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Transcranial Direct Current Stimulation and its Impact on Attention Networks in Tinnitus Patients

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Abstract

Background: Tinnitus is a prevalent condition often leading to disruptions in attentional functions. The effect of transcranial direct current stimulation (tDCS) on cortical attention networks has yielded inconsistent findings.

Objectives: This study aimed to examine the influence of tDCS on patients suffering from tinnitus on the efficacy of alerting, orienting, and conflict, as gauged by the Attention Network Test (ANT).

Methods: 30 tinnitus patients with chronic bothersome tinnitus longer than 6 months with moderate and high severities were placed into two separate groups at random. The control group (n=15) underwent sham tDCS, while the treatment group (n=15) received active tDCS, with the anodal electrode placed over the left dorsolateral prefrontal cortex (DLPFC) and the cathodal electrode over the right DLPFC. The ANT and the Electroencephalography (EEG) recording were used before and after interventions. The differences were analyzed using the MANCOVA test.

Results: There was a significant difference (P<0.01) between the control and tDCS groups only in terms of the mean post-test scores of conflict. However, no significant difference was observed in the means of alerting and orienting. This suggests that tDCS primarily influenced the conflict index, leading to its enhancement. EEG recording indicated a variety of significant changes in various frequency bands in different channel locations. Theta and high beta showed no significant difference in any channel, and most changes happened in the form of an increase in high alpha after tDCS. Absolute Power in theta and high beta frequency ranges showed no significant difference in any channel, and most changes in Absolute Power happened as an increase in high alpha frequency after tDCS.

Conclusion: tDCS potentially improves the attentional network in patients afflicted with tinnitus. More research is required to draw definitive conclusions, especially since only conflict demonstrated significance in the ANT test.

Keywords: Attention, Cognitive functions, EEG, Tinnitus, tDCS

1. Background

Tinnitus is characterized as the conscious perception of a tonal or composite auditory sensation that has no identifiable external source. The prevalence rate of tinnitus varies depending on the specific definition employed, but it is estimated that up to 30% of individuals have encountered this phantom auditory perception (1). Subsequently, this group of individuals often experiences various psychological, emotional, cognitive, and functional difficulties associated with their condition (2). The development of distressing and bothersome tinnitus is related to the dysfunction of attentional processes, which mostly happens at increased stress times and restrains cognitive resources (3) .

People experiencing tinnitus have noted challenges with focus and cognitive functions, likely attributed to the disruptive nature of persistent internal noise when engaging in tasks that require attention. (4). The attention network plays a role in directing the patient's focus toward the internal sound, and it also manages the emotional response by connecting to the tinnitus distress network. This connectivity, facilitated by the parahippocampus, hinders the habituation process (5). The attention system's functional neuro-architecture comprises three distinct networks: alerting, orienting, and executive control. The alerting system, which is broadly distributed spatially, supports the processing of temporally anticipated events that are not spatially localized. Orienting facilitates the allocation of resources toward the spatial location of anticipated or salient stimuli. Executive control, responsible for coordinating voluntary responses over involuntary or automatic ones (6). It has been shown that the dorsolateral prefrontal cortex (DLPFC) has modulatory effects on auditory memory (7), auditory processing (8), and attention (9). Studies have shown that the compromised top-down cognitive control of the DLPFC could significantly contribute to the persistence of tinnitus, disrupting habituation mechanisms and causing increased distress. Notably, the DLPFC's top-down control over other brain regions establishes it as a crucial connecting hub between networks associated with tinnitus. This underscores its significance as the preferred target for non-invasive neuromodulation techniques (10). Heeren et al. conducted an Attention Network Test (ANT) to determine if tinnitus patients were different from the control

group in terms of altering, selective, or executive networks. The findings indicated no general attention deficit in tinnitus patients but rather a precise impairment in the top-down executive control of attention (4).

Due to the central role of tinnitus, there has been an increasing utilization of neuromodulation techniques in its treatment, as well as the identification of an electrophysiological indicator of therapeutic efficacy (21). As one such technique, transcranial direct current stimulation (tDCS), has yielded promising results in mitigating or alleviating tinnitus and its associated distressing symptoms (22). Previous investigations have explored the possible impact of a single session of tDCS in comparison with multiple sessions, as well as the long- and short-term impacts of this technique in comparison with placebo in clinical trials (23). The findings of a study by Shekhawat et al. (24) revealed that tDCS stimulation targeting the right dorsolateral prefrontal cortex (DLPFC) and the left temporoparietal area (LTA) yielded comparable effectiveness in terms of the provision of relief from tinnitus and reducing symptom intensity. In another research performed by Hyvärinen et al. (25), the self-administration of tDCS at home resulted in favorable outcomes in terms of the quality of life of tinnitus patients, as assessed by the Tinnitus Handicap Inventory (THI).

Broadly speaking, the mechanism by which tDCS operates is connected to alterations in the patterns of excitatory and/or inhibitory activity that are reported in the pathophysiology of tinnitus. In fact, tDCS achieves this indirectly through the modulation of spontaneous neuronal activity using a low-intensity electric current, typically within the range of 0.5-2 mA (26). To comprehend the therapeutic efficacy of tDCS for patients suffering from tinnitus, the evaluation of behavioral factors both prior to and following tDCS treatment has been established. This has proven instrumental in gaining insights into the potential therapeutic benefits of tDCS in the management of tinnitus (27, 28).

2. Objectives

Therefore, taking into account the findings of the mentioned researchers, along with the potential mechanisms through which tDCS influences neural processes, employing EEG in research endeavors could elucidate the fundamental elements contributing to tinnitus. Additionally, it may aid in identifying physiological attributes that can serve as prognostic indicators of therapeutic advancements facilitated by tDCS. However, the findings of literature about ANT test and Absolute Power in various frequency ranges are not consistent throughout the studies and the potential benefits of tDCS related to attention problems of individuals with tinnitus are not well understood. Consequently, the main goal of the present research was to ascertain the potential of tDCS in ameliorating the attention deficits caused by tinnitus while simultaneously investigating its impact on modulating cortical frequency patterns.

