

Effects of transcranial direct current stimulation combined with tinnitus retraining therapy on sleep disorders in patients with chronic tinnitus

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Abstract. – OBJECTIVE: The aim of this study was to investigate the effects of transcranial direct current stimulation (TDCS) combined with tinnitus retraining therapy (TRT) on clinical efficacy and sleep disorder in patients with chronic tinnitus.

PATIENTS AND METHODS: 126 patients with chronic tinnitus treated in our hospital from May 2020 to June 2022 were retrospectively analyzed. These subjects were randomly divided into two groups: the electrical stimulation group and the combined group, in line with the random table method, with 63 patients in each group. Patients in the electrical stimulation group received TDCS treatment, and patients in the combined group were given TDCS combined with TRT. The clinical effects, tinnitus severity [Tinnitus Evaluation Questionnaire (TEQ) score and Tinnitus handicap inventory (THI) score], sleep status [Sleep Status Rating Scale (SRSS) score and Pittsburgh Sleep Quality Index (PSQI) score], psychological status [Hamilton Anxiety Scale (HAMA) score and Self Rating Depression Scale (SDS) score] and the quality of life (Quality of Life Scale) of these subjects in two groups were analyzed.

RESULTS: The clinical effect of simple TDCS was 82.53%, which was sharply lower compared to 95.24% in the combined group ($p < 0.05$). After the treatment, TEQ score, THI score, SRSS score, PSQI score, HAMA score, and SDS score were decreased in both groups ($p < 0.05$), and the combined group was much lower than the TDCS group ($p < 0.01$). Compared with the pre-treatment period, the scores of restrictions in daily living, medical resource utilization, somatic symptoms, and emotional disturbance were elevated in both groups after treatment, and the combined group had markedly higher scores than the TDCS group ($p < 0.05$).

CONCLUSIONS: TDCS combined with TRT had obvious effects in treating chronic tinnitus, which largely reduced the severity of tinnitus, improved

patients' sleep quality and psychological status, and improved the quality of life, indicating a certain worthy of clinical application and promotion.

Key Words:

Transcranial direct current stimulation, Tinnitus habit therapy, Chronic tinnitus, Clinical efficacy, Sleep disorders.

Introduction

Tinnitus refers to the perception of sound without external auditory stimulation. According to relevant statistics¹, over 20% of adults will experience tinnitus. Tinnitus is represented by auditory hallucinations, which can be explained by the plasticity change in brain adaptation caused by peripheral auditory input. The etiology of tinnitus is complex, and it may be accompanied by various manifestations caused by different causes. Currently, there is no clear treatment method for tinnitus, and some tinnitus may develop into refractory tinnitus, seriously affecting the quality of life of patients. Patients often have different comorbidities, such as anxiety, depression, and sleep disorders².

In recent years, non-drug technologies, such as cognitive behavioral therapy and hearing aids, have gradually been applied to the treatment of chronic tinnitus, and have achieved certain results, but the treatment effect is limited³. Therefore, finding more effective techniques to treat chronic tinnitus has an important role in reducing anxiety and improving sleep disorders in patients. Transcranial direct current stimulation (TDCS) is a non-invasive neuromodulation technique. Some studies⁴ have found that it has significant efficacy

in improving the cognitive function of healthy individuals and the symptoms of various neuropsychiatric diseases, such as depression, auditory language hallucinations, and chronic pain. Tinnitus retraining therapy (TRT) is a habit therapy that aims to use voice therapy to reclassify tinnitus perception as a central signal. Previous studies⁵ have found that TDCS and TRT can effectively reduce the symptoms of tinnitus. However, due to the high heterogeneity of the population with tinnitus, using only one treatment method may not achieve the desired effect.

In this study, 126 patients with chronic tinnitus treated in our hospital in the May 2020 to June 2022 period were optioned as the subjects. These subjects received transcranial direct current stimulation and tinnitus acclimatization therapy, aiming to compare the effects of two treatments on clinical efficacy and sleep disorder in patients with chronic tinnitus.

