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Original Article

A Randomized, Controlled Trial of Notched Music Therapy for Tinnitus Patients

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OBJECTIVE: To compare the tinnitus treatment outcomes of tailor-made notched music therapy and ordinary music.

METHODS: A double-blind, randomized, controlled trial was conducted on 104 Thai patients with chronic subjective tinnitus. Tinnitus matching was done on all subjects before they were randomly allocated to one of 2 groups: a treatment group (listening to tailor-made notched music) and a control group (listening to ordinary music). Each participant received their allocated intervention and was assessed at 1, 3, and 6 months.

RESULTS: The demographic data of the 2 groups showed no statistically significant differences. The Tinnitus Handicap Inventory and the total Visual Analong Scale also demonstrated no significant differences. However, the treatment group showed a greater reduction in their scores than the control group during the follow-up period.

CONCLUSION: Tailor-made notched music therapy is an optional treatment for patients with bothersome subjective tinnitus. However, more research is needed to draw firm conclusions about its benefits and cost-effectiveness.

KEYWORDS: Tinnitus, tailor-made music notched therapy, sound therapy

INTRODUCTION

Tinnitus is a bothersome symptom of noise perception without acoustic stimuli. Between 10% and 15% of the general population reports tinnitus, and around 1-6% state that their quality of life is considerably impaired.[1] The disorder can be classified into objective and subjective tinnitus. Objective tinnitus is a noise that can be perceived by the patient, the clinician, and sound-detecting devices. It results from noise generated by structures inside the body that is transmitted to the ear, such as stapedial muscle spasm and turbulent flow from vascular disorders within or adjacent to the temporal bone. Subjective tinnitus is more common and can be perceived only by the patients.[2] It is usually associated with hearing loss, and its prevalence increases with age. However, the underlying mechanism of subjective tinnitus is not well understood.[3,4] The discordant pathogenesis theory states that when the number of damaged outer hair cells is greater than the number of inner hair cells, tinnitus develops because of dorsal cochlear nuclei disinhibition.[2,5] The auditory plasticity theory explains that tinnitus is a compensatory reaction of the central nervous system to hearing loss caused by what has been termed "maladaptive auditory cortex reorganization", which is similar to the phantom pain experienced by amputated patients.[2] The pitch and loudness of subjective tinnitus, as well as its impact on daily life vary. In severe cases, tinnitus significantly impairs patients' abilities to work, sleep, and perform daily activities, and may contribute to the development of anxiety, depression, and sleep disorders.[5]

Currently, there is no standard treatment for subjective tinnitus.[2,3] The available options include cognitive behavioral therapy, tinnitus-retraining therapy, medications, acupuncture, neuromodulation, tinnitus masking, and sound therapy. The aim of these treatments is to make the tinnitus more manageable and tolerable for patients. Recently, a novel approach using music therapy

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was reported. Okamoto et al.[6] found that tailor-made notched music therapy (TMNMT) could significantly reduce tinnitus loudness and tinnitus-related auditory cortex activity. Other reports have also described improvements in tinnitus-related symptoms after receiving music notch therapy.[7,8] These findings can be explained by the suppression of cortical activity by the notched music through lateral inhibition[4] pathways in sensory neurons, coupled with the rewiring capability of the brain, often referred to as cerebral plasticity.

Okamoto et al.[6,9] reported that tinnitus loudness and auditory cortical response (N1m) were statistically significantly lower for patients who listened to notched music at their tinnitus pitch compared to control subjects. Teismann et al.[7] demonstrated a reduction of tinnitus loudness, tinnitus-related distress, and tinnitus-related auditory cortex activity after patients with a tinnitus pitch of less than 8 kHz were exposed to short-term, intensive notched music therapy. Stein et al.[8] conducted a study on 100 chronic tinnitus subjects randomly assigned to a specific-tinnitus-frequency notched music group (treatment), and a random-frequency notched music group (control). The tinnitus loudness was statistically significantly reduced using the frequency-notched music therapy.

