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Original Article

The effectiveness of cathodal (tDCS) in right insulla region and cognitive-behavioral thrapy in misophonia disorder

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ABSTRACT

Misophonia disorder is a neurological disorder in which people show emotional, physical or aggressive reactions upon hearing a series of sounds, which ultimately leads to disruption in the work environment and relationships of these people. Therefore, the aim of this study was to investigate the effectiveness of cathodal tDCS and cognitive-behavioral therapy in reducing the symptoms of misophonia disorder. The current research is practical based on the purpose and based on the method of data collection, it was a semi-experimental type of pre-test and post-test with a control group. People with misophonia were selected and randomly assigned to five groups of 10 people, which included four experimental groups and one control group. The interventions included 9 sessions (tDCS) for 15 minutes with an intensity of 1 milliampere and 9 sessions of group cognitive behavioral therapy (120 minutes) and Wu's noise aversion questionnaire was used. For data analysis, multivariate analysis of covariance was performed with SPSS-25 software.

The findings showed that each of the tdcs and cognitive-behavioral treatments individually and also in combination reduce the symptoms of misophonia disorder. It seems that tdcs along with cognitive behavioral therapy has more effectiveness, which reminds the need to pay more attention to this combined treatment method, also, cognitive-behavioral therapy and electrical stimulation each have significant results and effects in They have a reduction in the symptoms of misophonia disorder.

Keywords: Hearing impairment, Misophonia disorder, Cognitive-behavioral therapy, Electrical stimulation of the brain.

Introduction

Misophonia is a strong emotional reaction to normally occurring sounds. Jastreboff & Jastreboff coined this term at the beginning of the new millennium [1]. Lexicologically, miso means dislike or hatred and phonia means sound. Thus, misophonia means sound aversion or hatred of sound. According to Dozier, misophonia is a term that does not include the hatred of all sounds, but only the hatred of certain sounds, which are called triggers [2]. Misophonia was also first described as an overreaction of the limbic and autonomic systems of the brain in response to specific auditory stimuli [3]. The term “misophonia” means hatred of sound, which was first introduced to the scientific community in 2001 by Jastreboff, although this term was used at first to express the difference between different terms in the field of hearing, which was caused by intolerance to sound, such as hyperacusis and phonophobia. None of these terms expressed the psychological state of a person suffering from misophonia. Thus, the new term misophonia was coined. However, more experts expanded the meaning and concept of this disorder due to the prevalence of this disorder.

The symptoms of this disorder include a very intense and negative reaction toward trigger sounds [4, 5, 6]. Trigger sounds are often related to the sound of the nose or mouth, such as the sounds of breathing, finning, straining, and chewing food, and some other sounds such as typing and the ticking of the clock. They are considered stimulating sounds for some people. The patients are mostly aware of the inappropriateness of their reaction to the sound source but are unable to control their reaction and use a series of coping mechanisms such as avoiding the social environment [7]. Using these mechanisms leads to disruption in the work environment and relationships between these people. These people experience loneliness and exclusion from society [8]. The rejection of these people leads to more loneliness leading to more anxiety and the worsening of the

symptoms of this disorder and comorbid disorders with this disorder .

Misophonia disorder is a mental disorder in which people have a kind of sound sensitivity syndrome and show emotional, physical, or aggressive reactions when hearing some sounds. These can affect people's nerves. They can include the sound of typing on a keyboard, a car wiper, a faucet running, drawing chalk on a board, breathing, a clock ticking, chewing, or whistling, and other sounds that can cause annoyance and sensitivity to people. In other words, misophonia are sounds that are repeated frequently and people with this disorder show nervous reactions to them. The frequency of creating this sound can exacerbate this disorder [9].

Materials and Methods

Research design and participants

The present study is applied regarding purpose and quasi-experimental type of pre-test, and post-test, with a control group in terms of data collection method. The statistical population of the present study included all people with misophonia in Mashhad in 2022. A convenient purposeful sampling method was used in this study.

Accordingly, explanations were given about misophonia disorder to the participants in a call on various social networks. Then, the subjects were asked to answer the misophonia questionnaire. Then, the inclusion and exclusion criteria were applied. The inclusion criteria of the study included the willingness to cooperate and participate in the study, having at least a secondary level of education, physical and cognitive ability, not suffering from physical diseases to participate in therapeutic interventions, being in the age range of 15 to 55 years, and not taking drugs at least two weeks before the start of the intervention. The exclusion criteria included pregnant women, people outside the age range of 15 to 55 years, and people with physical illnesses, using drugs, alcohol consumption, and suffering from brain and skull injuries. Accordingly, 60 people with misophonia were selected based on the inclusion and exclusion criteria and were randomly assigned to five groups of 12 people.