Patients and Methods

General Materials

126 patients with chronic tinnitus who were retrospectively treated in Henan Provincial People's Hospital from May 2020 to June 2022, were selected as the subjects following the process in Figure 1. These subjects were randomized as the TDCS group and the combined group, in line with the random table method, with 63 patients in each group. A total of 35 males and 28 females formed the electrical stimulation group, with an

average age of 55.37 ± 7.26 years old and an average course of disease of 12.25 ± 3.76 months. In the combined group, 39 males and 24 females had an average age of (56.23 ± 9.81) years old and an average course of disease of 13.33 ± 3.41 months. Inclusion criteria: (1) All subjects met the diagnostic and treatment guidelines for tinnitus⁶, and the duration of the disease exceeded 10 months; (2) The patient had basic communication and reading and writing skills; (3) The clinical and pathological data of the patient was complete. The patient and their family members were informed and signed the informed consent form. Exclusion criteria: (1) Patients with significant abnormalities in liver and kidney function or cardiac function; (2) Patients with infectious diseases such as AIDS and hepatitis B; (3) Patients with autoimmune diseases such as diabetes and systemic lupus erythematosus; (4) Patients who could not receive electrical stimulation therapy. General data between the electrical stimulation group and the combined group had no significant difference ($p > 0.05$). This study was approved by the Ethics Committee of Henan Provincial People's Hospital and People's Hospital of Zhengzhou University and was conformed to the relevant principles of medical ethics (approval number: 202204).

Methods

Patients in the electrical stimulation group received transcranial direct current stimulation treatment. The patient took a comfortable sitting position and placed saline-soaked cathode and anode electrodes in both prefrontal cortexes

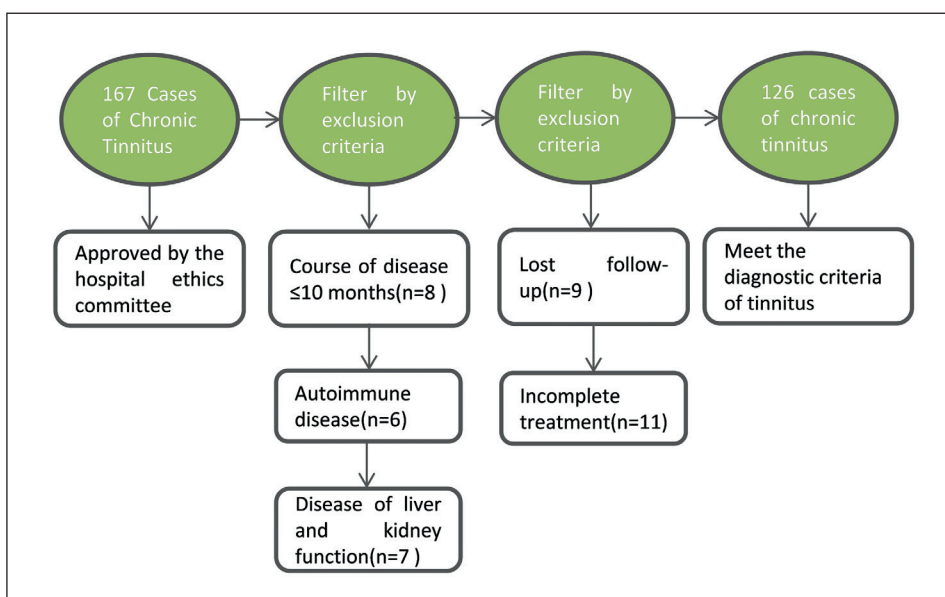


Figure 1. The selection process of general data.

for stimulation. The stimulation current intensity was set to 2 mA, and the stimulation duration was 20 minutes (both acceleration and deceleration times were 40 seconds). The treatment was performed 5 times per week for a total of 4 weeks.

