procedure

Participants were randomly assigned to either the active or control group using a simple randomization method based on a computer-generated random number table. Allocation was carried out by a researcher who was not involved in data collection or analysis, ensuring allocation concealment.

The experimental procedure began with baseline assessments, including quantitative electroencephalography (QEEG) to evaluate resting-state brain activity and determine the absolute power of specific frequency bands, particularly alpha and theta. Participants also completed the integrated visual and auditory continuous performance test (IVA-2), which provided objective measures of visual and auditory attention and impulse control. Following baseline testing, tDCS was administered using the ActivaDose device (ActivaTek Inc., USA). A constant current of 2 mA (peak) was delivered through saline-soaked sponge electrodes measuring 5×5 cm, with electrode placement following the international 10–20 EEG system: the anode was positioned over Fp1 and the cathode over Fp2, targeting prefrontal cortical areas associated with emotional regulation and attentional control (Figure 1). Electrodes were enclosed in saline-saturated sponges to ensure consistent conductivity and minimize skin irritation. Each stimulation session lasted 23 minutes and was administered three times per week over 5 weeks, totaling 15 sessions.

Participants in the experimental group received active tDCS for 15 sessions. In contrast, the control group received sham stimulation under identical conditions. For the sham protocol, the device was activated only during the initial ramp-up period (10 sessions with 2 mA in 30 minutes, every other day, in the same lobes), after which the current was discontinued. This condition ensured that participants experienced the initial tingling sensation associated with stimulation while avoiding actual neuromodulatory effects. This approach helped maintain participant blinding and minimize placebo-related bias. The study employed a single-blind design, wherein participants were unaware of their group assignment. However, it should be noted that no formal post-session assessment was conducted to evaluate blinding effectiveness, a recognized methodological limitation.

Data acquisition and analysis

Resting-state electroencephalographic (EEG) data were recorded using a 19-channel Ewave EEG system of Parto Danesh Co., with electrode placement conforming to the international 10–20 system and a default referential montage. All recordings were conducted in a sound-attenuated room with controlled lighting to minimize environmental interference. Participants were seated comfortably and instructed to remain relaxed, limit movement, and avoid excessive blinking throughout the procedure. EEG was recorded under two standardized conditions: 5 minutes with eyes open (EO) and 5 minutes with eyes closed (EC), for a total of 10 minutes. Signals were sampled at 500 Hz with a display scale of 60 μV. Artifact rejection was conducted manually by a trained technician to eliminate ocular and muscular artifacts, ensuring data integrity. Notably, no automated artifact removal algorithms or ICA-based corrections were applied to avoid the inclusion of spurious low-frequency components. For subsequent analysis, a one-minute artifact-free segment was extracted from the EC condition, which offers greater signal stability and reduced susceptibility to visual and motor interference. EEG preprocessing included bandpass filtering between 0.5–45 Hz and segmentation into non-overlapping epochs of equal duration. The data were processed using NeuroGuide software (Applied Neuroscience Inc.) and converted to quantitative EEG (QEEG) format. Spectral analysis was performed using fast Fourier transform (FFT) to compute absolute power (μV^2) in standard frequency bands: delta (0.5–4 Hz), theta (4–8 Hz), alpha (8–12 Hz), and beta (12–30 Hz). Primary analyses focused on changes in absolute power in the alpha and theta bands before and after the intervention. To complement the neurophysiological data, behavioral and cognitive performance was evaluated using the IVA-2, which assesses visual and auditory attention as well as impulse control. Both the EEG and IVA-2 assessments were repeated post-intervention, following the completion of the 15 tDCS sessions, to measure changes in brain function and attention-related outcomes.

All statistical analyses were conducted using SPSS software, version 20. Descriptive statistics, including Mean±SD, frequencies, and percentages, were used to summarize demographic data and baseline characteristics. To assess the effects of the tDCS intervention, a repeated-measures analysis of variance (RM-ANOVA) was performed, incorporating one within-subjects factor (time: pre-test vs post-test) and one between-subjects factor (group: active vs sham). Interaction effects were analyzed to determine whether changes over time differed significantly between the two groups. In addition, a multivariate analysis of covariance (MANCOVA) was employed to compare post-test outcomes across groups while statistically controlling for pre-test scores. This two-pronged approach allowed for the evaluation of both within-subject changes and between-group differences across multiple dependent variables, including EEG-derived power in the alpha and theta bands and IVA-2 performance metrics. Before conducting inferential analyses, assumptions of normality, homogeneity of variance (Levene's test), and homogeneity of covariance matrices (Box's M test) were verified and satisfied. A significance level of $P<0.05$ was used for all comparisons.

