



Original Article

# Multiple-Frequency Matching Treatment Strategy for Tinnitus

Yuan Tao, Xiaodong Chang, Sheng Ye, Guangxing Chu, Tian Guan, Jian Wang, Peiying Zeng

Department of Ear Nose and Throat, Peking University Shenzhen Hospital, Shenzhen, China (YT)

Graduate School at Shenzhen, Tsinghua University, Research Center of Biomedical Engineering, Shenzhen, China (XC, SY, GC, TG)

Shenzhen Institute of Information Technology, Electronics and Communication College, Shenzhen, China (JW)

Department of Immunology, Peking University Shenzhen Hospital, Shenzhen, China (PZ)

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**OBJECTIVE:** The first aim was to integrate commonly used tinnitus measures into a comprehensive questionnaire. Second, the effectiveness of a masking therapy based on multiple-frequency matching was verified in a clinical study. This study investigated the feasibility of a new treatment strategy for tinnitus, with two main foci.

**MATERIALS and METHODS:** Compare multiple-frequency matching with traditional masking therapy (Single-frequency matching) through clinical trials. The analysis indicated that the reliability and construct validity of the comprehensive questionnaire need to be improved, and the feasibility of the integration attempt remains uncertain.

**RESULTS:** The clinical results showed that the multiple-frequency matching method was more effective than single-frequency matching for tinnitus treatment.

**CONCLUSION:** The multiple-frequency approach should be used more often with tinnitus masking to promote the patients' recovery.

**KEYWORDS:** Tinnitus, multiple-frequency matching, masking therapy

## INTRODUCTION

Tinnitus, an auditory nerve disorder <sup>[1]</sup>, has a high morbidity rate in the general population and brings physical and psychological distress to patients <sup>[2]</sup>, seriously affecting their daily lives. At present, the pathogenesis of tinnitus is not clear <sup>[3]</sup>, and objective evaluations and treatments are not available for use in clinical practice. Doctors usually evaluate patients' conditions by subjective inquiry and using checklist questionnaires <sup>[4]</sup>. Patients are typically treated with the method of related medicine and sound masking <sup>[5]</sup>.

In multiple-frequency matched masking therapies <sup>[6]</sup>, narrow-band noise is used as an excitation to stimulate the hair cells of the cochlea, reducing spontaneous activity of these cells <sup>[7]</sup>. After a period of stimulation, the spontaneous activity of some or all of the hair cells can be recovered, reducing spontaneous discharge of auditory nerve activity and returning auditory nerve function to normal <sup>[8]</sup>. Damage to the central nervous system's memory of tinnitus can relieve tinnitus, and it will ultimately disappear.

In this approach, the nature of tinnitus is first classified. Then, an external sound closest to the tinnitus frequency and volume is used to mask the tinnitus sound. Following a doctor's instruction, the patient listens to the masking tone to achieve remission or eliminate the symptoms of tinnitus <sup>[9]</sup>.

Tinnitus sounds usually contain three to five dominant frequencies, and are thus difficult to match with pure tones. This method uses up to three sets of pure tones, the frequency and volume of which can be adjusted to match a patient's tinnitus parameters. This compound sound is the main tone used to mask the tinnitus sound.

In this study, we explored the effectiveness of a multiple-frequency matched masking therapy based on the Matlab platform (The commercial mathematics software produced by American MathWorks Company, Headquartered in Massachusetts, Neidikeshi, USA) for tinnitus. Since Matlab has a rich library functions and powerful GUI interface, so it is convenient to use Matlab platform to treat tinnitus.

**Corresponding Address:** Yuan Tao E-mail: 2437105032@qq.com

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## MATERIALS and METHODS

### Scale Validation

Newman<sup>[10]</sup> developed the Tinnitus Handicap Inventory (THI), a 25-item measure of tinnitus disability with three dimensions (functional effects, emotional effects, catastrophic effects) based on the subjective feelings of patients. Each item has three response options (e.g. poor sleep, anxiety and depression): never (score=4), sometimes (score=2), and always (score=0). The Chinese version of the THI has shown good reliability and discriminant validity, and it has been demonstrated to reflect patients' treatment response and quality of life<sup>[11]</sup>. We examined correlation between pairs of items.