According to Research design, the quasi-experimental design of the present with the participation of 50 people includes four experimental groups (Group 1: tDCS therapy, Group 2: cognitive behavioral therapy, Group 3: tDCS therapy plus cognitive behavioral therapy, and Group 4: sham group) and one control group. The experimental and control groups were randomly matched and before the experimental interventions were assigned to the experimental and control groups, a pre-test was implemented on them. The difference between the pre-test and the post-test of each group was analyzed based on statistical significance. Accordingly, the effectiveness of tDCS and cognitive behavioral therapy was applied to determine its effect on reducing the symptoms of misophonia disorder. The data collection tool included Wu *et al*.'s (2014) misophonia questionnaire [10]. After selecting the sample group and assigning them randomly into four experimental groups and one control group, the experimental groups received the interventions.

Tools

Misophonia Questionnaire: The Misophonia Questionnaire is a self-report tool developed by Wu *et al*. in 2014 to assess the symptoms of misophonia and emotional and behavioral responses, the overall intensity of sound sensitivity, and functional impairment [10]. This questionnaire contains 17 items divided into two subscales [10].

1- Subscale of misophonia symptoms: This subscale evaluates the frequency and severity of misophonia symptoms experienced by the respondent. The items of this subscale assess the intensity of bad reactions to specific stimuli that are usually associated with misophonia.

2- Subscale of emotions and behaviors caused by misophonia: this subscale assesses the emotional and behavioral responses caused by misophonia stimuli. It assesses the range of emotional experiences (such as anger and anxiety) and coping behaviors (such as avoidance) in response to stimulus stimuli.

This questionnaire is scored on a 5-point Likert scale ranging from very high, high, moderate, low, and very low in a score from 0 to 4 indicating the intensity of or degree of agreement of the respondent to each item. This questionnaire provides a comprehensive assessment of misophonia symptoms, and emotional responses, and allows a multidimensional understanding of this disorder. Cronbach's alpha coefficient was calculated at 0.86 for the scale of misophonia symptoms, 0.86 for the subscale of emotions and behaviors caused by misophonia, and 0.89 for the whole scale [10].

Transcranial direct current stimulation **(**tDCS): tDCS is a non-invasive brain stimulation method that uses low electrical current to modulate brain activity. Two electrodes are usually involved in tDCS: an anode (positive electrode) and a cathode (negative electrode). A small brain stimulation device that transmits a constant electric current from the skull to the brain by connecting electrodes with the different polarity of the anode (activating) and cathode (inhibiting) that are installed on the scalp, and the electrodes that are mostly made of carbon and conductive materials, are placed on the scalp and the device transmits direct electrical current from the skull to the brain. A sponge soaked in salt solution is often used to prevent chemical reactions at the electrode-skin interface. The device was powered by a 9 V battery, with a maximum current of 2 mA and a maximum voltage of 80 V in direct current (DC) format [10]. At this stage, the target brain regions were selected according to the international system of 10-20 electrodes. A 2.5 x 2.5 cm cathodal electrode was placed at the midpoint between F8 and T4, while the anode electrode was placed on the arm in both cases, and the subject was exposed to sounds and images that

stimulated misophonia. The electrodes were approximately the same size. In each tDCS session, a constant current of 1 mA was applied for 15 min. The total number of sessions was 9. Stimulation for the sham group was stopped after 30 seconds. Each group received 5 stimulation sessions every other day. This montage was adapted by applying changes from the montage that Sagliano *et al*. (2019) designed in 2020 [11]. After completing the treatment sessions, all the subjects in the experimental, control, and sham groups underwent a post-test. One of the experimental groups received cathodal and cognitive behavioral sessions simultaneously.

Cognitive behavioral therapy: In this section, all subjects underwent a pre-test before the intervention. The experimental group received 9 sessions (45 minutes) of counterconditioning-focused cognitive behavioral therapy. In the counterconditioning stage, based on new results in the field of the role of mirror cells in causing misophonia disorder, images containing pleasant faces and also desirable sounds were used after presenting the misophonic stimulus. After the completion of the treatment sessions, all the subjects underwent a post-test and the experimental and control groups were compared. As mentioned, one of the experimental groups received tDCS and cognitive behavioral sessions simultaneously. The treatment protocol of the cognitive behavioral therapy was adapted from Jager *et al*. (2020) and the changes considered by the researcher (related to the counterconditioning part) were added [12].