Patients in the combined group were given transcranial direct current stimulation combined with tinnitus practice therapy. The phases of therapy were as follows: (1) Learn about patients' current problems and provide detailed answers to alleviate their negative emotions and enhance their confidence in active treatment; (2) During training, patients could relax their mood and relax their nerves and muscles. Patients were treated twice a day for about 20 minutes each time; (3) In daily life, when patients feel tinnitus, they can divert their attention to tinnitus by listening to music, reading books, and other ways to alleviate the adverse physiological arousal of tinnitus. Enable patients to form a habit of tinnitus signals, and encourage patients to let the habit process proceed naturally; (4) Audiologists guided participants to wear a hearing nitus comprehensive diagnostic instrument as much as possible to listen to natural and pleasant sounds such as wind and rain, for about 5 hours per day. Patients were encouraged to enrich the sound environment at any time. The treatment lasted for 4 weeks.

Outcome Measures

The clinical efficacy of the treatment was evaluated by different degrees: 1. Recovery: tinnitus disappeared, accompanied by symptom disappearance, and no recurrence after 1 month of follow-up; 2. Marked effectiveness: The tinnitus level was reduced by more than 2 levels (including 2 levels); 3. Valid: tinnitus level was reduced by 1 level; 4. Invalid: There is no change in tinnitus level. Total effective rate = (healed + effective + markedly effective)/total number of cases \times 100%.

The severity of tinnitus was evaluated using the Tinnitus Evaluation Questionnaire (TEQ) score and the Tinnitus Handicap Inventory (THI) score⁸. The TEQ score includes 6 items, such as the environment in which tinnitus occurs and the duration of tinnitus, with a score of 0-21 points. A higher TEQ score suggested more serious tinnitus. A total of 25 items made up the THI score of 0 to 4 points each, with a score of 0 to 100 points. A higher THI score indicated a higher degree of tinnitus disability in the patient. Sleep disorder was evaluated using the Self Rating Scale of Sleep (SRSS) score⁹

and the Pittsburgh Sleep Quality Index (PSQI) score⁹. The SRSS scale includes 10 items, including "Do you feel like you have enough sleep at ordinary times?" and "Do you feel like you have had enough rest after sleep?". Each item has 1-5 points, with a total score of 10-50 points. Lower scores mean less sleep problems. The PSQI score consists of 18 items and 7 components, with each component scoring 0-3 points and a total score of 0-21 points. Higher PSQI score symbolizes poorer sleep quality of the patient.

The psychological status of patients was assessed using the Hamilton Anxiety Scale (HAMA) score¹⁰ and the Self Rating Depression Scale (SDS) score¹¹. The HAMA score includes 14 items such as anxiety, nervousness, and fear. Each item has a score of 0-4 points, with a total score of 0-56 points. The higher the score, the more severe the anxiety of the patient is. The SDS score includes 20 items, with a total score of 41 points. Lower SDS score stands for better patient's psychological status.

The quality of life of patients was evaluated using the Life Quality Scale¹² score. The Life Quality Scale has 20 items divided into 4 parts, including daily life limitations, medical resource utilization, physical symptoms, and emotional disorders. Each item has 0-5 points, with a total score of 100 points. Higher score implies higher life quality of the patient.

Statistical Analysis

The clinical effects and other enumeration data in this study were shown as [cases (%)] and compared following χ^2 test. Measurement data such as TEQ score, THI score, SRSS score, PSQI score, HAMA score, SDS score, and Life Quality Scale score were all tested for normal distribution, and they all conformed to normal distribution, using the form of ($\bar{x} \pm s$). The measurement data between the two groups were analyzed using an independent sample *t*-test. In this study, SPSS 23.0 software (IBM Corp., Armonk, NY, USA) was used for statistical data analysis, and $p < 0.05$ indicated a statistically significant difference.

Results

Clinical Effect of TDCS Combined with TRT on Patients with Chronic Tinnitus

The clinical effect of TDCS was 82.53%, which was sharply lower relative to 95.24% in the combined group ($p < 0.05$, Table I).

Table I. Clinical effect of TDCS combined with TRT on patients with chronic tinnitus [cases (%)].

Groups	TDCS group (n=63)	Combined group (n=63)	χ^2	<i>p</i>
Recovery	11 (17.46)	14 (22.22)		
Marked effectiveness	28 (44.44)	26 (41.27)		
Valid	13 (20.63)	20 (31.75)		
Invalid	11 (17.46)	3 (4.76)		
Efficiency	52 (82.53)	60 (95.24)	5.143	0.023

Effects of TDCS Combined with TRT on the Severity of Tinnitus in Patients

After the treatment, TEQ and THI scores were decreased in both groups ($p<0.05$), and the combined group showed much lower scores than the TDCS group scores ($p<0.01$, Table II and Figure 2).