Results

A total of 24 participants diagnosed with GAD were recruited from both public and private neuropsychiatric centers in Tabriz and randomly assigned to experimental and control groups. The study, which examines the efficacy of tDCS on the absolute power patterns of alpha and theta waves and on visual and auditory attention in patients with GAD, includes the following assessments. As shown in Table 1, the Mean±SD of pre-test and post-test scores for the study variables are presented for both the experimental and control groups. Additionally, this table includes the results of the Kolmogorov-Smirnov (K-S) test to assess the normality of variable distributions within the groups. According to this table, the Z-statistic for the K-S test was not significant for any variable, indicating that the distributions of these variables are normal. As evident in the post-test phase, the dependent variables demonstrate greater effectiveness with tDCS. To evaluate the efficacy of tDCS on visual and auditory attention components, MANCOVA was employed. The regression slope homogeneity test results for the pre-test and post-test variables in the experimental and control groups showed that the regression slopes were equal across groups. The results of the Levene's test for assessing homogeneity of variances revealed that the variances in visual split attention ($P<0.05$, $F_{2, 24}=2.794$), auditory split attention ($P<0.05$, $F_{2, 24}=2.012$), visual sustained attention ($P<0.05$, $F_{2, 24}=1.678$), auditory sustained attention ($P<0.05$, $F_{2, 24}=0.426$), visual focused attention ($P<0.05$, $F_{2, 24}=2.809$), auditory focused attention ($P<0.05$, $F_{2, 24}=0.002$), visual selective attention ($P<0.05$, $F_{2, 24}=1.963$), auditory selective attention ($P<0.05$, $F_{2, 24}=0.423$), visual attention shifting ($P<0.05$, $F_{2, 24}=0.383$), and auditory attention shifting ($P<0.05$, $F_{2, 24}=0.817$) were equivalent across groups. Therefore, the homogeneity of variances for the study variables was maintained. The M-Box test results for examining the equality of covariance matrices of dependent variables between the experimental and control groups showed that the covariance matrices were equivalent in both groups ($P<0.05$, $F=1.7$, M-Box $=74.32$).

After examining the assumptions of multivariate analysis of covariance, the results in Table 2 revealed a significant difference between the two groups in the visual and auditory attention components. To determine which specific components of visual and auditory attention the experimental and control groups differ in, the results of the multivariate analysis of covariance are presented in Table 2.

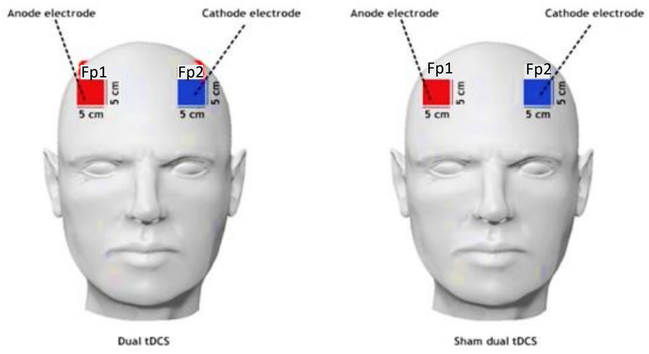

Figure 1. Channel location with tDCS Placement

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To assess participants' anxiety levels, the GAD-7 was employed. The Box's M test was conducted to evaluate the homogeneity of the covariance matrix. As shown in Table 3, the correlation between the studied variables is homogeneous, as the observed F value for this test is not statistically significant at the 0.05 level ($P<0.05$). Therefore, the assumption of covariance matrix homogeneity has been met.

The Levene's test was used to test the assumption of equal error variances. The contents of Table 4 indicate that the error variances of the variables in the study are homogeneous across the groups under investigation because the observed F value for this test is not statistically significant at the 0.05 level ($P<0.05$) for the variables studied. Therefore, the assumption of homogeneity of error variances is also satisfied.