At our department, about 3.2% of outpatients seek medical advice for tinnitus each year, and most have chronic subjective tinnitus. In 2014, we conducted a clinical pilot study of music notch therapy whereby tinnitus patients[10] received custom-made music notch therapy. After 3 months, the Tinnitus Handicap Inventory (THI) and the Visual Analog Scale (VAS) scores were statistically significantly reduced. We also found that residual inhibition test results were correlated with the outcomes of the music notch therapy, suggesting that they had potential to become a tool to predict post-treatment clinical response. Therefore, we decided to conduct a randomized, controlled trial using TMNMT and ordinary music in patients with tinnitus.

Objective

The objective was to compare the tinnitus treatment outcomes of TMNMT and ordinary music (control), which were assessed by using the THI questionnaire and a VAS.

MATERIALS AND METHODS

Study Design

This was a randomized, controlled trial of patients with chronic subjective tinnitus at the out-patient department. The treatment group received TMNMT while the control group received ordinary music (original songs without modification) therapy. The Institutional Review Board approved the study and clinical registration was applied for, for research registration and publication.

Participants

We recruited patients aged 18 years or older who had had continuous tinnitus for more than 3 months with tonal or narrow-band noise characteristics. To be enrolled, the patients needed to be willing to discontinue tinnitus pharmacological therapy for at least one month before initiation of the music therapy. All subjects understood the Thai language and independently gave their consent to participate. The exclusion criteria were: (1) a suspected or confirmed diagnosis of objective tinnitus; (2) active psychiatric or central neurological disorders; (3) broadband or white noise tinnitus; (4) intermittent tinnitus; (5) the pure-tone average of the better ear was greater than 70 dB HL; and (6) the initial THI score was less than 16.

The sample size was calculated using data from a previous clinical trial.[10] The Type 1 error was set at 5%, and the Type 2 error was set at 10%; hence, the Z_α and Z_β values were 1.645 and 1.28, respectively. The σ_1 (20.5), σ_2 (9.0), μ_1 (35.8), and μ_2 (22.2) values were derived from the mean (μ) and standard deviation (σ) of the pre-treatment (σ_1, μ_1) and the 3-month follow-up (σ_2, μ_2) periods of the total THI score. The dropout rate was estimated at 10%. The calculation indicated that 54 participants were needed for each group.

All participants underwent audiometry, auditory brainstem response, transient-evoked otoacoustic emission, and distortion product otoacoustic emission tests to exclude retro-cochlear lesions. Each participant provided informed consent, underwent the counseling process, received complete information about the treatment options, and made the decision to participate in consultation with their physicians. Each participant was able to withdraw from the research at any time after enrollment. After the 6-month experimental period, each participant was free to choose to continue listening to notched music or seek an alternative treatment.

Randomization

We used block randomization with a block size of 4. After the group type was allocated to each case number, envelopes labeled with case numbers were created. A third party inserted a symbol representing the assigned group into each envelope before sealing it. The investigators were blinded to this process. The envelopes were retrieved on the tinnitus-matching day and sent with the matching results to be unsealed only by the staff member responsible for the music notching process (described below).

Tinnitus Matching

Tinnitus matching was done using the Otometric Suite (Version 4) and Sennheiser HAD-200 high-frequency headphones. Details of the tinnitus pitch, loudness, and residual inhibition characteristics were collected. Participants were asked to listen to the tonal signal noise on the opposite ear and compare it with their tinnitus ear. If tinnitus was reported in both ears with different pitches or loudness, the test was done for each side separately. If tinnitus was reported without an identifiable side, the noise was applied to the better ear to prevent a cross-over effect. Two alternate octave frequencies were applied for pitch matching (two-forced-choice procedure). The noise most similar to the tinnitus was recorded in terms of pitch (Hz). The loudness (decibel sensation level; dB SL) was assessed by the participants. The participants were asked to evaluate the loudness level of the tinnitus at which the sound stimulated the opposite tinnitus ear. Narrow-band noise was used when patients were unable to distinguish between pure-tone noise and their own tinnitus.