Effects of TDCS Combined with TRT on Sleep Disorder in Patients

After the treatment, SRSS and PSQI scores were sharply decreased in both groups ($p<0.05$), and the score of the combined group was much lower than the score of the TDCS group ($p<0.01$, Table III and Figure 3).

Effects of TDCS Combined with TRT on the Psychological Status of Patients

After the treatment, HAMA and SDS scores were decreased in both groups ($p<0.05$), and the combined group score was much lower than the TDCS group score ($p<0.01$, Table IV and Figure 4).

Effects of TDCS Combined with TRT on Life Quality

Compared with the pre-treatment period, the scores of restrictions in daily living, medical resource utilization, somatic symptoms, and emotional disturbance were elevated in both groups after treatment, and the combined group had

Table II. Effects of TDCS combined with TRT on the severity of tinnitus in patients ($\bar{x} \pm s$, score).

Groups	Time	TDCS group (n=63)	Combined group (n=63)	<i>t</i>	<i>p</i>
TEQ score	Before treatment	13.30±5.14	13.48±5.02	0.199	0.843
	After treatment	10.37±4.05	7.95±3.40	4.205	<0.001
	<i>t</i>	3.554	7.239		
	<i>p</i>	0.001	<0.001		
THI score	Before treatment	52.74±13.62	53.53±13.44	0.328	0.744
	After treatment	41.19±10.86	35.35±9.08	3.275	0.001
	<i>t</i>	5.263	8.897		
	<i>p</i>	<0.001	<0.001		

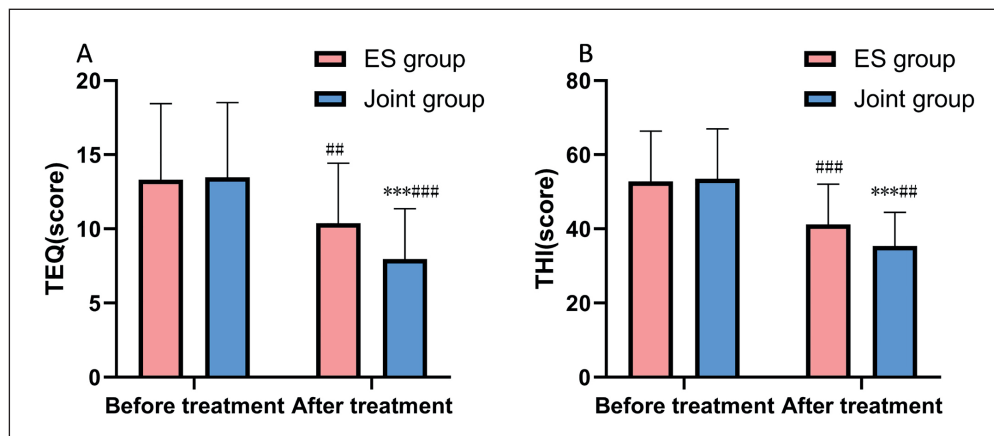


Figure 2. Comparison of tinnitus severity scores between two groups. **A,** Comparison of TEQ scores between two groups before and after treatment. **B,** Comparison of THI scores between two groups before and after treatment. ^{ns} $p>0.05$ compared to the TDCS group; ^{**} $p<0.01$, ^{***} $p<0.001$ compared to the TDCS group; ^{##} $p<0.01$, ^{###} $p<0.001$ compared to the same group before treatment.

Table III. Effects of TDCS combined with TRT on sleep disorder in patients ($\bar{x} \pm s$, score).