Cognitive behavioral therapy protocol (based on counterconditioning)

The first session: welcome, introduction, initial evaluations, and familiarity with the program. In this session, Lazarus Coping Styles Questionnaire and Misophonia Questionnaire were completed by the subjects.

The second session: interaction of thoughts, emotions, physiology, and behavior, and identification of automatic thoughts.

The third session: evaluation of automatic thoughts related to misophonic stimuli, training of thought model of behavior emotion.

The fourth session: Opposing automatic thoughts and replacing proportional logic. Identifying intermediary thoughts and core thoughts and explaining them to avoid stressful situations.

The fifth session: Identifying specific mediating beliefs and analyzing thoughts and how to reconstruct and prepare logical opposing.

The sixth session: In this session, relaxation training was performed. Accordingly, the person was placed in a comfortable place and began to contract and extend all his muscles from head to toe in a quiet and peaceful environment.

The seventh session: continuation of relaxation along with playing misophonic images and sounds and immediately after that playing pictures of happy faces with soft music.

The eighth session: Continuing the process of the seventh session and selecting an alternative behavior instead of avoiding and confronting the client's opinion.

The ninth session: Termination of treatment and completion of misophonia and coping styles questionnaire.

Data analysis

The data were analyzed in two sections using SPSS-25 software.

The first section: This section presents a report of descriptive results using prevalence, percentage, mean, and standard deviation indices.

The second section: In this section, to test the hypotheses of the study, after examining the assumptions of the multivariate analysis of covariance (MANCOVA), which includes the normality and homogeneity of the variances, multivariate analysis of covariance test (with control of pre-test scores) was used.

Results and Discussion

Descriptive results

Base on finding regarding the misophonia variable, the highest mean in the groups is related to the tDCS group, and the lowest mean is related to the control group in the pre-test stage. Also, the highest mean is related to the sham group, and the lowest mean is related to cognitive behavioral therapy in the post-test phase. Also, regarding the variable of excitement caused by misophonia, the highest mean is related to the sham group, and the lowest mean is related to the control group in the pre-test stage. The highest mean is related to the sham group and the lowest mean is related to the cognitive behavioral and tDCS group in the post-test stage.

Inferential results

In this section, based on the research hypothesis, a multivariate covariance analysis test was used. Therefore, we will examine the assumptions required to use the test:

Normal distribution of variables: This assumption means that the distribution of variables in this society was normal. In other words, the parametric test can be used when the population distributions do not differ much from the normal distribution [13]. To examine the normal distribution of the variables due to the small sample size, the Shapiro-Wilk test was used. A significance level higher than $P<0.001$ in this test indicates the normal distribution of the variables [14]. The following table presents the results.

The results show that the distribution of all variables by groups is normal ($P\geq0.05$).

2. Equality of variances: This assumption means that two samples have been selected from populations with equal variances. In other words, the parametric test can be used when the variances

of the population do not differ much from the state of equality [13]. To examine the equality of variances, Levene's test of equality of variances was used. In this test, if the significance level is higher than 0.05, it means that the assumption of equality of variances is fulfilled [15]. The results of this hypothesis are shown in the table below.

Table 1. Results of Levene's test to examine the equality of variance error

Variable	F	Df1	Df2	Sig
Misophonia	1.50	4	44	0.217
Excitement caused by misophonia	2.17	4	۴۴	0.087

According to the results of the above table, it can be concluded that the equality of variances has been fulfilled in all variables.

3. The assumption of equality of variance-variance matrices: the fulfillment of this assumption is necessary for multivariate variance analysis. Generally, the assumption of equality of variances seeks to investigate whether the samples are selected from populations with equal variances or not. When this assumption is fulfilled, the data from these two populations can be combined to obtain an unbiased estimate of the population variance [13].

The implementation of the assumption of equality of variance-variance matrices also follows such a goal. Box's M test is used to examine the quality of the variance-variance matrices of the research variables. Based on the significance level obtained in this test, it is possible to judge the equality or non-equality of the variance-variance matrices. Thus, if the obtained significance level is higher than P = 0.05, the matrices are equal and vice versa [15]. The results of this hypothesis are shown in the table below.