Notched Music

After the tinnitus was matched, the required information along with the case-number envelope were sent to the staff member responsible for the music notching process. The participants were free to bring their favorites songs in MP3 format or simply allow the study staff to arrange songs from available playlists. We used the Audacity

software to produce the notched music created by removing one-octave width centered at the individual's tinnitus frequency from the music energy spectrum. For the control group, no modification was made to the music.

Listening to Music

Participants were asked to listen attentively and daily to the music at a comfortable volume. After completing the listening period, participants were free to continue listening, take a break, or stop listening on that day. Subjects recorded their listening periods in a daily log book.

Outcome Measurements

We used the THI questionnaire and total VAS score to access the severity of the tinnitus symptoms and treatment outcomes. The THI was created by Newman et al.[11]; a translated version was subsequently developed and validated[12] to apply in this study. As for the use of VAS to assess the severity of tinnitus, the total score has 7 components: tinnitus loudness perception, annoyance, moodiness, insomnia, distraction, hearing difficulty, and fear of dreadful disease. Each of those aspects is scored separately on a scale from 0 to 100; the mean score of the 7 scales is then calculated to determine the total VAS score. Follow-up assessments using THI and VAS questionnaires were scheduled for 1, 3, and 6 months after the participants started listening to the music.

Statistical Analysis

The statistical analyses were conducted using IBM SPSS Statistics for Windows (Version 21.0; IBM Corp., Armonk, NY, USA). Chi-square tests were used for the comparisons of the categorical data. Independent-sample *t*-tests and Mann–Whitney U-tests were used to analyze the variables based on the distribution pattern of the data. Demographic data were described as number (%), mean (+/- standard deviation), or median (range). Measurements of outcome (total THI and total VAS score) were repeated at a number of separate time points for each patient. Thus, linear mixed model analysis was used to estimate the mean of each score category. A P value of $< .05$ was considered statistically significant.

RESULTS

In all, 141 patients with tinnitus were identified between August 2017 and February 2019. Of those, 33 were excluded, leaving 108 patients enrolled. That meant that 54 patients each were randomized into the treatment and control groups (Figure 1). Subsequently, one participant from each group withdrew because their continued participation would prove inconvenient, another