Groups	Time	TDCS group (n=63)	Combined group (n=63)	t	p
SRSS score	Before treatment	26.62±8.50	26.90±7.95	0.191	0.849
	After treatment	21.43±5.35	15.69±4.28	6.650	<0.001
	t	4.102	9.855		
	p	<0.001	<0.001		
PSQI score	Before treatment	15.13±3.09	14.22±2.41	1.843	0.068
	After treatment	9.79±3.04	6.91±2.73	5.595	<0.001
	t	9.778	15.933		
	p	<0.001	<0.001		

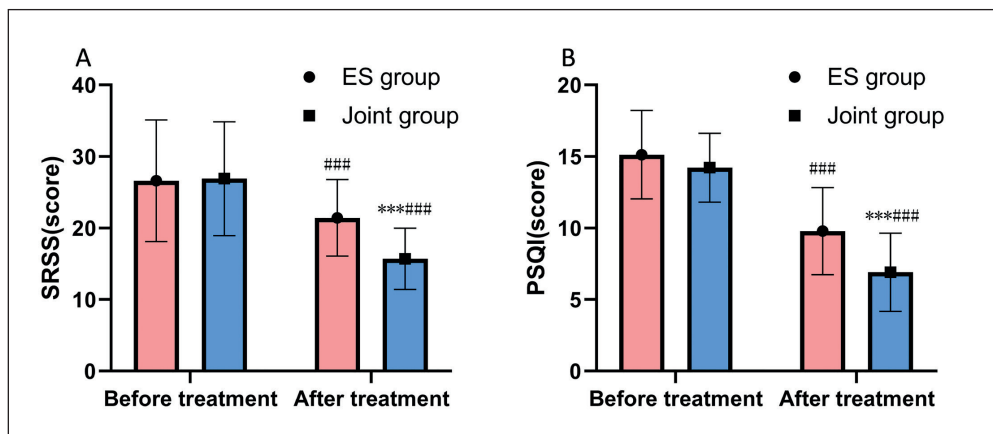


Figure 3. Comparison of tinnitus sleep disorder scores between two groups. **A**, Comparison of SRSS scores between two groups before and after treatment. **B**, Comparison of PSQI scores between two groups before and after treatment. ^{ns}*p*>0.05 compared to TDCS group; ^{**}*p*<0.01, ^{***}*p*<0.001 compared to TDCS group; ^{###}*p*<0.001 compared to the same group before treatment.

markedly higher scores than the TDCS group (*p* <0.05, Table V and Figure 5).

Discussion

Tinnitus is defined as a ringing, hissing, clicking, or growling sound that individuals consciously perceive without external auditory stimulation, and is a frequent symptom in modern society. The pathogenesis of tinnitus is relatively

complex, and tinnitus perception may begin at the level of cochlear afferent nerve block. Neuronal changes from the central auditory system to non-auditory areas (such as the limbic system) may be the main factor causing chronic tinnitus^{13,14}. Thus, understanding the pathogenesis of tinnitus and exploring treatment methods are important for alleviating the symptoms of tinnitus.

There is no unified treatment method for tinnitus. Currently, the focus of tinnitus treatment is to reduce or mask tinnitus, rather than stop

Table IV. Effects of TDCS combined with TRT on psychological status of patients ($\bar{x} \pm s$, score).

Groups	Time	TDCS group (n=63)	Combined group (n=63)	t	p
HAMA score	Before treatment	13.57±4.42	13.64±3.56	0.098	0.922
	After treatment	10.79±2.84	7.38±2.73	6.871	<0.001
	t	4.200	11.075		
	p	<0.001	<0.001		
SDS score	Before treatment	54.21±5.36	53.28±4.62	1.043	0.299
	After treatment	50.15±4.20	42.14±3.54	11.575	<0.001
	t	4.732	15.192		
	p	<0.001	<0.001		