3. Methods

Subjects and Study Procedures

The present investigation was a randomized, double-blind, placebo-controlled clinical trial performed on individuals afflicted with Non-pulsatile chronic tinnitus (more than 6 months), with moderate to high severiries irrespective of the laterality of their symptoms. The necessary permits from Ardabil University of Medical Sciences and Ardabil Medical Council were obtained and after explaining the research to an otolaryngologist and a neurologist, a total number of 165 tinnitus patients were referred to the Niusha Hearing Clinic. The evaluation of hearing and tinnitus was done in the hearing clinic by an experienced audiologist with audiometry (two-channel audiometer, Maico MA53) and tympanometry (Maico MI34) tests. 30 people were randomly selected through available sampling and according to the strict criteria of the research. After homogenization in terms of the matching criteria, they were randomly divided into two experimental and control groups. The criterion for normal hearing was 0 to 20 dBHL of hearing in frequencies of 250 Hz, 500 Hz, 1000 Hz, 2000 Hz, 4000 Hz, and 8000 Hz during air conduction and bone conduction tests in audiometry. Specifically, the control group (n=15) received sham tDCS, whereas the treatment group (n=15) was subjected to active tDCS, with the anode and cathodal electrodes positioned over the left and right DLPFCs, respectively. The participants and the technician of the tDCS were unaware of the group each participant belonged. Before the interventions, participants of the study were subjected to ANT and evaluation of brain activity using EEG. During three weeks, the patients participated in 10 sessions of tDCS (3 times a week). 24 hours after the interventions, the patients' EEG recordings, ANT, and tinnitus severity were reassessed. The assessment procedures were conducted according to previous research studies (20).

The inclusion criteria for tinnitus participants were as follows: 1) possession of normal-range auditory thresholds, 2) experiencing moderate to severe distress attributable to tinnitus, as indicated by a score of ≥48 on the THI, 3) the

absence of ongoing treatment for tinnitus, including tDCS or other forms of neuromodulation, and 4) the absence of metallic objects or medical devices implanted in the cranial region. Conversely, the exclusion criteria were the following: 1) the concurrent usage of psychotropic medications for mental health conditions, 2) the history of neurological disorders or existing neurological conditions (such as brain tumors, seizures, hemorrhages, or strokes), 3) the presence of moderate to severe mental health disorders or conditions that could impact the neurofeedback investigation (including moderate or severe depression, psychosis, bipolar disorder, or ADHD), and 4) substance abuse. The procedure of the study is represented in Figure 1.

The matching criteria for dividing the participants into two groups included age, gender, and tinnitus severity.

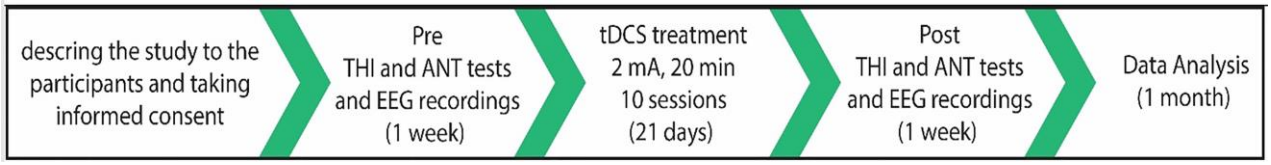

Figure 1. Procedure of different steps of the study. The times inside the parantheses represent the duration of each section. THI, Tinnitus Handicap Inventory; tDCS, Transcranial Direct Current Stimulation; EEG, Electroencephalography, ANT, Attention Network Test

Clinical Evaluation

Participants were subjected to pure-tone audiometry to ascertain their hearing thresholds. The clinical evaluation of tinnitus included an assessment of tinnitus severity utilizing the THI administered both prior to and following the interventions. The THI was conducted via an interview format, wherein the participant answered 25 questions based on a three-point scale, including "yes" (4 points), "sometimes" (2 points), or "no" (0 points). Each question pertained to functional, emotional, or catastrophic aspects. The cumulative scores were within the range of 0-100. Based on the resultant score, the extent of tinnitus-related impairment of the patients was categorized as light or no handicap (0-16), mild (18-36), moderate (38-56), severe (58-76), or catastrophic (78-100) (30).

Attention Network Test

The objective of the ANT is to accurately and efficiently determine the direction (left or right) of a central arrow, referred to as the target, which appears either above or below a fixed point on a computer screen (31). The ANT consists of a total of 288 trials, which are further organized into three blocks, with each block containing 96 trials. Additionally, a practice block precedes these three primary blocks. Importantly, there are 48 possible trial combinations that are randomly presented, including four types of cues, three types of flankers, two target directions (left or right), and two target positions (above or below the fixation cross). Each trial combination is repeated twice within every training block (Figure 2).

Every individual presentation target is preceded by one of four potential cue conditions: the absence of any cue, central cue, double cue, or spatial cue. Additionally, there exist three distinct flanker conditions. In congruent trials, the central target is accompanied by two arrows positioned on either side, pointing in the same direction as the target. Conversely, in incongruent trials, the two flanking arrows point in the opposite direction from the central arrow. Furthermore, the central target presents lonely in neutral trials.

Each experimental trial follows a specific sequence comprised of the following stages. First, the presentation begins with a central fixation cross, which remains on the screen for a randomly determined duration from 400 to 1600 ms. Afterward, a cue is displayed for 100 ms. Another central fixation cross is then presented for a fixed duration of 400 ms. The target stimulus then appears either higher or lower than the fixation cross. In case of lack of response, the target remains visible for a duration of 1,700 ms at most. Afterward, an inter-trial interval ensues, during which a central fixation cross is displayed on the screen. This interval lasts for 4,000 ms minus the combined time taken for fixation and reaction.