Anxiety scale (SAS) has a total of 20 items (e.g. I feel nervous and anxious than usual.). Each item has "not yet", "sometimes", "most of the time" and "most of the time" four options, each option score respectively, 1 points, 2 points and 3 points and 4 points. Therefore, each item of equipment to set a variable and recorded for A1-A20, each of the variables are respectively provided with a "1", "2", "3" and "4" four level.

Depression scale (SDS) consists of 20 items (e.g. I want to cry), each item "never or occasionally", "sometimes", "often" or "always," four options, each option score respectively, 1 points, 2 points and 3 points and 4 points. Therefore, each item of equipment to set a variable were recorded for D1-D20. Each of the variables respectively, "1", "2", "3" and "4" four level.

Based on Tinnitus Handicap Inventory (THI) scale, anxiety scale (SAS) and depression scale (SDS), a comprehensive scale was obtained. Tinnitus handicap scale (THI) retained variables T1, T5, T9, T10, T12, T15, T16, T19, T21, T24 and T25 total 11 questions. Anxiety scale (SAS) reserved variables A1, A3, A6, A9, A11, A13, A16 and A19 a total of 8 items; Depression Scale (SDS) table reserved variable D1, D2, D6, D10, D12, D16, D18 and D20 a total of 8 items. The items of each scale to retain the integration, get a comprehensive scale, for a total of 27 items, each item set for a variable, were recorded options for C1-C35 and comprehensive scale in each item option settings and their respectively corresponding to the original scale of the same.

### Patients and Study Design

This experiment was supported by government of the Shenzhen. All volunteers volunteered for experiments, and the experiment was harmless to humans.

This study involved 30 patients who come to the hospital for treatment with nervous tinnitus for more than 12 months. The patients underwent pure-tone and acoustic immittance audiometric examinations to characterize tinnitus; those with conductive tinnitus were excluded, and patients with nervous tinnitus were selected. Before the mask treatment, the scale was used to determine the severity of tinnitus. Multiple-frequency masking for tinnitus treatment will begin according to the result of scale. After the treatment, patients fill out the scale. Through these two results of scale, conclusion can be determined whether the treatment is effective.

From Table 1: The patients were assigned randomly to single-frequency (group A) and multiple-frequency (group B) matching treatment groups (n=15/group). In group A, a tone with signal frequency and vol-

ume matching the tinnitus sound was mixed with white noise. In group B, a compound tone (consisting of three tone of different frequencies and volumes) matching the tinnitus sound was mixed with white noise. All patients were treated twice a day (15 min/session) for 20 days per course, with the total treatment consisting of three courses.

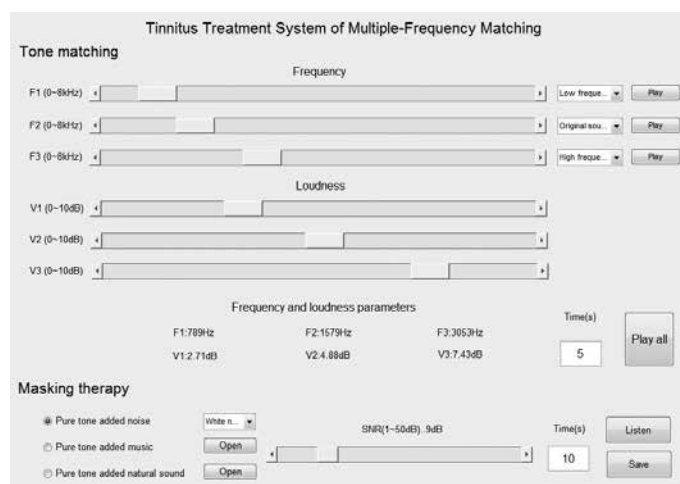
### Treatment Procedure

The main operation interface for the masking therapy is illustrated in Figure 1. The system consists of two modules for tone matching and masking therapy. In the pure-tone matching module, tinnitus parameters are matched by adjusting the frequency and volume of tones arbitrarily within the ranges of 0–8 kHz and 0–10 dB, respectively. In the masking therapy module, the matched composite tone is processed again to generate a masking sound for tinnitus treatment.