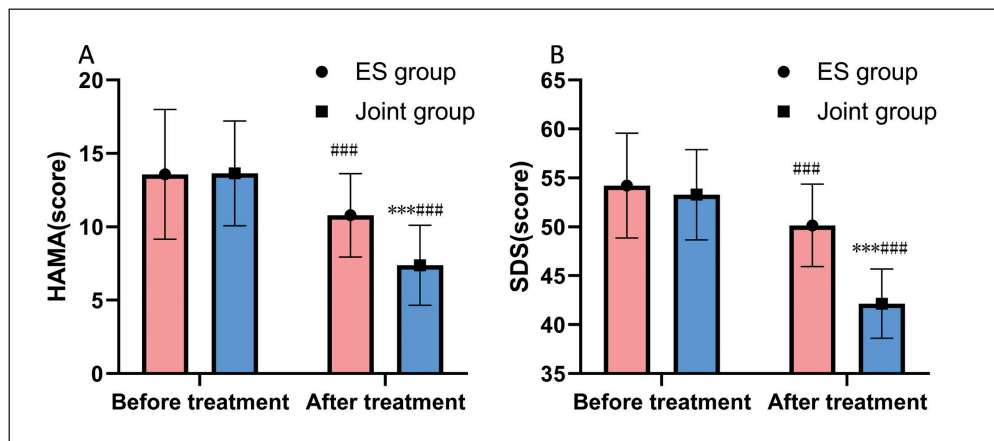


Figure 4. Comparison of psychological status scores between two groups. **A**, Comparison of HAMA scores between two groups before and after treatment. **B**, Comparison of SDS scores between two groups before and after treatment. ^{ns} $p > 0.05$ compared to TDCS group; ^{***} $p < 0.001$ compared to TDCS group; ^{###} $p < 0.001$ compared to the same group before treatment.

tinnitus¹⁵. Tinnitus masking, tinnitus retraining, or personalized music therapy combined with medication can be effective in the treatment of tinnitus patients. In these methods, personalized music therapy may be a better treatment than tinnitus masking and tinnitus retraining therapy after nine months of treatment¹⁶. TDCS is a popular method of brain stimulation, which can utilize the characteristics of weak direct current flowing through nerve tissue to trigger changes in subthreshold action potential. It has been shown¹⁷ that TDCS can change the activity and excitability of cerebral cortical neurons to a certain extent,

thereby inducing changes in brain function, and its application value in patients with brain injury has been proven. Some studies¹⁸ have found that TDCS, as a neuroregulatory technique, can enhance cortical plasticity and improve motor function in a range of neurological diseases. Some scholars found that¹⁹, when patients with tinnitus were treated with TDCS, the tinnitus function index and the total score of the tinnitus questionnaire significantly increased over time. TDCS can significantly improve the tinnitus sensation in patients. TRT is an internationally recognized habit-based treatment that combines educational

Table V. Effects of TDCS combined with TRT on life quality ($\bar{x} \pm s$, score).

Groups	Time	TDCS group (n=63)	Combined group (n=63)	t	p
Restrictions in daily living	Before treatment	14.59±3.22	14.32±2.25	0.546	0.586
	After treatment	16.11±3.45	17.74±5.14	2.090	0.039
	t	2.557	4.838		
	p	0.012	<0.001		
Medical resource utilization	Before treatment	8.47±2.97	8.39±3.82	0.131	0.896
	After treatment	12.26±3.43	15.22±2.19	5.773	<0.001
	t	6.630	12.312		
	p	<0.001	<0.001		
Somatic symptoms	Before treatment	25.91±3.02	25.73±2.94	0.339	0.735
	After treatment	34.66±4.16	37.66±3.10	4.590	<0.001
	t	13.510	22.163		
	p	<0.001	<0.001		
Emotional disturbance	Before treatment	17.13±3.57	16.71±3.40	0.676	0.500
	After treatment	20.26±4.11	22.57±5.92	2.544	0.012
	t	4.564	6.813		
	p	<0.001	<0.001		
Total score	Before treatment	66.10±12.78	65.15±12.41	0.423	0.673
	After treatment	83.29±13.15	93.19±10.35	4.696	<0.001
	t	7.441	13.773		
	p	<0.001	<0.001		