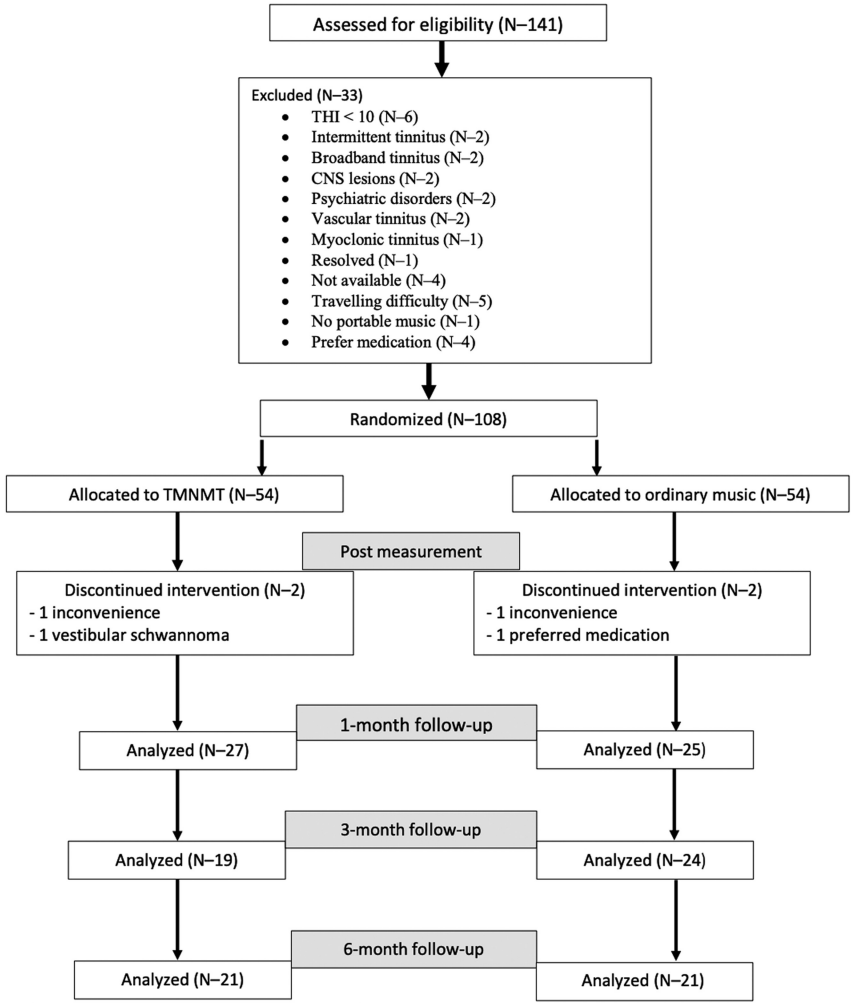

Figure 1. Study flow diagram of all recruited participants. Ordinary music, placebo; THI, Tinnitus Handicap Inventory questionnaire; TMNMT, tailor-made notched music therapy.

participant from the placebo group preferred to continue with a medication, while one from the treatment group was diagnosed as having vestibular schwannoma. Thus, there were finally 52 subjects in each group at enrollment. At the 1-month follow-up session, there was a total of 52 participants present (27 from the treatment group; and 25 from the control group). The 3-month follow-up session had 43 participants (treatment, 19; and control, 24), while 42 participants attended the 6-month follow-up (treatment, 21; and control, 21; Figure 1). The median (range) age was 59 (27-80 years) for the treatment group, and 57 (24-75 years) for the control group. The median durations and ranges of the tinnitus were 24 (3-365) months for the treatment group, and 22 (3-667) months for the control group. There were no statistically significant differences in the age or duration of tinnitus between the 2 groups. However, there was a significant difference in gender, in that the female-to-male ratio for the treatment group was 0.79, compared with 1.74 for the control group ($P = .049$). In the treatment group, 15 patients (28.8%) had central tinnitus, 13 (25%) had right-sided tinnitus, 14 (26.9%) had left-sided tinnitus, and 10 (19.2%) reported bilateral tinnitus. In the control group, 10 (19.2%) had central tinnitus, 13 (25%) had right-sided tinnitus, 24 (46.2%) had left-sided tinnitus, and 5 (9.6%) had bilateral tinnitus. There were no statistically significant differences in the underlying diseases of the patients between the treatment and control groups (Table 1).

The audiological testing median of pure-tone average (PTA) was about 20 dB HL and word recognition score (WRS) was about 100% in both groups. There were no statistically significant differences in the values of the 2 parameters between the treatment and control groups. Data for the transient-evoked otoacoustic emission and distortion-product otoacoustic emission tests showed poor signal-to-noise ratios for both groups, without statistical significance (Table 2).

Tinnitus Characteristics

The median values of the pitch for the 3 subgroups of patients (right-sided, left-sided, and bilateral tinnitus) ranged from 4000 to 8000 Hz for the treatment group, but was 8000 Hz for each subgroup of the control group. There were no significant differences in the values. The tinnitus loudness medians ranged from 5.5 to 15 dB SL, and from 5 to 11 dB SL, for the treatment and control groups, respectively. There was no statistically significant difference between treatment and control groups. There were no significant differences in the THI and VAS scores between the groups (Table 1).