From Figure 1: The system is operated as follows. The doctor adjusts the frequency ( $\geq 75$ -Hz change per adjustment) of a tone until the frequency best matching the tinnitus pitch is determined by patient feedback. This frequency is recorded as F1. Then, the doctor adjusts the volume, recording the matching volume as V1. The tone produced by the F1 and V1 parameters is then played to check whether it approximates the patient's tinnitus sound. Based on patient feedback, further subjective adjustments are made to obtain accurate matching parameters. These steps are repeated while playing the first tone to obtain a second set of matching parameters (F2, V2), and repeated a third time to obtain a third parameter set (F3, V3). In this manner, a final compound tone most similar to the tinnitus sound is created. This tone serves as the main tone for masking therapy.

As the human auditory system has the characteristics of frequency multiplication chaos, a pure tone has twice the frequency relationship of the human ear is not easy to distinguish. Thus, a frequency test must be conducted at each stage of the frequency matching process. Doctors can choose a low-frequency or high-frequency multiplication sound to determine the true tinnitus frequency. As irregular drift of tinnitus frequency and volume may occur, the compound tone should be readjusted after 7 days.

A complex pure tone has better frequency targeting, but it is monotonous and piercing, making it difficult for patients to tolerate long-



**Figure 1.** The system of Matlab platform includes two modules of tone matching and masking therapy.

**Table 1.** Information of patients (part)

Subject	Gender	Age	Disease age	Ear	Career
S1	0	65	5	Right	None
S2	0	30	0.5	Both	Engineer
S3	1	27	3	Both	Teacher
S4	0	33	0.5	Right	Engineer
S5	1	34	2.5	Both	Technician
S6	1	45	5	Left	None
S7	0	37	10	Right	Staff
S8	0	46	7	Both	Clerk
S9	0	48	9	Right	Staff
S10	1	52	2	Both	None
S11	0	28	6	Both	Staff
S12	0	33	4	Left	Clerk
S13	0	42	10	Both	Staff
S14	0	24	2.5	Both	Student
S15	1	63	1.5	Both	None
S16	0	29	3	Both	Staff
S17	1	38	4.5	Both	Doctor
S18	0	54	8	Left	None
S19	1	29	3	Both	Staff
S20	0	27	1.8	Both	Staff
S21	1	37	4	Both	Doctor
S22	1	52	6	Both	None
S23	1	60	20	Both	None
S24	0	18	0.5	Left	Student
S25	1	39	2.5	Both	Clerk
S26	0	41	5.5	Left	Doctor
S27	1	58	7	Both	Staff
S28	0	44	2	Both	Clerk
S29	0	27	1	Both	Student
S30	1	23	1	Both	Student