The experiment utilized Inquisit 5 software (Millisecond, Seattle, WA, USA) to administer the test. The distance between the display screen and the ocular region of the participant was maintained within 60-65 cm. Responses of participants were captured by left mouse clicks for targets pointing leftward and right mouse clicks for those pointing rightward. Prior to the test, a preliminary trial ensured that participants verified the visibility of stimuli and their comprehension of the task. Three factors involving altering, orienting, and conflict were extracted from the ANT (Cortex software, Shahid Beheshti University) based on the relevant reaction times (RT) and equations below:

Altering = RT (no-cue) – RT (double-cue)
Orienting = RT (center-cue) – RT (spatial-cue)
Conflict = RT (incongruent) – RT (congruent)

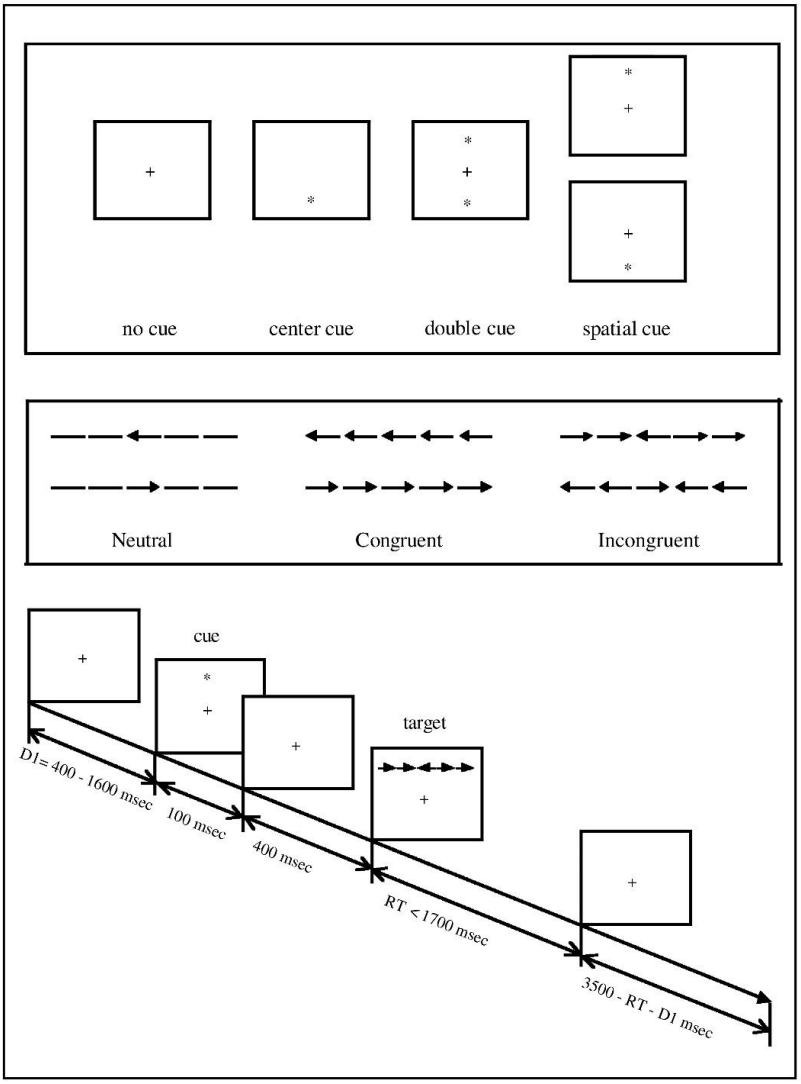

Figure 2. Overview of the Attention Network Test. The diagram depicts the four potential cues (upper section), the six potential targets (middle section), and an exemplification of the trials employed in the task (lower section). Source: Adapted from Fan et al. [38].

During the ANT, the higher scores of altering and orienting indicate a better cognitive performance, however, a lower score of conflict indicates a better performance (6).

tDCS Protocol

Before administering tDCS, a thorough examination of the patients' scalp was conducted to identify any potential deviations (such as irritation, lacerations, or lesions) which might impede the application of the technique. Afterward, silicone conductive electrodes measuring 5×7 cm (35 cm^2) were utilized, which were saturated with saline solution (0.9% NaCl) and positioned according to the 10-20 EEG system (32). Specifically, the anode and cathode were positioned over the left (F3) and right DLPFC (F4), respectively.

The tDCS was administered at a current intensity of 2 mA (equivalent to 0.057 mA/cm2) for 20 min, employing a tDCS stimulator (model: Neurostim, Medina Teb Gostar, Iran). The stimulation protocol involved a gradual increase and decrease in current intensity, with a 30-sec ramping period at the commencement and conclusion of the stimulation. The tDCS was administered over 20 days, encompassing 10 sessions scheduled every other day (with three sessions per week). The control group underwent sham stimulation, while the treatment group received active stimulation. In the sham group, the same electrode montage was employed; however, the tDCS device ceased delivering electrical current after 30 sec of stimulation initiation, a process repeated for all of the 10 sessions.

Acquisition and Processing of EEG Data

The electrical activity of the brain was recorded using EEG with a 19-channel EEG recorder (e Wave by Parto Danesh Co.). A total of 19 active electrodes made of Ag-AgCl were placed based on the 10-20

International System, and the sampling rate was set at 500 Hz. The frontal, parietal, temporal, and occipital regions were monitored. The recording sessions consisted of five minutes each, with participants instructed to keep their eyes open and then closed, resulting in a total recording time of 10 min. Data collection commenced once the impedance of all electrodes dropped below 10k. The patients were assessed before and after the intervention. The data were collected in a quiet room. During the eyes-open situation, a fixation spot was positioned on a wall to minimize potential movements of the eye. Participants were ordered to focus their gaze on the spot throughout the five-minute recording period. The EEG measurements during the eyes-open situation followed the recommendations of the European research network TINNET (https://tinnet.tinnitusresearch.net/) regarding the standardization of EEG and MEG procedures in tinnitus research (https://tinnet.tinnitusresearch.net/index.php/243-standardisation-of-m-eeg-procedures-in-tinnitus-research).

NeuroGuide software (Applied Neuroscience, Russia) was utilized to process the data. Initially, specific parameters were employed, including a low cutoff of 0.1 Hz, a high cutoff filter of 70 Hz, and a notch filter set at 50 Hz. Additionally, careful scrutiny of the data was conducted to identify and eliminate any artifacts. Independent component analysis (ICA) was employed to eliminate vertical and horizontal movements of the eye. Furthermore, the data were referenced by the linked ear method.