Outcome Analysis

The outcome measurements of the total THI and total VAS scores were calculated by a linear mixed model. The estimated mean score of the control group was deducted from the mean score of the treatment group to obtain the total THI and total VAS score differences. There were no significant differences in any variable of the treatment and control groups (Table 3). The total THI scores of the participants who had at least one follow-up session are detailed in Figure 2, while comparisons of the estimated mean total THI and VAS scores of the treatment and control groups are illustrated in Figures 3 and 4. The *P* values below the X-axis are those values calculated by comparing the corresponding scores of each group for each follow-up time point, while the *P* values at the right side of the graphs represent the values calculated by comparing the graph slopes of the 2 groups. There were no statistically significant differences.

Table 1. Baseline Demographic Data of the Treatment- and Control-Group Participants

	Number (%)		
Group	**Treatment ($N = 52$)**	**Control ($N = 52$)**	***P***
Age (years) [a]	59 (27-80)	57 (24-75)	.644
Gender			**.049***
Male	29 (55.8%)	19 (36.5%)	
Female	23 (44.2%)	33 (63.5%)	
Duration of tinnitus (months)[a]	24 (3-365)	22 (3-667)	.668
Underlying diseases			
Diabetes mellitus	7 (13.5%)	6 (11.5%)	.767
Hypertension	17 (32.7%)	12 (23.1%)	.274
Renal disorders	1 (1.9%)	2 (3.8%)	.558
Old CVA	1 (1.9%)	3 (5.8%)	.308
SSNHL	4 (7.7%)	5 (9.6%)	.727
Meniere's disease	2 (3.8%)	0 (0%)	.153
Others	25 (48.1%)	29 (55.8%)	.432
Side of tinnitus			.151
Central	15 (28.8%)	10 (19.2%)	
Right	13 (25.0%)	13 (25.0%)	
Left	14 (26.9%)	24 (46.2%)	
Bilateral	10 (19.2%)	5 (9.6%)	
Pitch of tinnitus (Hz) [a]			
Right	4000 (500-18 000)	8000 (250-14 000)	.199
Left	6000 (750-18 000)	8000 (450-14 000)	.444
Bilateral	8000 (2000-16 000)	8000 (4000-18 000)	.204
Loudness (dB SL) [a]			
Right	15 (0-65)	10 (0-55)	.691
Left	15 (0-50)	11 (0-60)	.892
Bilateral	5.5 (0-38)	5 (0-30)	.555
THI total score [b]	37.15 (19.34)	37.5 (19.75)	.848
Emotional score	11.62 (8.12)	12 (8.65)	.868
Functional score	13.65 (10.20)	14.20 (8.92)	.535
Catastrophic score	11.88 (3.62)	11.69 (4.72)	.802
VAS total score[b]	25.22 (11.92)	25.04 (8.65)	.480
Loudness perception	52.63 (17.59)	49.08 (21.16)	.556
Annoyance	32.37 (22.95)	37.13 (26.74)	.489
Moodiness	27.69 (24.13)	27.83 (24.91)	.812
Insomnia	39.54 (29.56)	37.08 (27.61)	.725
Distraction	33.40 (27.41)	32.62 (24.30)	.922
Hearing difficulty	30.69 (23.51)	29.92 (22.17)	.830
Fear of dreadfulness	35.9 (24.88)	42.46 (27.16)	.307

CVA, cerebrovascular accident; dB, decibel; Hz, Hertz; MML, minimum masking level; SL, sensation level; SSNHL, sudden sensorineural hearing loss; THI, Tinnitus Handicap Inventory; VAS, Visual Analog Scale.

[a]Data expressed as median (range).

[b]Data expressed as mean (SD).

*Indicates statistical significance (a *P* value of < .05, calculated from the Mann–Whitney *U*-test).