To examine the assumption of canonical correlation among the dependent variables, Bartlett's test of sphericity was used. The results indicate a canonical correlation between the variables (Table 5), and these variables have combined to create a new weighted variable because the calculated Bartlett's index ($X=169.85$) is statistically significant at the 0.01 level ($P<0.01$).

The results in Table 6 show that transcranial electrical stimulation has a statistically significant effect on visual and auditory attention. Specifically, beta and theta waves have decreased, while delta and alpha waves increased significantly. Additionally, visual and auditory attention have significantly improved, and these changes, as indicated in Table 1, suggest that transcranial electrical stimulation in the post-test group has led to an overall increase in all subcomponents of visual and auditory attention.

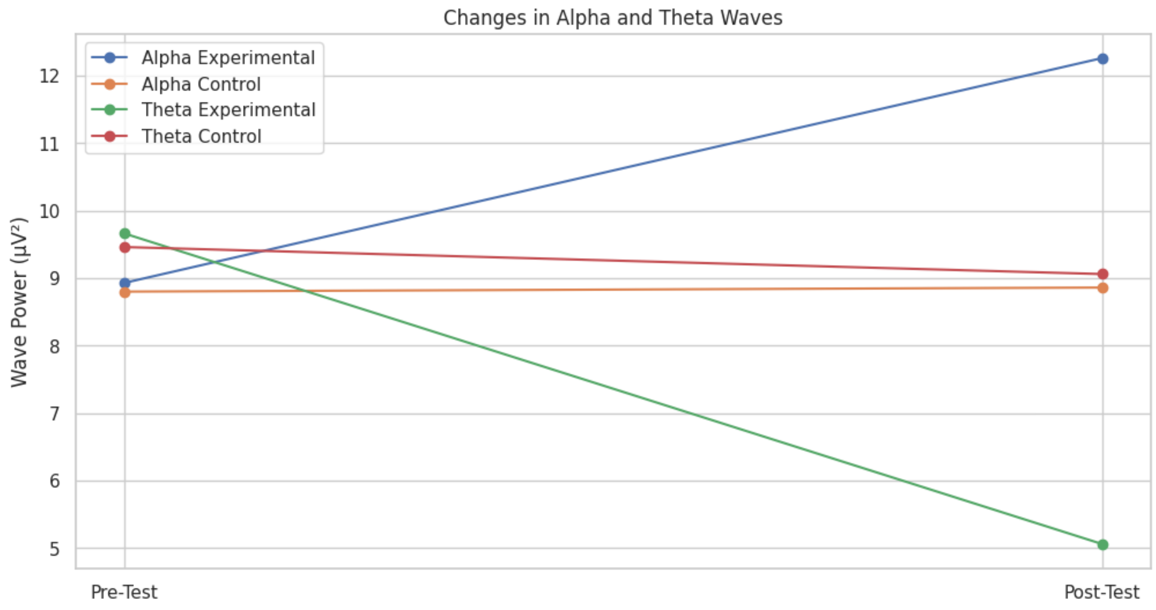

Figure 2. The mean changes in alpha and theta waves

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Table 1. Descriptive indices of pre-test and post-test scores for the experimental and control groups (n=24)

Parameter	Condition	Group	Mean±SD	K-SZ	P
Attention split visual	Pre-test	Experimental	176.08±20.01	0.213	0.111
		Control	176.23±18.48	0.161	0.235
	Post-test	Experimental	197.15±12.29	0.255	0.102
		Control	175.32±18.75	0.159	0.212
Attention split auditory	Pre-test	Experimental	194.31±24.44	0.126	0.238
		Control	178.08±14.1	0.164	0.241
	Post-test	Experimental	203.85±13.73	0.159	0.205
		Control	188.23±13.4	0.153	0.278
Continuous attention visual	Pre-test	Experimental	255.38±53.99	0.243	0.095
		Control	239.62±55.48	0.215	0.103
	Post-test	Experimental	307.23±29.64	0.206	0.100
		Control	242.23±52.77	0.226	0.069
Continuous attention auditory	Pre-test	Experimental	225.31±45.44	0.205	0.138
		Control	225±36.58	0.137	0.341
	Post-test	Experimental	251±28.7	0.178	0.220
		Control	225.54±39.24	0.095	0.368
Focused attention visual	Pre-test	Experimental	160.38±39.09	0.246	0.086
		Control	159.69±46.6	0.228	0.064
	Post-test	Experimental	192.69±29.76	0.213	0.097
		Control	161.08±43.6	0.241	0.050
Focused attention auditory	Pre-test	Experimental	143.92±36.71	0.177	0.213
		Control	136.69±39.1	0.162	0.215
	Post-test	Experimental	176.31±17.87	0.184	0.203
		Control	137.08±38.37	0.151	0.323
Selective attention visual	Pre-test	Experimental	239.08±59.41	0.198	0.098
		Control	224.38±79.29	0.198	0.170
	Post-test	Experimental	283±44.16	0.242	0.068
		Control	225.62±75.85	0.175	0.132
Selective attention auditory	Pre-test	Experimental	228.77±48.62	0.204	0.144
		Control	206.77±55.21	0.200	0.164
	Post-test	Experimental	263.31±38.93	0.266	0.052
		Control	207.15±53.89	0.127	0.365