Following the data segmentation process in the analyzer, the application of a neuroGuide software facilitated the computation of Absolute power (V) values associated with distinct EEG frequency bands, including delta (0.5-4 Hz), theta (4-8 Hz), alpha (8-12 Hz), beta (12-30 Hz), and gamma (30-70 Hz). These values were subsequently extracted for every study condition (pre- and post-intervention, as well as open- and closed-eyes) to enable a comparative analysis between the two groups.

Statistical Analysis

To guarantee the accuracy and reliability of the analysis, it is imperative to take into account the demographic variables. Ignoring these variables can potentially distort the outcomes, leading to erroneous interpretations. The objective was to verify if the demographic variables were similar in both groups. The Chi-squared test and Fisher's exact test were used for categorical demographic variables (including gender, education level, wearing glasses, tinnitus laterality, and tinnitus intensity).

For scale demographic variables, the Shapiro-Wilk test results showed that the three variables of age, right ear PTA, and left ear PTA followed a normal distribution. On the other hand, the history of tinnitus involvement and tinnitus frequency did not have a normal distribution. For variables with a normal distribution, the T-test was used for comparison of the two independent samples. For those that were not normally distributed, the non-parametric Mann-Whitney U test was employed to compare the two groups.

Furthermore, the Pearson correlation coefficient was employed to evaluate the relationship between the post-intervention value of the THI variable and the post-intervention values of the alerting, orienting, and conflict variables. In the case of no significant linear relationship, a T-test for two independent samples was employed to compare the post-test THI means between the control and tDCS groups.

The multivariate analysis of covariance (MANCOVA) was also employed to investigate the effects of alerting, orienting, conflict, and EEG frequency bands.

Ethical Consideration

The data presented in this article were gathered within a dedicated audiology clinic located in Ardabil, Iran, from December 2022 to March 2023. The research protocol was ethically approved by the Research Ethics Committee of the University of Tabriz (IR.TABRIZU.REC.1401.029) and was registered in the Iranian Registry of Clinical Trials (IRCT20220625055275N1). It should also be mentioned that written consent by means of an authorized consent form was obtained from all participants. Moreover, the voluntary nature of their participation and their unrestricted right to withdraw from the study at any time, without any requirements for justification or potential consequences were explained to them.

4. Results

Demographics and Clinical Scores

Figure 3 displays the demographic details of study participants in both the treatment and control groups. This includes specifics on participants' gender, educational background, tinnitus side, eyewear use, and tinnitus severity.

Out of the 30 participants, 12 were women, and 18 were men. The control group consisted of 11 females and 4 males, whereas the tDCS group included 8 females and 7 males, as shown in Figure 1a. Regarding their educational backgrounds, 18 of the participants had completed secondary education, while 12 had pursued post-secondary studies. Figure 1b provides a detailed breakdown of the participants' educational backgrounds in both groups. In terms of tinnitus laterality, 8 participants had tinnitus in both ears with equal frequencies, 6 individuals had

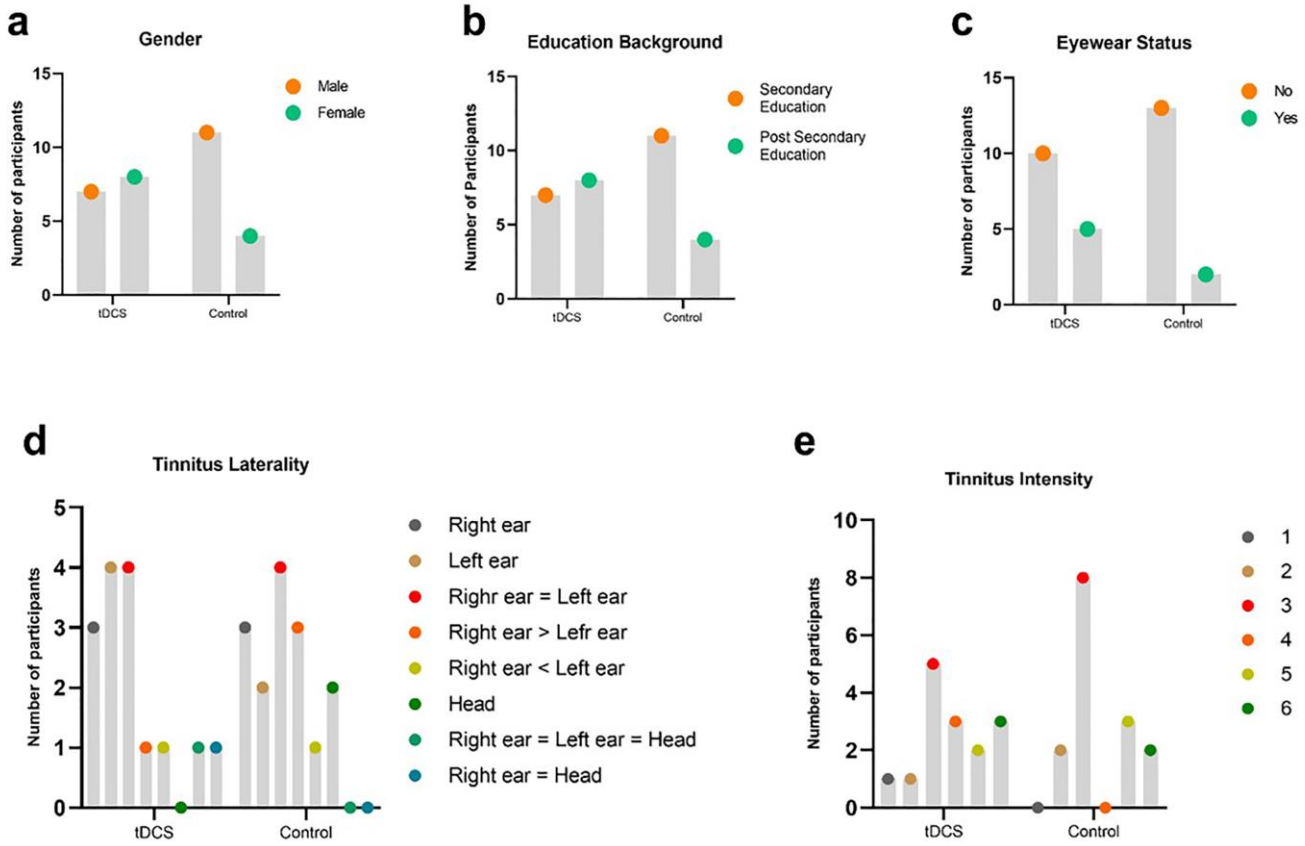

Figure 3. Demographic characteristics of the participants in the treatment and control groups