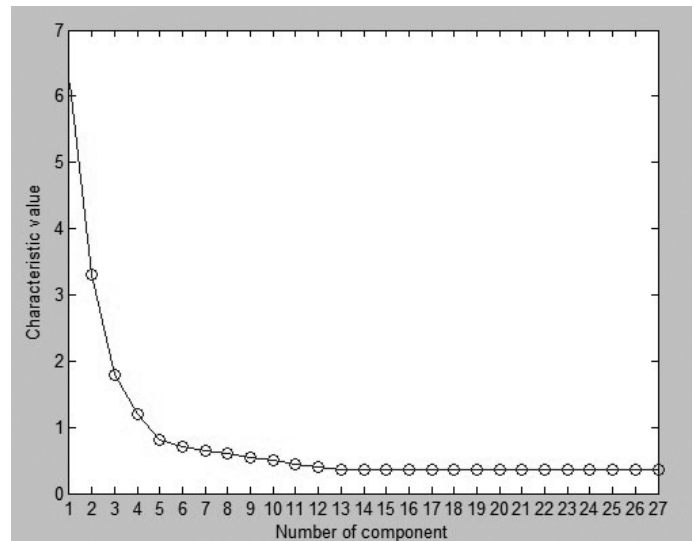
A total of 30 patients (17 male patients and 13 female patients) completed the follow-up treatment. The range of patients' age was 18 to 65 years old. The course of disease was 6 to 720 months.

term treatment. Thus, we chose to use white noise as a pure compound background sound. For SNR (SIGNAL-NOISE RATIO), the signal was the compound tone and the noise was the background sound. Patients could manually adjust the SNR volume in the range of 0–50 dB to a comfortable level to mask the tinnitus sound.

Because tinnitus parameters change frequently and are strongly subjective, matched sounds were readjusted weekly. Treatment was stopped immediately when a patient had any adverse reaction, such as nausea, dizziness, or hearing loss.

### Statistical Analysis

The scale was used to determine the severity of tinnitus *before the mask treatment*. After single-frequency masking and multiple-fre-



**Figure 2.** The number of this factor is four and their contribution rate reaches 96.17%. They can well explain the scale of all variables and illustrate the validity of the scale is very good.

quency masking for tinnitus treatment, patients fill out the scale too. Through these two results of scale, conclusion can be determined whether the treatment is effective. Through a significance level of  $p < 0.05$ , analyses were conducted using SPSS (Statistical Product and Service Solutions) software. SPSS basic functions include data management, statistical analysis, charting, output management, and so on. SPSS statistical analysis including descriptive statistics, comparison of means, general linear model, correlation analysis, regression analysis, log-linear model, cluster analysis.

## RESULTS

### Scale Validity

In the scale, The Cronbach's  $\alpha$  coefficient of the tinnitus disability scale was 0.81, with a standard value of 0.956, indicating good internal consistency and a high level of reliability. Correlation between pairs of items 1, 2, 9, 18, and 20 was good ( $r > 0.5$ ), and that between pairs of items 3, 10, 14, 21, and 25, and between pairs of items 5, 11, 19, and 23, was also good ( $r > 0.6$ ). These results are consistent with the three dimensions of the tinnitus disability scale. In the item total statistics, the removal of items 2, 4, 6, 7, 14, 17, 20, 21, 22, and 23 one by one significantly improved the Cronbach's  $\alpha$  value. Thus, these variables were placed under consideration for deletion.

From Figure 2: Validity analysis yielded a KMO test value of 0.83. The Bartlett spherical test is the significant level ( $p < 0.001$ ), indicating that factor analysis could be applied. Principal component analysis was used to select factors with eigenvalues  $> 1$ . Four factors variance contribution rate reached 96.17% (Figure 2). Thus, the scale showed good validity.

### Therapeutic Effect of Multiple-Frequency Masking

From Table 2: Thirty patients (17 men, 13 women) aged 18 to 65 years completed the three treatment courses. Disease courses ranged from 6 months to 20 years. Patient information is presented in Table 1 (0 = male, 1 = female).