Parameter	Condition	Group	Mean±SD	K-SZ	P
Attention shift visual	Pre-test	Experimental	352.31±46.36	0.193	0.207
		Control	349.62±47.75	0.125	0.300
	Post-test	Experimental	398.69±42.54	0.186	0.183
		Control	348.39±49.23	0.119	0.262
Attention shift auditory	Pre-test	Experimental	322.69±34.61	0.157	0.270
		Control	343.31±30.89	0.164	0.256
	Post-test	Experimental	355.31±30.8	0.200	0.160
		Control	344.15±31.69	0.105	0.418

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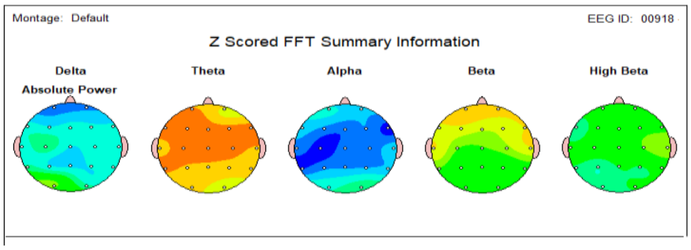
To enhance the interpretability and clinical significance of the findings, effect size estimates were calculated for both behavioral and neurophysiological outcomes. Within-group comparisons in the experimental group showed large Cohen's d values across nearly all visual and auditory attention subcomponents. Notably, the following changes were observed in Table 7.

These values reflect substantial improvements in attentional functioning following the tDCS intervention. Additionally, partial eta squared (η^2_p) was computed for key between-group comparisons derived from the RM-ANOVA and MANCOVA analyses. The following effect sizes were obtained in Table 8.

All η^2_p values fall within the large effect size range (η^2_p >0.14), underscoring the strong impact of tDCS on both EEG activity and attentional performance. These results not only support statistical significance but also indicate robust clinical and cognitive benefits of the intervention. The Pearson correlation coefficients were calculated between baseline GAD-7 scores and pre-to-post change scores in alpha and theta power, and in visual and auditory attention within the experimental group. Results revealed significant negative correlations between baseline anxiety and changes in theta power (r=-0.68, P<0.01) and positive correlations with increases in alpha power (r=0.71, P<0.01). Additionally, baseline GAD-7 scores were significantly correlated with improvements in visual focused attention (r=0.65, P<0.01) and auditory attention (r=0.60, P<0.05). These findings suggest that participants with higher initial anxiety symptoms benefited more from the intervention.

a)



b)

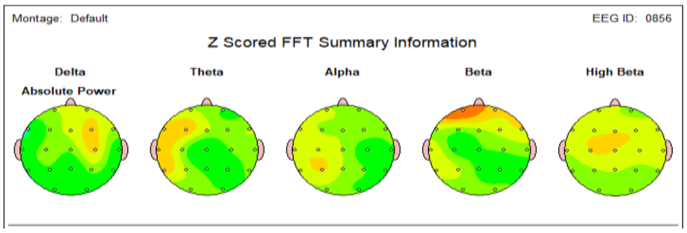


Figure 3. The pre- (a)and post-intervention (b) EEG heatmap

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Table 2. Results of MANCOVA related to the effectiveness of transcranial electrical stimulation on visual and auditory attention components