in the right ear, and 6 individuals in the left ear. This is further detailed in Figure 1d. Regarding tinnitus intensity, 13 participants had 3dBSL loudness, and 5 had of 1 and 6, as illustrated in Figure 1e. Additionally, 7 participants wore glasses, while the remaining 23 did not.

Even though the two groups were not pre-matched, statistical analyses were conducted to assess the differences in demographic variables between them. Initially, we used the Chi-squared test and Fisher's exact test for categorical variables, including gender, education level, use of glasses, tinnitus laterality, and tinnitus intensity. The outcomes of these tests indicated that all these categorical variables were independent of the grouping variable and showed no significant associations.

Considering the demographic data, the Shapiro-Wilk test showed that age, right ear PTA, and left ear PTA were normally distributed. In contrast, the time spent suffering from tinnitus and the frequency of tinnitus were not. Consequently, the parametric T-test was employed for independent samples to compare the control and treatment groups in terms of the means of the first three variables. For the latter two variables, the non-parametric Mann-Whitney U test was used. Levene's test confirmed that variances for age, right ear PTA, and left ear PTA were homogeneous (P>0.05). The T-test revealed no significant differences between the two groups regarding the means of these three variables (P>0.05). Similarly, according to the Mann-Whitney U test, the two groups had no significant difference in terms of tinnitus history and frequency (P>0.05). The mean (SD) and P-values related to each test are presented in Table 1.

Tinnitus Handicap Inventory

The value of the THI variable for each subject was calculated based on a standard 25-item questionnaire. The Cronbach's alpha coefficient of this questionnaire for the studied sample was 0.79, indicating the good reliability of the data obtained from this questionnaire.

The relationship between the conflict effect and the self-reported intensity of tinnitus was evaluated using the Pearson correlation coefficient. The results showed that the post-intervention THI values had no significant linear relationship with any of the post-intervention values of alerting, orienting, or conflict. For this reason, the post-intervention THI values were analyzed separately between the control and tDCS groups using the T-test. Furthermore, the post-intervention THI data in the control and tDCS groups had a normal distribution (Shapiro-Wilk test, P>0.05). Based on the results of this test, there was a significant difference in the post-intervention score of the THI between the two groups of the study. It can be said that the tDCS method had a significant impact on

the THI scores of the subjects as is represented in Figure 4.

The pre-intervention score of the THI was also tested between the control and tDCS groups. The Shapiro-Wilk test rejected the normality of the pre-intervention score distribution of the THI variable in the control group (P=0.021). Therefore, the mean values of the two groups were compared using the non-parametric Mann-Whitney U test. The results of this test showed no significant difference between the pre-intervention scores of the THI variable in the study groups (P=0.512).

Attention Network Test

For the evaluation of the effects of tDCS on altering, orienting, and conflict, firstly, the pre-intervention scores of these three variables were checked between the control and tDCS groups. Based on the results, the assumption of equality of means was rejected only for the pre-intervention score of the orienting variable. In addition, based on the results of Leven's test, the homogeneity of variances was not rejected for any of the pre-test scores of the three stated variables.

Therefore, the MANCOVA test was performed with the grouping variable (control and tDCS) as the independent variable, the post-intervention values of the alerting, orienting, and conflict as dependent variables, and the pre-intervention value of the alerting, orienting, and conflict as auxiliary variables. The Box test did not reject the assumption of equality of covariance matrices between the two groups (P=0.862). According to the obtained results, only the mean post-intervention scores of conflict were significantly different between the control and tDCS groups (P=0.01). In the case of alerting and orienting, the equality of means was not rejected. In other words, the tDCS method has only had a significant effect on the conflict index, leading to its decrease. The results of altering, orienting, and conflict are shown in Figure 5.

Table 1. Demographic and clinical characteristics of the participants

Demographic measures	Mean (SD)		Statistical test	P-value
	Control Group	tDCS group		
Age (year)	39.33 (11.57)	41.36 (9.27)	T test	0.772
Time of suffering from tinnitus (year)	5.10 (5.89)	5.47 (6.86)	Mann–Whitney U test	0.949
Right ear PTA	16.33 (3.88)	11.84 (3.95)	T test	0.940
Left ear PTA	17.66 (5.61)	17.56 (3.54)	T test	0.775
Tinnitus frequency	4325 (2760.29)	4964.29 (3187.43)	Mann–Whitney U test	0.285
Laterality	-	-	Chi-square	0.579

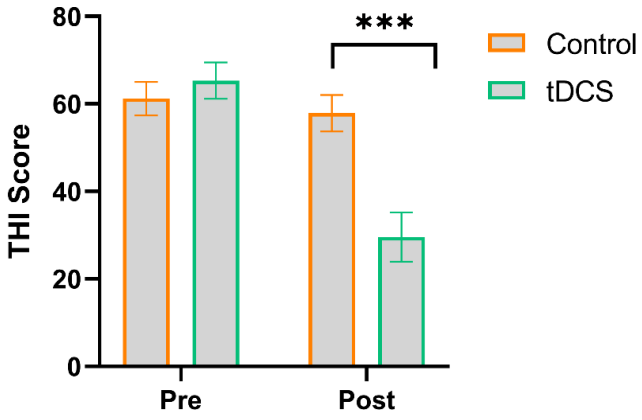

Figure 4. THI score for the study groups. tDCS, Transcranial Direct Current Stimulation; THI, Tinnitus Handicap Inventory