Table 2. Audiological Test Results of Treatment and Control Groups at Baseline

	Number (%)			Number (%)		
Side:	**Right Ear**			**Left Ear**		
Group:	**Treatment**	**Control**	***P***	**Treatment**	**Control**	***P***
Total audiometry	52 (100%)	52 (100%)		52 (100%)	1 100%)	
PTA (dB HL) [a]	22 (5-88)	18 (5-63)	.292	21 (7-102)	20 (7-67)	.679
WRS (%) [a]	100 (12-100)	100 (52-100)	.102	100 (0-100)	100 (36-100)	.244
Total TEOAE	19 (100%)	9 (100%)		16 (100%)	1 100%)	
Poor SNR	14 (73.7%)	8 (88.9%)	.36	14 (87.5%)	11 (100%)	.223
Total DPOAE	37 (100%)	24 (100%)		37 (100%)	1 100%)	
Poor SNR	19 (51.4%)	14 (58.3%)	.593	18 (48.6%)	22 (57.9%)	.422

dB, decibel; DPOAE, distortion product otoacoustic emission; HL, hearing level; PTA, pure-tone average threshold; SNR, signal-to-noise ratio; TEOAE, transient-evoked otoacoustic emission; WRS, word recognition score.
[a]Data expressed as median (range).

DISCUSSION

Two patients from each group had long-term tinnitus which had increased in intensity and become a problem between 3 and 6 months before the start of the trial. However, for our study purposes, we collected details of the duration since the onset of tinnitus rather than of the period since an individual's tinnitus came to be perceived as a problem. This is why the duration of tinnitus experienced by the subjects in both the treatment and control groups had a wide range. Nevertheless, there was no significant difference in the durations between the 2 groups. Except for gender, the groups were similar, suggesting that the subject randomization had been effective. The participants' female-to-male ratio in total was about 1.16 (56 : 48). This showed that women were more concerned about tinnitus than men.

In all, 108 participants were recruited. Unfortunately, many were lost to follow-up (treatment group: 25/52 participants the 1 month, 33/52 at 3 months, and 31/52 at 6 months; control group: 27/52 at 1 month, 28/52 at 3 months, and 31/52 at 6 months). Four subjects also withdrew after enrollment. We planned to use the repeated measure ANOVA for statistical analysis, but the linear mixed model was used to accommodate the many missing values. The outcome data used in our analyses came from those participants who had attended at least one follow-up session. While there were no statistically significant differences, the treatment group's total THI and total VAS scores trended lower at each follow-up interval (Figures 3 and 4). This finding was consistent with those of previous studies.[9, 13] The total THI was categorized into slight (THI 0-16), mild (THI 18-36), moderate (THI 38-56), severe (THI 58-76) and catastrophic handicap (THI 78-100).[14] At the initial evaluation of total THI score, there were 64 (61.5%) participants with mild, 22 (21.2%) participants in moderate, 14 (13.5%) participants in severe and 4 (3.8%) participants in catastrophic grading. The participants who did not attend follow-up sessions were mainly in the mild handicap group from the initial evaluation, which were 22 participants at 1-month, 38 participants at 3-month and 40 participants at 6-month follow-up sessions. About 50% of the subjects stated that the main reasons for not attending all or some of the follow-up sessions were a lack of time and difficulties in traveling. Other reasons included migrating to a distant area in Thailand or to another country, or changing a contact telephone number or residence without notifying our support staff. Even though we could not reach all of the participants, we expect that they would have gained improvements after exposure to the music.

Table 3. Results of the Outcome Measurements of the Treatment and Control Groups

	Estimated Mean			
Group	**Treatment**	**Control**	**Difference[a]**	***P***
Total THI score				
• Pre-treatment	39.5446	38.1624	1.3822	.7625
• 1-month follow-up	33.9867	35.0766	1.0899	.8019
• 3-month follow-up	26.7828	31.5582	4.7755	.3346
• 6-month follow-up	25.7566	32.9141	7.1575	.1777
Total VAS score				
• Pre-treatment	25.9916	26.1474	0.1558	.9549
• 1-month follow-up	24.3316	25.292	0.9604	.7107
• 3-month follow-up	21.9265	24.2529	2.3264	.4473
• 6-month follow-up	20.6061	24.3734	3.7674	.256

THI, Tinnitus Handicap Inventory; VAS, Visual Analog Scale.
[a]Difference between estimated mean score of each group, calculated by the score of the control group deducted from the score of the treatment group.