Parameter	Pre-test				Post-test			
	Experimental Group		Control Group		Experimental Group		Control Group	
	Mean±SD	No.	Mean±SD	No.	Mean±SD	No.	Mean±SD	No.
Delta	5.26±0.59	12	5.46±0.51	12	2.8±0.67	12	5.13±0.51	12
Theta	9.66±0.59		9.46±0.91		5.06±0.7		9.06±0.7	
Alpha	8.93±0.59		8.8±0.56		12.26±1.75		8.86±0.63	
Beta	5.66±1.83		5.4±1.95		8.8±0.77		5.13±0.63	
Visual attention	120.13±1.55		120.6±1.8		190.86±3.64		120.65±1.8	
Auditory attention	118.73±1.98		119.46±3.04		150.33±3.88		119.5±3.04	

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Table 3. The Box's M test for the assumption of homogeneity of covariance matrices

Box's M test	First Degrees of Freedom	Second Degrees of Freedom	F	P
44.65	21	2883.55	1.62	0.3

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Table 4. Levene's test for homogeneity of error variances

Parameter	F Coefficient	First Degrees of Freedom	Second Degrees of Freedom	P
Delta	0.06	1	28	0.79
Theta	0.05		28	0.81
Alpha	2.61		28	0.11
Beta	0.41		28	0.52
Visual attention	0.09		28	0.92
Auditory attention	0.01		28	0.99

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Moreover, Figure 2 illustrates the mean changes in alpha and theta wave power across experimental and control groups pre- and post-intervention. In the experimental group, a significant increase in alpha wave power is observed after the intervention, reflecting improved relaxation and cognitive efficiency associated with tDCS. Conversely, theta wave power shows a marked decrease post-intervention in the experimental group, indicative of reduced anxiety and enhanced emotional regulation. In contrast, no substantial changes are observed in the control group, highlighting the specific efficacy of tDCS in modulating neural oscillations relevant to anxiety

Table 5. Bartlett's test of sphericity

Chi-square Value	Degrees of Freedom	P
169.85	20	0.001

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Table 6. MANCOVA

Parameter	MM	MS	Degrees of Freedom	F	P
Delta	34.97	34.97		89.85	
Theta	108.28	108.28		99.44	
Alpha	73.66	73.66	1	175.33	0.01
Beta	84.77	84.77		45.35	
Visual attention	596.86	596.86		1836.34	
Auditory attention	503.57	503.57		1850.30	

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Table 7. The Cohen's d results for the experimental group

Measure	Pre-test Mean	Post-test Mean	Cohen's d
Attention split visual	176.08	197.15	1.27
Attention split auditory	194.31	203.85	0.48
Continuous attention visual	255.38	307.23	1.19
Continuous attention auditory	225.31	251	0.68
Focused attention visual	160.38	192.69	0.93
Focused attention auditory	143.92	176.31	1.12
Selective attention visual	239.08	283	0.84
Selective attention auditory	228.77	263.31	0.78
Attention shift visual	352.31	398.69	1.04
Attention shift auditory	322.69	355.31	1.00

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Table 8. η^2_p results

Measure	F	η^2_p
Alpha power	108.28	0.831
Theta power	84.77	0.794
Delta power	89.85	0.803
Beta power	45.35	0.673
Visual attention	73.66	0.770
Auditory attention	175.33	0.889
IVA visual score	1836.34	0.988
IVA auditory score	1850.30	0.988
Multivariate attention effect	34.97	0.614

IVA: The integrated visual and auditory.

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Figure 4. F Values from analysis of variance in various metrics

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regulation and cognitive enhancement. Figure 3 depicts baseline neural activity across key regions of interest in the experimental group. Post-intervention, the heatmap reveals increased activity in regions associated with cognitive and emotional regulation, particularly those influenced by the applied tDCS protocol. The visual representation of changes highlights the localized effects of tDCS, with notable modulation of power in the alpha and theta frequency bands. These findings align with the hypothesis that tDCS optimizes cortical excitability and connectivity, thereby improving cognitive and emotional outcomes.

Figure 4 demonstrates the statistical significance of differences across key metrics (alpha waves, theta waves, visual attention, and auditory attention). High F values and corresponding P values below 0.05 indicate that the intervention had a significant effect on these measures, particularly for the experimental group. Furthermore, Figure 5 outlines the gender-specific changes in alpha and theta wave power for experimental and control groups. Male and female participants in the experimental group exhibit notable improvements in alpha power and reductions in theta power, while changes in the control group are minimal. This analysis suggests that the effects of tDCS are robust across genders, providing further support for its efficacy.