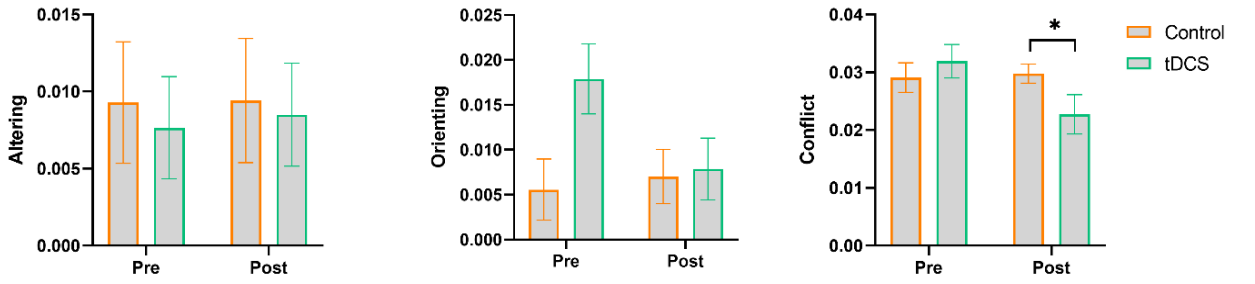

Figure 5. Results of attention network test between the study groups. tDCS, Transcranial Direct Current Stimulation

Absolute power

For the EEG analysis, we examined nine frequency bands, including alpha, alpha1, alpha2, beta, delta, gamma, theta, high beta, and high gamma, across 19 brain regions. We used data from closed-eye EEG sessions to eliminate visual distractions. In this analysis, the post-intervention values for each of the nine bands mentioned served as dependent variables. The group type (control or tDCS) was the independent variable, while the pre-intervention values were treated as covariates.

The analysis of the data revealed that the two groups were significantly different in terms of various regions of the brain across different frequency bands. The results indicated no significant differences between the two groups in the theta and high beta bands in any of the brain regions. The alpha2 frequency band exhibited the greatest number of brain regions, including F3, F4, F8, FZ, FP1, FP2, PZ, P3, P4, O2, T4, T5, and T6, showing significant differences between the control and treatment groups. In the alpha1 frequency band, the CZ and P4 regions displayed significant differences between the two groups. In the delta and high gamma bands, only the FZ and T3 regions were significantly different between the groups, respectively. Table 2 represents the brain regions for each frequency band with significant differences between the control and treatment groups. Absolute power of Alpha2 band in F3 and T4 regions of the brain was also demonstrated in Figure 6.

The P-values for each analysis are indicated in parentheses. The upward and downward arrows indicate an increase and decrease, respectively, following tDCS in each comparison.

Table 2. Results of the Absolute power analysis across various brain regions and frequency bands.

Delta	FZ (0.032↑)
Alpha	C3 (0.043↓), PZ (0.046↑), O1 (0.013↑), T4 (0.037↓)
Alpha1	CZ (0.016↓), P4 (0.022↑),
Alpha2	F3 (0.040↑), F4 (0.024↑), F8 (0.020↑), FZ (0.020↑), FP1 (0.037↑), FP2 (0.030↑), PZ (0.003↑), P3 (0.003↑), P4 (<0.001↑), O2 (0.049↑), T4 (0.040↑), T5 (0.009↑), T6 (0.001↑)
Beta	C4 (0.027↓), F4 (0.008↑), FZ (0.010↓)
Gamma	C4 (0.018↓), CZ (0.036↓), P4 (0.019↓)
High Gamma	T3 (<0.001↑)

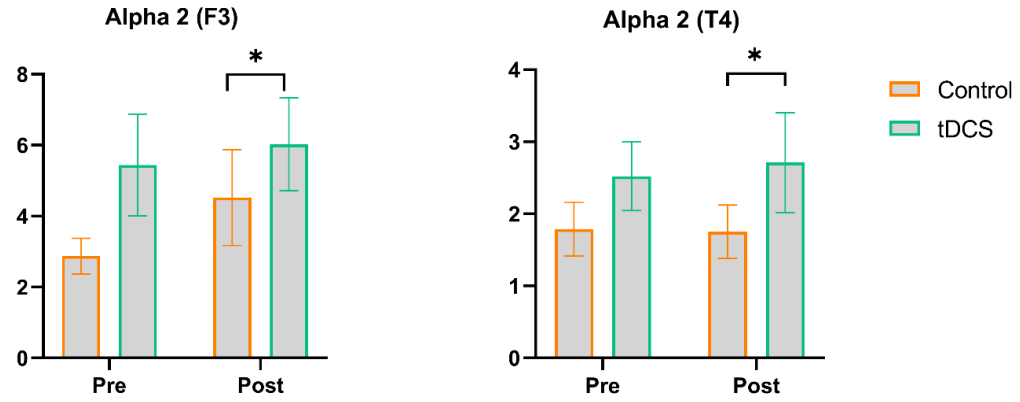

Figure 6. Absolute Power of Alpha2 frequency band in F3 and T4 regions of the brain. tDCS, Transcranial Direct Current Stimulation; Absolute Power (*P<0.05)