Compared to other studies,[6-8] ours had an intermediate follow-up period (6 months). Wunderlich et al.[15] demonstrated that 3 months of listening to TMNMT led to a decrease in tinnitus severity. In other work, Okamoto et al.[6] followed their patients for up to 12 months. Their control group received randomly notched music; the researchers also compared the treatment group results with those of another group of patients who preferred to only have their symptoms observed without any intervention. Nevertheless, the researchers did not find a significant loudness of tinnitus after 6 months of follow-up.

Stein et al.[8] used half-octave-width notched music with an equalized energy spectrum and an amplified edge of the notched frequency band. According to Wunderlich et al.,[15] the notch width of the music should have no effect on the outcomes of the study; still, the amplified edge of the notched frequency band might explain the effectiveness of the treatment through increased lateral inhibition. This

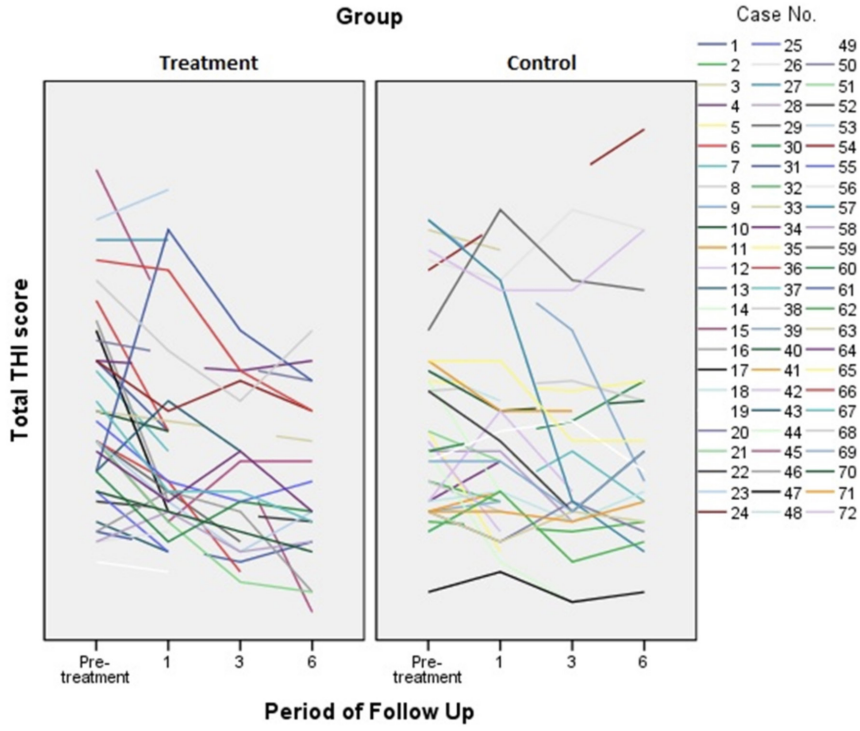

Figure 2. Spaghetti plot graph of the total THI score of each participant who had at least one follow-up session.

was in contrast with the current study; we did not amplify the edge of the notched frequencies, which may have led to less significant outcomes. Nevertheless, previous studies[16-18] showed reduction in neuronal activity evoked by tinnitus as well as in perception of tinnitus loudness in the human auditory cortex after listening to notched music. It has been purposed that the effect of lateral inhibition, neural reorganization, and behavioral adaptation after exposure to TMNMT decreases tinnitus severity.[16,18] Although this present study did not show statistical significance between treatment and control groups, there were trends of decrease in tinnitus severity (Figures 3 and 4). The lateral inhibitory effect of the notched music and central auditory neural plasticity are the main mechanisms which explain why the therapy effectively reduces tinnitus loudness and the cortical activity related to tinnitus.[6,16,19] Thus, TMNMT should be considered as one optional treatment which is enjoyable and a low-cost therapy for tinnitus patients.