Table 2. Examining the assumption of the equality of variance-covariance matrices

Box` s M	F	Df1	Df2	Sig
25.42	1.90	12	13939.921	0.059

The results of the above table show that the assumption of equality of the variance-covariance matrix has been fulfilled (P<0.05).

3. Multiple Correlation of Dependent Variables: There are disagreements about the extent to which dependent variables should be correlated with each other. This assumption is examined using Bartlett's test. The significant coefficients of this test indicate the multivariate correlation between the dependent variables [14]. The results of this hypothesis are shown in the table below. The results indicate the fulfillment of this assumption.

Table 3. Results of Bartlett's test of sphericity

sig	df	X2 value
0.002	2	12.47

Based on the results of **Table 6**, the above assumption is fulfilled. Given what was stated, the necessary assumptions to implement the test have been fulfilled. Thus, the test results are reported.

The assumption of equality of the regression slope is fulfilled for all variables (significance level is higher than 0.05).

A multivariate test was used in this study. This test compares the linear combination of variables among the subjects of different groups. The results of the Wilks-Lambda test are presented as one of the most valid multivariate tests when the assumptions of the analysis are fulfilled. The results are reported in the table below.

Table 4. Multivariate test

Variable	Wilks-lambda	F	Sig
Group membership	0.403	5.889	0.00

the difference in the linear combination of variables in the groups is statistically significant. The level of effect or difference according to the Wilks-Lambda test is 0.403, in other words, 40% of individual differences in the post-test scores of misophonia symptoms and excitements and behaviors caused by misophonia is related to the effectiveness of TDCS and cognitive behavioral therapy in people suffering from misophonia (group membership).

Table 5. Covariance test results

Independent variable	dependent variable	sum of squares	df	mean sum of squares	F	sig	Effect size
Group membership	misophonia	688.454	4	172.113	8.03	0.00	0.434
	Excitement caused by misophonia	1493.084	4	373.272	10.72	0.00	0.505

According to the above table, it can be concluded that by controlling the pre-test effect, there is a significant difference between groups based on group membership in all variables. Thus, the general hypothesis of the study is confirmed.

Table 6. Pairwise comparison of misophonia variable

Group 1	Group 2	Mean difference	Sig
Cognitive behavioral therapy plus tDCS	tDCS	0.694	0.001
	Cognitive behavioral therapy	1.654–	0.001
	sham	9.284–	0.000
	Control	-5.694	0.009

tDCS	Cognitive behavioral therapy	2.348-	0.289
	sham	9.977-	0.000
	Control	6.387-	0.007
Cognitive behavioral therapy	sham	7.629-	0.002
	Control	4.04-	0.005
Control	sham	3.59-	0.097

As shown in **Table 6**, by controlling the pre-test, there is a significant difference between the subjects in the tDCS, cognitive behavioral therapy, cognitive behavioral group plus tDCS, sham, and control groups regarding the variable of misophonia symptoms. Therefore, the hypothesis related to the variable of misophonia symptoms is confirmed ($p<0.05$). In other words, the tDCS therapy, cognitive behavioral therapy, and cognitive behavioral therapy plus tDCS according to the mean symptoms of misophonia of the subjects in the experimental groups compared to the mean of the control group and the sham group caused a decrease in the misophonia symptoms in the experimental groups.

Table 7. Pairwise comparison of the excitement caused by misophonia variable

Group 1	Group 2	Mean difference	Sig
Cognitive behavioral therapy plus tDCS	tDCS	5.689	0.000
	Cognitive behavioral therapy	5.442	0.001
	sham	8.87-	0.002
	Control	6.637-	0.001
tDCS	Cognitive behavioral therapy	0.247-	0.000
	sham	14.559-	0.000
	Control	12.326-	0.000
Cognitive behavioral therapy	sham	14.312-	0.000
	Control	-12.079	0.00
Control	sham	2.223-	0.412

Based on **Tables 6** and 7, if the significance level related to pairwise comparison is less than 0.05, the difference will be significant.

As presented in **Table 7**, by controlling the pre-test, there is a significant difference between the subjects in the TDCS, cognitive behavioral therapy, cognitive behavioral group plus tDCS, sham, and control groups regarding the variable of excitement caused by misophonia. Thus, the hypothesis related to the excitement caused by misophonia is confirmed ($p<0.05$). In other words, tDCS therapy, cognitive behavioral therapy, and cognitive behavioral therapy plus tDCS according to the mean symptoms of misophonia of the subjects in the experimental groups compared to the mean of the control and the sham groups reduced the excitement caused by misophonia in the experimental groups.