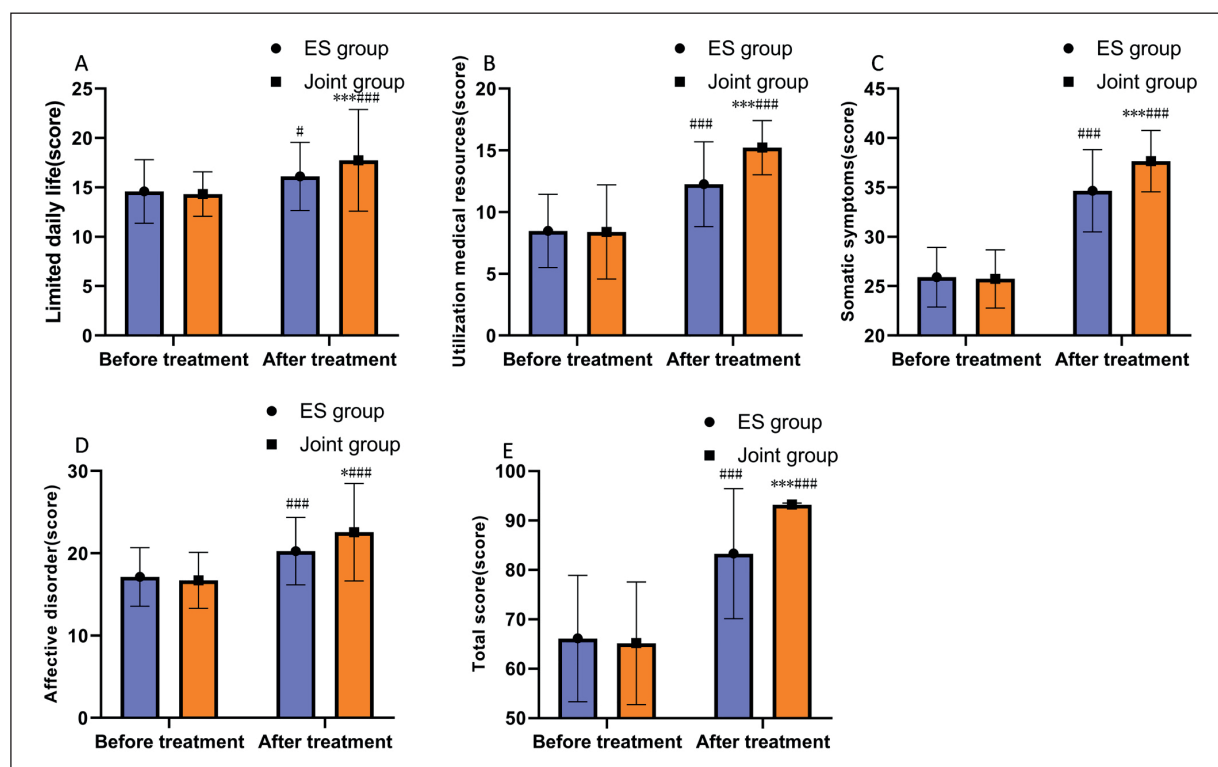


Figure 5. Comparison of life quality scores between two groups. **A**, Comparison of daily living restriction scores before and after treatment. **B**, Comparison of medical resource utilization scores before and after treatment. **C**, Comparison of somatic symptom scores before and after treatment. **D**, Comparison of emotional disorders scores before and after treatment. **E**, Comparison of total scores before and after treatment. ^{ns} $p > 0.05$ compared to TDCS group; * $p < 0.05$, *** $p < 0.001$ compared to TDCS group; # $p < 0.05$, ### $p < 0.001$ compared to the same group before treatment.

counseling for tinnitus to help patients become accustomed to perceiving tinnitus. TRT treatment reduces the impact of tinnitus on health-related life quality by reducing negative emotions in patients. In some studies, it has been evaluated that TRT can obviously improve the response rate of patients with tinnitus, reduce the THI score, and alleviate the symptoms of tinnitus²⁰. The results of this study indicated that TDCS combined with TRT had a better clinical effect on chronic tinnitus compared to TDCS, and could largely reduce the symptoms of tinnitus. The above results suggested that TDCS combined with TRT was an effective treatment for chronic tinnitus.