From Table 3 and Table 4: In the first and second courses of treatment, therapy type (single-frequency masking vs. multiple-fre-

**Table 2.** The first course of treatment results

Group	Patients number	Effective number	Invalid number	Effective rate
A	15	2	13	13.33%
B	15	3	12	20.00%

**Table 3.** The second course of treatment results

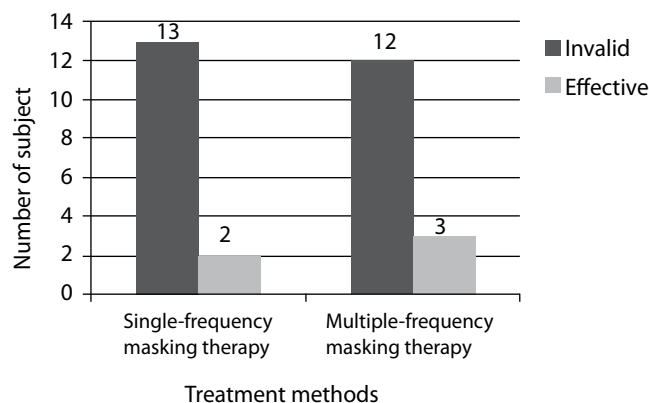
Group	Patients number	Effective number	Invalid number	Effective rate
A	15	3	12	20.00%
B	15	5	10	33.33%

**Table 4.** The third course of treatment results

Group	Patients number	Effective number	Invalid number	Effective rate
A	15	5	10	33.33%
B	15	12	3	80.00%

**Table 5.** The first course of treatment results

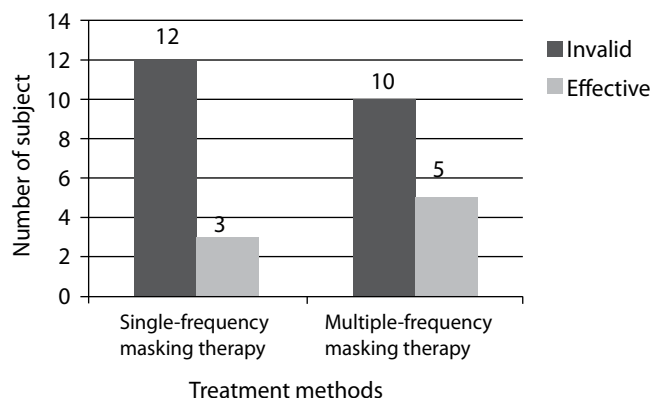
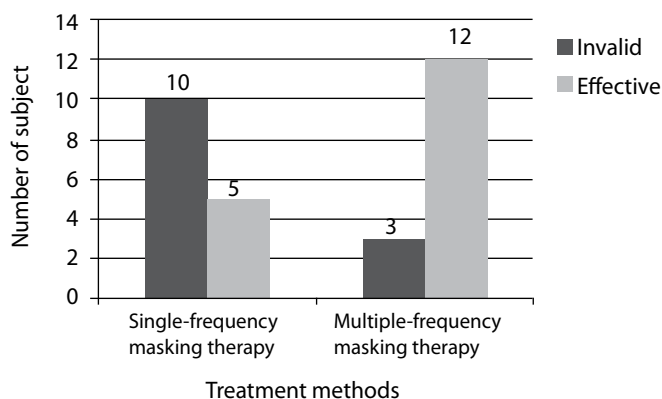
Results of cross over trials		
Course of treatment	$\chi^2$	p
First course of treatment	0.240	0.624
Second course of treatment	0.682	0.409
Third course of treatment	6.652	0.010

**Figure 3.** Result of the first course of treatment, single-frequency masking compare with multiple-frequency masking.

cy masking) had no significant effect on response to treatment (Tables 2 and 3, the corresponding statistics are shown in figures 3 and 4); the effect was significant in the third course of treatment (Table 4, the corresponding statistics are shown in figure 5). The therapeutic effect of multiple-frequency masking therapy was superior to that of single-frequency masking therapy.

#### Results of Cross Over Trials

In the Table 5, we can find clinical trials have shown that multi-frequency masking therapy is more effective than single-frequency masking therapy in improving tinnitus symptoms in patients. In the first course

**Figure 4.** Result of the second course of treatment, single-frequency masking compare with multiple-frequency masking.**Figure 5.** Result of the third course of treatment, single-frequency masking compare with multiple-frequency masking.

of treatment and second course of treatment, compared with single-frequency masking therapy, multi-frequency masking therapy did not show advantages. But in the third course of treatment, the effectiveness of multiple-frequency masking therapy was greatly increased, while the effective number of single-frequency masking therapy was not significantly increased. Multi-frequency masking therapy has significant advantages over single-frequency masking therapy.