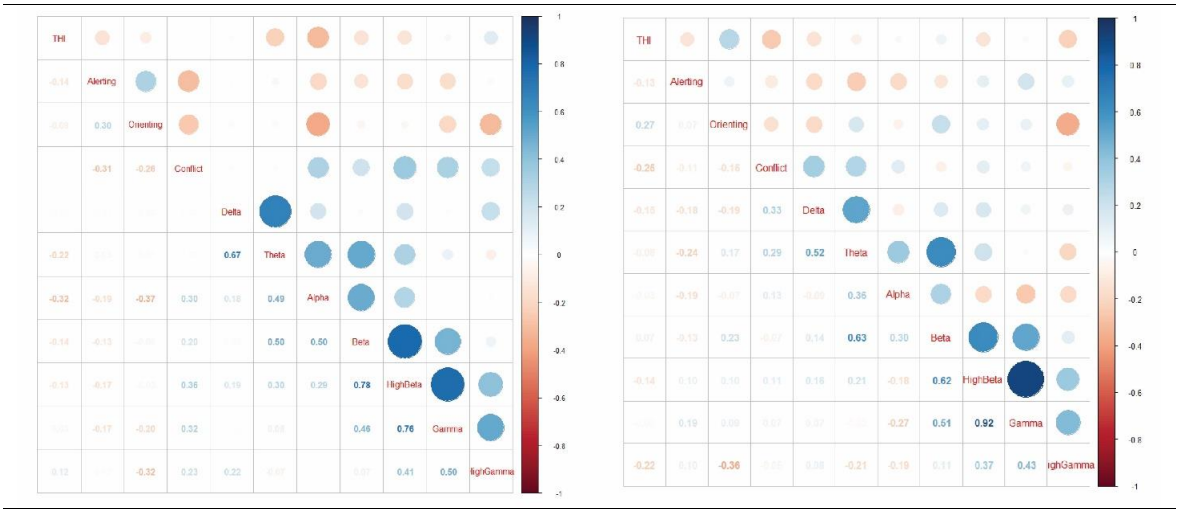

Figure 7. Correlation diagram between post-pre difference (right side) and post values (left side) of research variables in F3 area. THI, Tinnitus Handicap Inventory

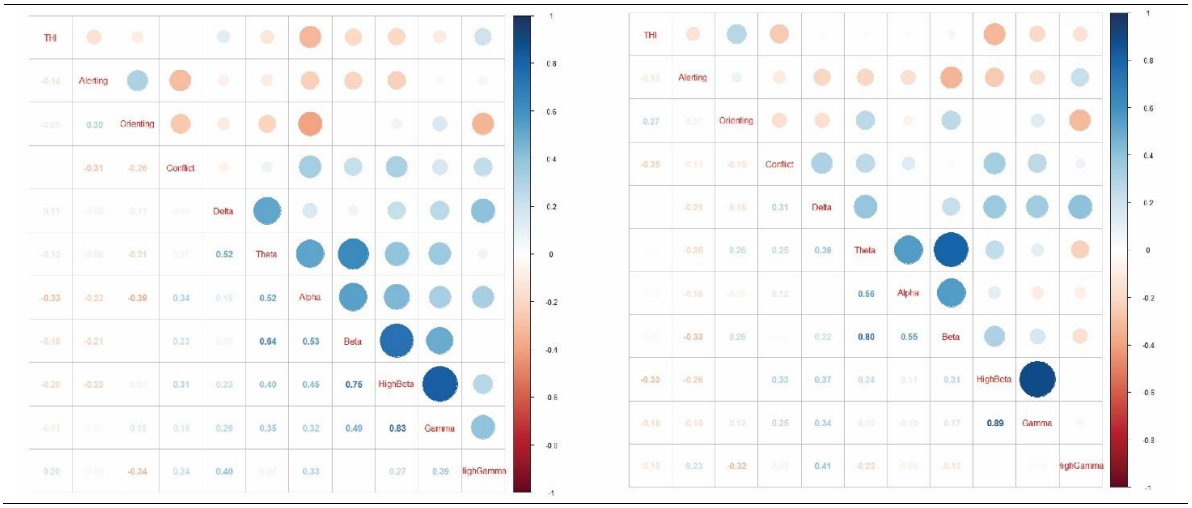

Figure 8. Correlation diagram between post-pre difference (right side) and post values (left side) of research variables in F4 area. THI, Tinnitus Handicap Inventory

Correlation analysis

The results of correlation analysis between the pre-post difference of the research variables along with the state of correlation between the post values of these variables in the F3 and F4 regions was drawn in Figure 7 and Figure 8, respectively. In these graphs, a larger circle with darker color indicates a stronger relationship between the two variables, and vice versa. Blue and red colors indicate the direct and inverse relationship of two variables, respectively. Based on these graphs, in both F3 and F4 regions, although there seems to be no relationship between the post-THI values and ANT indicators, there is a significant relationship between the pre-post values of these variables. Also, in the case of posterior values, alpha has an inverse significant relationship with THI and orienting and a direct significant relationship with conflict.

5. Discussion

The main goal of this research was to explore the impact of anodal tDCS on the left DLPFC in tinnitus patients, especially compared to sham stimulation. The focus was on its impacts on the alerting, orienting, and executive networks of attention, as well as the Absolute Power across various EEG frequency bands. This study also sought to determine if there was any notable enhancement in the attention network of tinnitus patients post-tDCS. Previous research has indicated attention deficits in tinnitus patients. The present findings suggest that any observed improvements in attention after tDCS in tinnitus sufferers might largely stem from an enhanced ability to discern and address conflicts between task-related stimuli and the distractions caused by unrelated stimuli.

In addition, previous research has revealed that tinnitus patients tend to have longer reaction times compared to those without it (33). This suggests that those with tinnitus may have impaired executive control abilities. Such abilities are crucial

for concentrating on task-related information (such as the central arrow in ANT) and blocking out distracting or irrelevant stimuli (such as incongruent flankers). Heeren et al. were the first to directly examine the integrity of attentional networks in individuals with tinnitus using the ANT (20). Their study revealed that these individuals do not suffer from a broad attentional deficit. Instead, they have a specific shortfall in top-down ECA. This particular deficit closely ties with the duration of their tinnitus and how frequently they use coping mechanisms to ease their daily tinnitus-related distress. The present findings align with recent neurobiological theories suggesting a potential connection between tinnitus habituation and activity in the PFC. On the other hand, the study indicates that alerting and orienting attentional networks remain intact in tinnitus sufferers, showing they can leverage cues to enhance their performance.

In contrast to the results of Heeren et al. (20) and the prevailing views in much of the literature (34, 35), a previous study found that tinnitus and ECA impairment had no relationships (31). Specifically, the treatment group did not experience more difficulty in resolving conflict on incongruent trials compared to the control group. In simpler terms, participants with tinnitus in this study demonstrated no signs of compromised ECA.