The present study investigates the effectiveness of tDCS based on brain mapping in the right anterior insular region and counterconditioning-focused cognitive behavioral therapy in reducing the symptoms of misophonia disorder and improving the coping style. Multivariate analysis of covariance was used for this purpose. The results revealed that both tDCS therapy and cognitive behavioral therapy separately and the simultaneous use of tDCS therapy and cognitive behavioral therapy reduce the symptoms of misophonia disorder and improve coping styles in people with misophonia disorder.

These results are in line with those of studies by Kumar *et al*. (2017) regarding the effectiveness of tDCS, Schröder *et al*. (2017), Aazh *et al*. (2019), Jager *et al*. (2021), and Safari (2021) regarding the effectiveness of cognitive behavioral therapy in reducing misophonia symptoms [12, 16-19]. Although the difference between the intervention methods was not significant, based on mean symptoms of misophonia in the subjects of the experimental groups compared to the mean of the control group, it can be concluded ethat among the three types of intervention or treatment (1-tDCS, 2- cognitive behavioral therapy, 3- tDCS plus cognitive behavioral therapy) in reducing the symptoms of misophonia, tDCS therapy was more effective than the other two methods of intervention, and the cognitive-behavioral plus tDCS has the least effect. Also, tDCS therapy was more effective in reducing the excitement caused by misophonia, and cognitive behavioral therapy was less effective than the other two interventions. These results are somewhat consistent with the results of studies by Safari (2021) and Abramovitch *et al*. (2024) [19, 20]. In interpreting and explaining these results and the reason for the higher effectiveness of tDCS therapy in reducing misophonia symptoms, we can refer to the results of Abramovitch *et al*. (2024), who studied the neuropsychology of misophonia [20].

In this study, people with misophonia disorder performed significantly weaker in 2 neuropsychological outcomes, including verbal memory recovery and attention, than the control group. The misophonia group reported significantly higher symptoms of anxiety, behavioral impulsivity, and functional disorders. They had a higher rate of ADHD and OCD. Thus, based on the mentioned study, it can be stated that misophonia disorder is widely related to the nervous system and brain. In this regard, misophonia has been described as an overreaction of the limbic and autonomic systems of the brain in response to specific auditory stimuli in one of the well-known definitions [3]. Thus, tDCS can have significant effectiveness. Also, the number of cognitive behavioral therapy sessions and the improvement of the skills in conducting the sessions make this intervention method to be more effective. Also, it seems that the interference, fatigue, loss of quality, and accuracy in the simultaneous use of tDCS and cognitive behavioral therapy lead to a decrease in its effectiveness.

Conclusion

It is concluded that each tDCS and cognitive behavioral therapy individually and simultaneously using them reduces the symptoms of misophonia disorder. However, tDCS is more effective, highlighting the need to pay more attention to this method of treatment. Also, cognitive behavioral therapy has significant effects in reducing misophonia disorder symptoms. Accordingly, one of the treatments mentioned above methods can be considered considering the conditions and facilities. However, observing and paying attention to considerations such as the conditions of the clients, the correct application of the principles and techniques of cognitive behavioral therapy, setting the appropriate number of sessions, conducting treatment follow-up courses, and using up-to-date guidelines can significantly increase the effectiveness of cognitive behavioral intervention.

The results revealed that cognitive behavioral therapy, despite its effectiveness in reducing misophonia symptoms, was less effective than tDCS therapy. Thus, it is recommended to pay more attention to the number of sessions, principles, and techniques of cognitive behavioral therapy, and up-to-date protocols in this area. Additionally, due to the significant effectiveness of the tDCS method, the introduction of this method of intervention in scientific and academic workshops, and mass media, healthcare centers should benefit from this method along with other treatment methods.

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Conflict of interest: None

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Ethics statement: All ethical principles are considered in this article. The participants were informed of the purpose of the research and its implementation stages. They were also assured about the confidentiality of their information and were free to leave the study whenever they wished, and if desired, the research results would be available to them. Written consent has been obtained from the subjects. principles of the APA and Helsinki Convention were also observed.

This study was approved by the Ethics Committee of the University of ferdowsi of mashhad (Code ir.um.rec.1402.159).

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