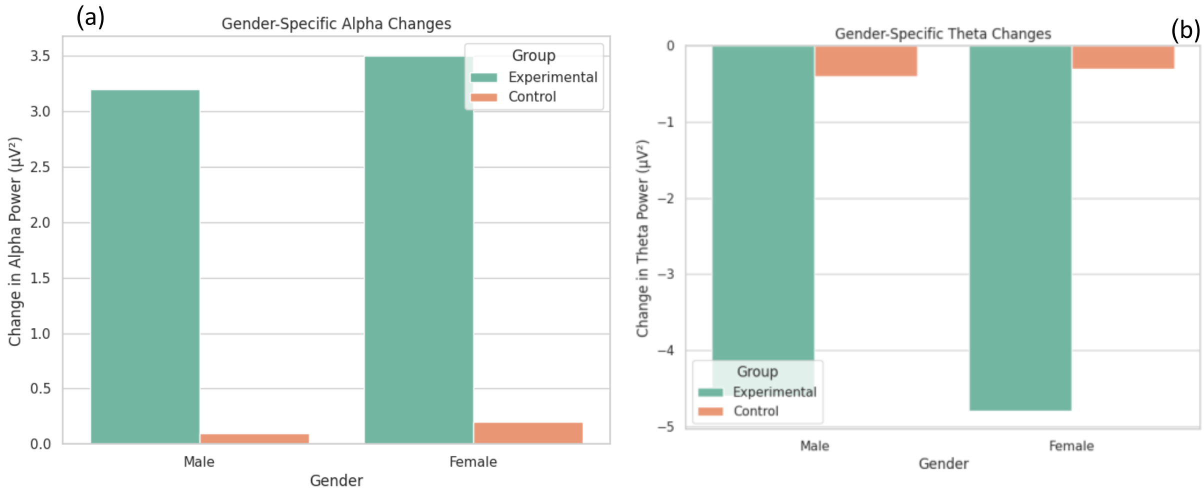

Figure 5. Gender-specific analysis

a) Alpha changes, b) Theta changes

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Discussion

In this study, the primary objective was to investigate the efficacy of tDCS on the absolute power of alpha and theta brain waves and its impact on improving visual and auditory attention performance in individuals with GAD. GAD is a common psychiatric disorder characterized by pervasive anxiety, chronic worry, and diminished concentration. Non-invasive brain stimulation methods, such as tDCS, represent emerging therapeutic approaches for modulating neural activity and enhancing cognitive function (Qi et al., 2024; Xie et al., 2024; Zheng et al., 2024).

In this research, the stimulation targeted the OFC, specifically the Fp1 and Fp2 regions, diverging from many prior studies that predominantly focused on the dlPFC and regions F3 and F4 (Qi et al., 2024; Shiozawa et al., 2014; Wu et al., 2022; Zheng et al., 2024). This choice was based on the OFC's critical role in cognitive processes, particularly emotion regulation and stress management (Rolls, 2023).

The orbitofrontal cortex is integral to emotional regulation, stress control, and decision-making, with direct associations to executive and affective functions. Given its involvement in anxiety management, modulating OFC activity through tDCS could alleviate GAD symptoms (Vicario et al., 2020). While previous research has linked DLPFC stimulation to reduced anxiety and improved attention Andrews et al., 2011; Antal et al., 2022; Frings et al., 2018; Moslemi et al., 2021; Qi et al., 2024; Shiozawa et al., 2014; Wu et al., 2022; Xie et al., 2024; Zheng et al., 2024), fewer studies have examined the OFC's stimulation effects (Qi et al., 2024; Xie et al., 2024; Zheng et al., 2024). Thus, this study aimed to evaluate tDCS effects across different brain regions to identify the optimal target for enhancing cognitive performance in GAD patients.

The results demonstrated that tDCS significantly modulated brain wave activity and enhanced attentional performance. Notably, absolute alpha power, typically associated with relaxation and anxiety reduction, increased post-intervention, while theta power, often linked to anxiety and attentional deficits, decreased. These neurophysiological changes corresponded with improvements in both visual and auditory attention tasks, as participants showed better responsiveness and sustained focus on stimuli.