Yuan et al. found that tDCS offers moderate to significant relief from tinnitus symptoms (36). Similarly, Shekhawat et al. noted that stimulating the LTA and DLPFC was equally effective in reducing both tinnitus intensity and annoyance (37). This is consistent with the results of a study performed by Joos et al. regarding the effects of tDCS polarity (anodal or cathodal) on the annoyance and loudness experienced by 175 tinnitus patients (22). In the aforementioned study, notable improvements in tinnitus loudness and annoyance were reported, specifically after anodal tDCS. Interestingly, the tDCS suppressed tinnitus perception regardless of its application to either the left or right auditory cortex. Several other research papers have also highlighted the positive impacts of anodal tDCS on the DLPFC and LTA in decreasing tinnitus annoyance (32, 38).

However, in some research, no significant improvement has been reported regarding the annoyance and severity of tinnitus after tDCS (27, 28). For instance, Pal et al. did not observe any decrease in tinnitus annoyance or severity after applying cathodal tDCS to the auditory cortex and placing the anode over the PFC (28). Similarly, Forogh et al., even after using anodal tDCS over LTA on 22 participants with chronic tinnitus, did not report any notable benefits, either short-term or long-term, in reducing loudness or distress (VAS) (27). These inconsistent findings could be due to differences in the tDCS protocols (anodal vs. cathodal) and the varied criteria used to assess tinnitus symptoms (annoyance/severity vs. loudness distress).

Earlier trials exploring the potential of tDCS to suppress tinnitus showed that anodal stimulation over the LTA often resulted in positive effects, with notable reductions in annoyance (38, 39). At first glance, this might seem contradictory. After all, anodal tDCS has excitatory properties, and tinnitus is often linked to hyperexcitability in the cortical regions (40). However, this can be partly explained by the focality of the tDCS. The electrodes employed in these stimulations have broad coverage (35 cm2), which means they might also be stimulating other parts of the neural network tied to tinnitus, thereby activating nearby cortical areas. Through either competitive processes or inhibitory connections, this could reduce hyperexcitability in regions linked to the symptoms. Therefore, in essence, anodal stimulation might decrease hyperactivity in adjacent areas, either due to competition or through direct inhibition (39).

In a recent study, the present authors observed a notable decrease in THI scores from before to after the treatment in the intervention group, but not in the control group. Additional research was thus performed to determine the impact of tDCS on tinnitus severity. The findings aligned with those of Hyvarinen et al., who reported reduced tinnitus severity after 20 min of anodal tDCS over the LTA (25). Similarly, Lee et al. observed that 14 tinnitus patients experienced a 50% or greater improvement in THI scores after bilateral tDCS over the DLPFC, with the anode over F4 and the cathode over F3 (41). However, not all studies corroborate these findings. Frank et al., for instance, found no positive effects from repeated sessions employing the same tDCS montage on the THI scores of 31 tinnitus patients (42). Similarly, Pal et al. did not notice any reduction in severity after applying cathodal tDCS to the auditory cortex with the anode positioned over the PFC (28). The differences in target areas and stimulation polarity between these studies and the present one could explain the varying outcomes.

When it comes to brain electrical activity, research highlights that the theta rhythm in the frontal areas is linked to cognitive functions, such as concentration, sustained attention, working memory, and emotions (43). In the context of tinnitus, studies have indicated a rise in low-frequency Absolute Power, such as delta and theta, typical of the condition's underlying pathology (7). Notably, after tDCS treatment, a decrease was seen in theta activity, hinting at a potential decrease in attention to the symptom. The heightened activity in this band in the frontal areas corresponds with levels of prolonged attention and cognitive prowess, as established in earlier studies (43). However, no

difference was observed between the study groups in the theta frequency band.

The most notable finding of the present study in the EEG spectra of the intervention group was an enhancement in the alpha Absolute power. This heightened cortical activity aligns with a prior MEG study that reported an excess of power across all frequency ranges associated with positive symptoms (11). Furthermore, the current findings indicate a significant uptick in the delta band post-tDCS in the frontal region. This, however, contrasts with an earlier study that showed reduced and increased average total power in tinnitus compared to normal males and females, respectively (44). Such discrepancies might be attributed to the sample size, the selection criteria for the patient groups, and the specific frequency bands chosen for the statistical analysis.

Research into tinnitus and EEG has largely centered on uncovering the electrophysiological mechanisms behind the symptoms. Weisz et al. carried out a study to compare the spontaneous neuronal activity between participants with and without tinnitus (45). Their findings indicated a reduction in alpha and an increased Absolute power in the theta frequency band for the tinnitus group, compared to the control group. Moazami-Goudarzi et al. noted enhanced Absolute power in both theta and beta frequencies, predominantly in the left auditory cortex and the frontal cortex (7). Additionally, Vanneste et al. showed a heightened synchronization of beta and alpha activities in the anterior cingulate cortex for patients with tinnitus and stress in comparison with those without it. They concluded that beta activity might play a role in the neural network responsible for intense distress, mirroring the patterns observed in post-traumatic stress disorder (46).

Considering the heightened Absolute power observed in the alpha and beta frequency bands in the temporal regions, as highlighted in the aforementioned studies, the diminished activity in these frequency bands in the frontal and temporoparietal areas following tDCS, along with the clinical improvements seen in the actively treated group, suggests a therapeutic advantage from the stimulation. This positive impact is backed up by multiple tDCS studies, which report a decrease in auditory discomfort and a reduction in the severity and occurrence of symptoms (22, 37). These reports are not completely aligned with the current results of increased alpha Absolute Power in parietal and occipital areas after tDCS. In this study, the alpha frequency band in the temporal region decreased after tDCS, while the alpha2 frequency band increased after tDCS. These subtle differences might be due to differences in the procedures for applying tDCS and differences in subjects compared to other studies.

6. Conclusion

A limitation of this study is the exclusive application of tDCS to the left DLPFC. Future research should customize the tDCS stimulation side based on the tinnitus symptoms' laterality, possibly employing left, right, or both-sided anodal tDCS to enhance its effectiveness. Additionally, this study assessed the outcomes shortly after the intervention. Upcoming studies should explore the duration of these beneficial effects. Such insights can better inform tDCS treatment strategies for individuals with tinnitus.

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None.

Conflicts of interest

The authors declare that they have no conflict of interest.

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