Limitations

Although we successfully recruited the planned number of participants, many failed to subsequently attend some or all of the follow-up sessions for various reasons. Moreover, the limited time available for the study and an inability to assess the electrophysiological data of the participants to make objective measurements played a limiting role. Finally, the reason we were unable to demonstrate any

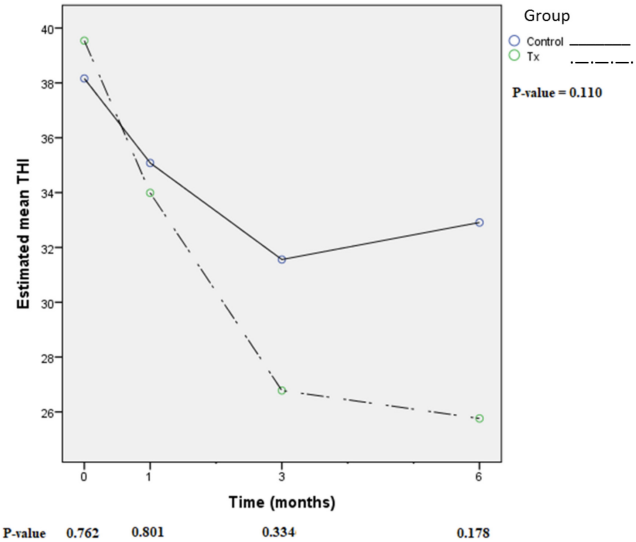

Figure 3. Comparison of the THI scores of the treatment and control groups. Tx, Treatment.

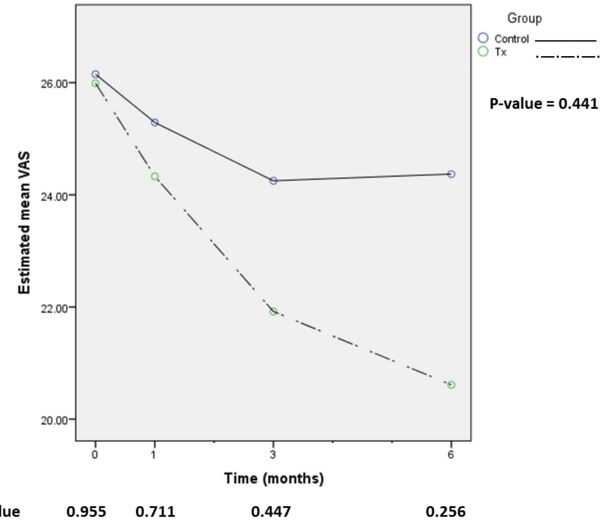

Figure 4. Comparison of the VAS scores of the treatment and control groups. Tx, Treatment.

significant differences between the treatment and placebo groups may have been due to insufficient follow-up data.

CONCLUSION

Tinnitus is a bothersome symptom with no known curative treatment. The possibility that we could reduce the severity of the disorder by listening to music brings hope to many patients. Although we cannot conclude from our study that TMNMT is more helpful than ordinary music, we did observe some trends in the data suggesting an improvement. TMNMT remains an optional treatment for patients with subjective tinnitus.

Ethics Committee Approval: All procedures performed in studies involving human participants were in accordance with the ethical standards of the Siriraj Institutional Review Board (NO.249/2560, EC3) and registered with Thai clinical registration (TCTR20190222001).

Informed Consent: Informed consent was obtained from all participants included in this study.

Peer Review: Externally peer-reviewed.

Author Contributions: Concept – A.S., S.L.; Design – S.A., S.L.; Supervision - S.A., S.L.; Resource -K.S., S.P., K.T., J.T., S.L.; Materials - K.S., S.P., K.T., J.T., S.L.; Data Collection and/or Processing - J.T., S.L.; Analysis and/or Interpretation - J.T., S.L.; Literature Search – J.T., S.L.; Writing - J.T., S.L.; Critical Reviews - S.A.

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