#### DISCUSSION

This study confirmed that multiple-frequency masking therapy is more effective than single-frequency therapy in improving the symptoms of patients with nervous tinnitus. Among the numerous tinnitus treatment methods, masking therapy is used commonly because it is simple, safe, and has no obvious adverse effect, its mechanism remains unclear<sup>[12]</sup>. Although previous studies have found that the masking effect of tinnitus is more than that of the cochlea. Cross masking and other phenomena suggest that higher-level neural mechanisms should be involved in the masking process in addition to the cochlea<sup>[13]</sup>. Psychologically, patients are more likely to accept and be able to ignore an external sound compared with the internal tinnitus sound. At the same time, such a sound can transfer a patient's attention to the sound of tinnitus, which causes the sound of tinnitus cannot be heard. Customized multiple-frequency masking can improve the success rate of tinnitus treatment<sup>[14]</sup>.

In recent years, further study on the mechanism of tinnitus, no matter the primary site of tinnitus exists in the peripheral or central nervous system, and its further processing, perception and maintenance of the process are located in the central nervous system. Regardless of the primary location of the tinnitus. The development of functional brain imaging technology has enabled the location of tinnitus in the central nervous system<sup>[15]</sup>. The use of masking and medication methods to suppress tinnitus has been studied. Positron emission tomography has shown differences in regional cerebral blood flow before and after the inhibition of tinnitus. The results support the above points, and show that there is a relationship between the auditory centre and the limbic system, the attention, emotion, memory and other functional areas of the frontal lobe<sup>[16]</sup>. This involvement explains the frequent accompanying symptoms related to the nervous system (e.g. poor sleep, anxiety, depression) in patients with tinnitus<sup>[17]</sup>. According Jastreboff's neuropsychological model of tinnitus, auditory centre activity hierarchy are regulated by external acoustic signal input, you can reduce the external auditory masking sound excited pathways, making it difficult to detect the presence of the central auditory tinnitus<sup>[18]</sup>.

The observed response after the third treatment course in this study is consistent with the long-term nature of tinnitus treatment. The choice of treatment method and duration of treatment are known to have significant influences on treatment effects<sup>[19,20]</sup>. Thus, the treatment of tinnitus must be prolonged and sustainable. In this study, we examined the effects of only three courses (60 days) of treatment; further research with more long-term monitoring is needed to verify our preliminary results.

## CONCLUSION

This study demonstrated that multiple-frequency matching masking therapy is more effective than single-frequency therapy for the treatment of tinnitus. As tinnitus is subjective, its volume and frequency, psychological characteristics, and severity are generally accepted to be unstable. In addition, its prognosis is not predictable. These factors make the development of objective, quantitative evaluation criteria and choice of appropriate treatment method difficult. The THI is a reliable and valid scale that can be used for global comparison of tinnitus treatment responses. Using scale and subjective tinnitus severity classification is the criteria for our study. Ultimately, the quality of life of patients with tinnitus can be greatly improved, reflecting the benefits of the physiological to psychological to social medical model.

**Ethics Committee Approval:** All the experiments were done cooperating with doctors in the hospital. Ethics committee approval was received for this study from the ethics committee.

**Informed Consent:** All subjects gave informed consent and agreed to participate in the study.

**Author Contributions:** Concept - S.Y., G.C.; Design - Y.T., X.C.; Resources - P.Z.; Materials - T.Ç.; Data Collection and/or Processing - T.G., J.W.; Analysis and/or Interpretation - T.G., J.W.; Literature Search - Y.T., X.C.; Writing Manuscript - Y.T.

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**Conflict of Interest:** No conflict of interest was declared by the authors.

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