The causes of tinnitus are complex, and occupational or recreational noise exposure is closely related to the occurrence of tinnitus. When tinnitus occurs, persistent, annoying, and irritating noise can affect the patient's social interaction and social functions, reducing the joy of life. In addition, tinnitus can be amplified in a quiet environment. Tinnitus, which worsens before bedtime, can seriously affect sleep quality, leading to daytime fatigue and lethargy²¹. The results of

this study indicated that TDCS combined with TRT could largely improve sleep disorders in patients with chronic tinnitus. In addition to sleep quality, tinnitus can also seriously affect the mental health of patients. It is often associated with adverse psychological emotions such as anxiety and depression. Research^{22,23} found that tinnitus patients had a stronger increased incidence rate of anxiety and depression than healthy subjects. Sleep disorders may promote the occurrence of anxiety, exacerbate the severity of most anxiety symptoms, and may increase the risk of emotional distress in patients with tinnitus. The results of this study proved that TDCS combined with TRT decreased HAMA scores and SDS scores and improved anxiety, depression, and life quality in patients. In fact, TDCS, combined with TRT, can enhance patients' confidence, divert patients' attention, improve patients' sleep disorders, and alleviate patients' negative emotions such as anxiety and depression.

Negative emotions related to tinnitus can also activate the pressure response of the limbic system, causing increased sympathetic responses

and dysfunction, increasing the sensitivity and subjective discomfort of patients to tinnitus, and reducing tolerance. TDCS delivers a weak direct current of 0.5 to 2 mA to the scalp to stimulate the prefrontal cortex, auditory cortex, and left temporal parietal region. By this method, TDCS induces changes in cortical excitability, thereby regulating tinnitus-related anxiety and depression. Research²⁴ found that TDCS improved patients' negative emotions and improved their quality of life. The purpose of TRT is to adapt to tinnitus, mainly through retraining the conditioned reflex, so that patients can achieve adaptation to tinnitus. TRT can help patients reduce neuromuscular tension and alert the state of the body by reducing attention to tinnitus signals. TRT alleviates adverse emotions caused by tinnitus, stabilizes patients' psychological state, and improves quality of life. The results of this study showed that the scores of daily living limitations, medical resource utilization, physical symptoms, and emotional disorders were significantly higher in the combined group than in the TDCS group. The above results indicated that TDCS combined with TRT could effectively improve patients' daily life limitations and physical symptoms, improve the utilization of medical resources, alleviate emotional disorders, and improve quality of life.

Limitations

In general, TDCS combined with TRT had obvious effects in treating chronic tinnitus, which largely reduced the severity of tinnitus, improved patients' sleep quality and psychological status, and improved the quality of life, indicating a certain worthy of clinical application and promotion. However, due to the limited sample size and research time of this study, the long-term effect of TDCS combined with TRT in the treatment of chronic tinnitus patients is still unclear. In the later stage, the research time will be extended and the sample size will be expanded for further identification.

Conclusions

This study confirmed the effectiveness of TDCS combined with TRT in patients with chronic tinnitus. After 4 weeks of treatment, the combination therapy had a significant advantage in reducing the symptoms of chronic tinnitus. In addition, no significant adverse reactions were found during the treatment, indicating that the therapy had a high safety profile.

This study provides a new combination therapy for the treatment of chronic tinnitus, which has important guiding significance for clinicians in their practical work. First, TDCS combined with TRT brings more active treatment options to patients with chronic tinnitus, which is helpful in improving treatment compliance and satisfaction. Secondly, combination therapy focuses on individualized treatment and develops a personalized plan according to the patient's condition and needs, which is conducive to improving the treatment effect. During the treatment process, doctors should pay close attention to the changes in the patient's condition and adjust the treatment plan in time to ensure that the treatment is safe and effective.

Ethics Approval

This study was approved by the Ethics Committee of the Henan Provincial People's Hospital, People's Hospital of Zhengzhou University (approval number: 202204).

Informed Consent

Not applicable, due to the retrospective design of the study.

Availability of Data and Materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Conflict of Interest

The authors declare that they have no competing interests.

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None.

Authors' Contributions

H.-J. L. confirmed the authenticity of all the raw data and edited the manuscript. X.-D. J. and Y.-K. L. collected and processed data. C.-C. X. and X.-L. D. performed the statistical analysis. S.-G. D. revised the manuscript. All authors read and approved the final manuscript.

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