These findings align with previous literature and provide compelling evidence supporting the use of tDCS to improve attentional deficits and reduce anxiety symptoms (Antal et al., 2022; Moslemi et al., 2021; Qi et al., 2024; Shiozawa et al., 2014; Wu et al., 2022; Xie et al., 2024; Zheng et al., 2024). This study emphasizes the therapeutic potential of non-invasive stimulation techniques like tDCS in managing anxiety disorders.

Specifically, the study analyzed changes in absolute alpha and theta power, key frequencies involved in attention and anxiety. Post-tDCS, alpha activity rose and theta activity diminished in the targeted cortical regions, correlating with enhanced visual and auditory attention. This finding offers deeper insight into how tDCS influences brain oscillations and cognitive function in GAD.

Importantly, correlational analyses demonstrate that individuals with higher baseline anxiety showed greater improvements in both neurophysiological markers (increased alpha, reduced theta) and attention scores, suggesting that tDCS may be particularly beneficial for patients with more severe symptoms.

Before, studies have also validated the efficacy of transcranial electrical stimulation, particularly tDCS, in modulating brain rhythms and improving attentional and anxiety-related dysfunctions (Antal et al., 2022; Moslemi et al., 2021; Qi et al., 2024; Shiozawa et al., 2014; Wu et al., 2022; Xie et al., 2024; Zheng et al., 2024). This research reinforces those findings, with statistical analyses and brain mapping confirming significant post-intervention changes.

Furthermore, the study highlights the need for continued research to optimize stimulation protocols and examine long-term effects. Limitations included a relatively small sample size, the presence of comorbid psychiatric conditions in some participants, and a lack of longitudinal follow-up. Future work should expand sample sizes, explore effects on other anxiety disorders and executive functions such as memory and decision-making, and utilize advanced neuroimaging techniques like fMRI or high-resolution EEG to characterize neural changes better.

In conclusion, this study confirms the positive impact of tDCS on improving attentional performance and reducing anxiety symptoms in GAD patients. As an innovative therapeutic approach, tDCS shows promise for broader clinical application in anxiety disorder treatment and may inform future development of targeted neuromodulation protocols aimed at enhancing cognitive-emotional functioning and quality of life.

Conclusion

In conclusion, this study's findings demonstrate that tDCS targeting the orbitofrontal cortex via Fp1/Fp2 significantly reduces anxiety, modulates alpha and theta brainwave activity, and improves visual and auditory attention in individuals with GAD. These results highlight the potential of tDCS as a non-pharmacological, neurophysiologically-informed intervention for anxiety disorders. Future research should aim to replicate these findings in larger samples, include healthy and clinical control groups, utilize enhanced EEG analysis protocols, and incorporate long-term follow-up assessments. Moreover, further investigations are needed to optimize stimulation parameters and explore differential effects of DLPFC versus OFC stimulation across anxiety subtypes.

Study limitations

This study is not without limitations. First, the relatively small sample size may have reduced statistical power and generalizability. Second, the absence of a healthy control group limits our ability to isolate tDCS-specific effects from general clinical improvement. Third, the single-blind design, though supported by a sham protocol, was not validated with post-session blinding checks. Fourth, automated artifact rejection was used in EEG preprocessing without manual inspection or ICA, potentially affecting the precision of EEG findings. Finally, no long-term follow-up was conducted, and thus, the persistence of tDCS effects remains unclear. The choice of the Fp1/Fp2 montage, although theoretically justified based on recent OFC research, diverges from the more common DLPFC protocol. Future studies should directly compare these montages to determine the most effective stimulation target for anxiety modulation.

Ethical Considerations

Compliance with ethical guidelines

This study was approved by the Research Ethics Committee of Tabriz University of Medical Sciences, Tabriz, Iran (Code: IR.TABRIZU.REC.1402.131). The study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki.

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Authors' contributions

Study implementation, patient diagnosis and screening: Farrokh Bakht shady; Writing the original draft: Mohammad Reza Gholipour Fallahy; Validation and statistical analyses: Shahram Vahedy; Review and editing: Leila Mehdizadeh Fanid, Shahram Vahedy, and Mahdi Jafari Asl;

Conflict of interest

The authors declared no conflict of interest.

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